Results: Electrophysiological integration of transplanted fetal and induced pluripotent stem cell-derived cardiomyocytes

M. Haab1, G. Penkofler1, S. Baumgartner1, B. Krausgrill1, A. Fatima1, J. Hescheler1, T. Saric1, J. Mueller-Ehmsen2. 1University of Cologne, Department of Internal Medicine III, Cologne, Germany; 2University Medical Center Gottingen, Department of Pharmacology, Gottingen, Germany

Purpose: A functional integration and maturation of transplanted cardiomyocytes prevents arrhythmias and enhances synchronous contractions of transplanted and host tissue. We compared the electrophysiological integration and properties of transplanted fetal cardiomyocytes (FCM) and induced pluripotent stem cell-derived cardiomyocytes (IPSCM), which are regarded as promising cell type for cardiac cell replacement therapy.

Methods: FCM from transgenic mice expressing eGFP under control of the α-actin promoter were isolated at day 13.5-15.5 p.c. Murine IPSCM, expressing eGFP and a purinergic resistance under control of the alpha MHC promoter, were prepared from human induced pluripotent stem cells (hiPSCs) at day 16. FCM and IPSCM were injected into adult mouse hearts (2 injections, ~500,000 cells per site). 6-9 days after transplantation, recipients were sacrificed and viable ventricular tissue slices (thickness: 150 μm) were prepared. Slices were locally stimulated by a unipolar electrode placed in host tissue. Recordings of action potentials (AP) were performed by glass microelectrodes in transplanted cells, which could be identified by their green fluorescence, and in neighboring host cardiomyocytes within the tissue slices.

Results: Coupling of FCM and IPSCM to host tissue could be clearly demonstrated. Transplanted FCM and IPSCM showed no conduction blocks even at high stimulation frequencies of up to 8 Hz, while others had blocks at lower stimulation frequencies or were not electrically integrated at all. 80% of FCMs and 60% of IPSCMs were integrated. The delay between stimulus and AP upstroke was significantly longer in IPSCM (~13 ms) than in FCM (7.9 ms). In host tissue, the delay was 6.9±1.0 ms. IPSCM had a lower maximal diastolic potential, amplitude and upstroke velocity than FCM and host cardiomyocytes, pointing to a very immature electrophysiological stage of IPSCM. Repolarization was characterized by a very fast phase 1 in host cells, which was not present in IPSCM and FCM.

Conclusions: FCM and IPSCM are able to integrate electrically into host tissue, but conduction blocks and deactivations occur. The quality of integration is higher in FCM than in IPSCM. Action potential properties of transplanted IPSCM differ considerably from those of adult host cardiomyocytes. IPSCM are also more immature as compared to transplanted FCM, which have typical neonatal AP properties at the time point studied.

Figure 1. 30-day and 360-day cardiomyocytes

1. 30-day cardiomyocytes
2. 360-day cardiomyocytes
**Induced pluripotent stem cells in action / The metabolic kick to heart failure**

**231**

**Derivation and characterization of transgene free induced pluripotent stem cell derived cardiomyocytes from an Asian patient with long QT syndrome**

A. Mehta1, G.L. Sequiera1, Y. Sudoyo1, L. Jun1, P. Wong2, R. Liew2, W. Shim1, *National Heart Centre Singapore, Development and Research Unit, Singapore*; 2*National Heart Centre Singapore (NHCS), Singapore*

**Purpose:** Long QT syndromes are associated with prolonged ventricular repolarization and predisposed patients to risk of sudden cardiac death. We establish a unique reprogrammed model to better understand electrical manifestations of Long QT Syndrome type 2 (LQT2) in vitro.

**Methods and Results:** Dermal fibroblasts from a patient harboring a mutation of ASL1 (corresponding to C1682T base pair) in KCNQ1 gene that encodes Ikr potassium ion channel were reprogrammed using transgene free episomal based vectors to generate human induced pluripotent stem cells (hiPSC). They were differentiated into cardiomyocytes that manifested the LQT2 syndrome phenotype. While no difference in cell morphology and cell number of these cardiomyocytes, they demonstrated prolonged repolarization period whereby field potential duration was significantly affected in comparison to normal controls (patient vs. control; 346±48 ms vs. 228±69 ms, p < 0.05). Extracellular field potential recording following exposure of E-4031 in these LQT2 cardiomyocytes induced an overt ventricular tachycardia-like waveforms leading to contraction arrest. We further evaluated effects of commonly prescribed beta-blockers, in conjunction with beta-agonist stimulation, to mimic clinical management of such patients.

**Conclusions:** We report the first generation of viral-free hiPSC-derived cardiomyocytes from Asian patient with Long QT syndrome that respond appropriately to clinical drugs that could provide a clinical relevant model for LQT2 for better understanding of inherited cardiac arrhythmias.

**232**

**Human induced pluripotent stem cells as in vitro model for hypertrophic cardiomyopathy**

S. Dambrak1, S.R. Braam1, C.M.A.H. Freund2, S. Van De Pas2, D. Ward-Van Oostwaard1, D.E. Atsma1, C.L. Mummery2, *Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands*; 2*Leiden University Medical Center, Department of Anatomy and Embryology, Leiden, Netherlands*

**Purpose:** The in vitro study of genetic cardiac diseases is thwart by many obstacles, especially because of the difficulty to obtain cardiomyocytes from patients and to expand and maintain those cells in long term cultures. Hypertrophic cardiomyopathy (HCM) is a genetic cardiac disease characterized by increased heart size and wall thickening in the absence of other cardiac or systemic diseases. It affects 1:500 individuals and is the leading cause of sudden cardiac death in young adults. In the Dutch population three founder mutations in the myosin binding protein C have been discovered, accounting for nearly one fourth of HCM cases in the Netherlands. MYBPC3 is a cardiac specific sarcomeric protein involved in modulations of force contraction modulation through intracellular calcium regulated phosphorylation. Recently it has become possible to reprogram somatic cells from patients into pluripotent stem cells (induced pluripotent stem cells (iPSC)). Similar to human embryonic stem cells (hESC), iPSC can be readily differentiated into cardiomyocytes. In this study we investigated whether iPSC-derived cardiomyocytes from patients with HCM reflect the diseased phenotype.

**Methods:** Skin fibroblasts from HCM patients was obtained with informed consent and reprogrammed into iPSC. hESC or iPSC from healthy individuals were used as controls. Pluripotent cells were differentiated into cardiomyocytes by using End-2 co-culture, spin EBs or monolayer methods. Beating areas containing cardiomyocytes were dissociated into single cells. Hyper trophy in control cells was induced by addition of phenylephrine (PE). A disease phenotype was determined by cell size, NFAT localization and changes in calcium sensitivity.

**Results:** Preliminary results on dissociated HCM-iPS derived cardiomyocytes show a 2-fold increase in cell surface area when compared to control cardiomyocytes and 1.5-fold increase in size compared to PE-induced control cardiomyocytes. Localization of NFAT to the nucleus was seen in the PE-induced and HCM-iPS derived cardiomyocytes but not in the control cardiomyocytes. In addition, a significant alteration in response to changes in external calcium of HCM-iPS derived cardiomyocytes was observed compared to three independent control lines (determined by changes in beating frequency).

**Conclusions:** These results suggest the ability of the model to recapitulate a disease phenotype. However additional experiments as well as further investigations into alterations in MYBPC3 protein levels and phosphorylation (western blot) as well as adenovirus AT1Pase activity are currently being developed.

**237**

**DPP4 inhibitor vildagliptin reverses diastolic left-ventricular dysfunction via the SDF-1αa-dependent mechanisms in diabetes independently of glycemic control**

T. Shigeta, Y. Kurichi Bando, M. Aoyama, A. Moriya, T. Mitsu, X.W. Cheng, T. Muramura, Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

**Purpose:** Small molecule DPP4 inhibitors are widely used to treat diabetes. We aimed to explore clinical significances of DPP4 activity as the diagnostic marker and therapeutic target for diabetic heart failure by examining the effect of vildagliptin on diabetes–induced cardiac remodeling and diastolic left ventricular dysfunction (DHF) using streptozotocin-induced diabetic male rats (19 weeks old).

**Methods and Results:** Diabetes increased the cardiac DPP4 activity that exhibited. Cardiac catheterization and echocardiography revealed that vildagliptin (VIL: 10 mg/kg/day) ameliorated the diabetes-induced DHF (dp/dt: 6374.5±202.1 for veh and 9491.3±1115.4, VIL, Tau (msec): 20.0±1.7 (veh) and 15.5±3.2 (VIL), peak E (msec): 1.28±0.09 (veh) versus 1.49±0.2 (VIL), Dct (msec): 48.5±3.4 (veh) versus 64.2±0.9 (VIL) independently of glycemic control. Immunohistochemical analysis revealed that vildagliptin treatment reversed the decline in the cardiomyocyte size and capillary density in diabetic rats. Cardiac SDF-1αa level in the diabetic heart was decreased, which was reversed by VIL. The phosphorylation levels of eNOS and Akt were attenuated in diabetic subject and found that both reductions were reversed by VIL. We additionally evaluated the impact of genetic DPP4 deficiency using F344 rats and found that non-pharmacological loss of DPP4 activity consistently reversed the diabetes-induced DHF and remodeling.

**238**

**Calmodulin kinase II deteriorates mitochondrial dysfunction by increasing ROS production in STZ-induced diabetic rat heart**

T. Saito, S. Nishio, N. Takashashi, L.C. Thuc, S. Saito, A. Fukui, C. Kume, M. Hara, M. Nakagawa, Y. Teshima, Oita University, Oita, Japan

**Purpose:** Increased reactive oxygen species (ROS) is one of the mechanisms of cardiac dysfunction in diabetes mellitus. In ESC congress 2011, we presented that sequential activation of Na+H exchanger and Na-Ca exchanger and subsequent Ca overload contributes to ROS increase in cultured neonatal cardiomyocytes exposed to high glucose concentration. In the present study, we focused on Ca2+ (calmodulin-dependent protein kinase II (CaMKII) as a mechanism of ROS increase working in the downstream of Ca overload using an animal model of diabetes mellitus.

**Methods:** Diabetes mellitus was induced by a single injection of STZ (60 mg/kg) into the tail vein of 250-300g Sprague-Dawley rats. Age matched control rats were injected with an equivalent volume of citrate buffer solution. Four weeks after the STZ injection, plasma glucose concentration of rats were >300 mg/dL, and they were used for experiments.

**Results:** First, we confirmed that Ca level was increased in adult cardiomyocytes isolated from STZ-induced diabetic rat compared to those from control rat by ratiometric analysis of Fluor-3/Fura Red. Next, we investigated the ROS level in the heart of diabetic rat. Level of O2•-H2O2 was significantly higher in STZ diabetic rats than that in control; however, this increase was attenuated by the treatment with KN-93, an inhibitor of CaMKII, and apocynin, a NADPH oxidase inhibitor. Consistently, the expression of phosphorylated CaMKII was up-regulated in STZ-induced diabetic cardiomyocytes but not in the control cardiomyocytes. Furthermore, the expressions of p47phox and p67phox, which are components of NADPH oxidase, were up-regulated in the heart of diabetic rats in a KN-93-inhibitable manner. These results indicate that activation of CaMKII works upstream of NADPH oxidase and increases ROS.
The soluble guanylate cyclase activator cinaciguat improves cardiac dysfunction in diabetes mellitus

T. Radovits1, A. Olah1, B. Nemeth1, L. Hidi1, E. Birtalan1, G. Kokenyi1, G. Szabó1, B. Merkely2, S. Semmelweis University, Heart Center, Budapest, Hungary; 1Semenwets University, Department of Pathophysiolog, Budapest, Hungary; 2University Hospital of Heidelberg, Department of Cardiac Surgery, Heidelberg, Germany

Purpose: Patients with diabetes mellitus exhibit cardiovascular dysfunction along with increased oxidative stress and decreased nitric oxide – cyclic guanosine monophosphate (cGMP) signaling. It has been reported, that elevated intracellular cGMP levels contribute to an effective cytoprotection against oxidative stress. In this study we investigated the effects of cinaciguat, a newly developed soluble guanylate cyclase activator on myocardial dysfunction in type 1 diabetes mellitus.

Methods: In male Sprague-Dawley rats diabetes was induced by a single ip. injection of streptozotocin (60mg/kg). In the treatment groups, cinaciguat (10mg/kg/d) was applied orally for 8 weeks. Rats of the control groups received vehicle for the same time. After the treatment left ventricular (LV) pressure-volume relations were measured by using a microt Millar pressure-volume conductance catheter, and indexes of contractility (e.g. preload recruitable stroke work (PRSW)) were calculated. Blood plasma and myocardial tissue samples were collected for determination of cGMP-levels and immunohistochemical analysis, respectively. Myocardial gene expression analysis has been performed by quantitative real-time polymerase chain reaction (qRT-PCR).

Results: When compared to the non-diabetic controls, diabetic rats showed impaired left ventricular contractility (PRSW: 49.5±3.3 vs. 80.3±5.9mmHg; p< 0.05) and a marked diastolic dysfunction (time constant of LV pressure decay, Tau: 17.3±0.8 vs. 10.3±0.9ms, which was significantly improved by cinaciguat (PRSW: 66.8±3.6mmHg, Tau: 14.9±0.6ms in the diabetes-cinaciguat group). The treatment had no hemodynamic effects in non-diabetic control animals. Diabetic patients were increased with associated myocardial immunoreactivity for transforming growth factor beta (TGF-β) along with enhanced gene expression for atrial natriuretic peptide (ANP), heat shock protein 70 (Hsp70) and matrix metalloproteinase 9 (MMP-9), which were all reversed after cinaciguat treatment. Efficacy of the therapy was reflected by markedly elevated levels of cGMP in the diabetes-cinaciguat group compared to control (44.2±11.4 vs. 16.1±2.0pmol/ml plasma).

Conclusions: Our results demonstrate that cinaciguat prevents diabetes-associated deleterious myocardial changes and improves diabetic cardiac dysfunction in our rat model. Pharmacological soluble guanylate cyclase activation might represent a novel therapy approach for diabetic cardiomyopathy.

Conclusion: For the first time we directly recorded human mitoCx43 hemichannels which were inhibited by 43GAP27. Our results indicate endogenous protective adaptation mediated via enhanced basal mito-Cx43 hemichannel activity through hyper phosphorylation of the mitochondrial Cx43 fraction in heart failure.

Glucon-like peptide-1 receptor activation ameliorates cardiac steatosis and reverses pathological remodeling by quality control of mitochondria via cAMP/PKA axis

A. Monji, Y. Kureishi Bando, M. Aoyama, T. Shigeta, T. Mitsu, T. Murohara, Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Purpose: Glucagon-like peptide-1 receptor (GLP-1R) agonist exendin-4 facilitates cardiac contractility in systolic dysfunction model in rodents and patients with heart failure. However, the impact of GLP-1R on cardiac steatosis remains unclear.

Methods and Results: Male KK/AY mice (16-week-old) were allocated into exendin-4 (24 nmole/kg/day, 40 days; KK-ex4) and vehicle group (KK-v). Male C57BL/6 mice were fed with high fat diet for 3 months (DIO) and subjected to exendin-4 treatment at the age of 16 week old (DIO-ex4 and DIO-v). KK-ex4 inhibited decline in heart weight (16.5% vs KK-v) without body weight loss. Oil-red-O staining revealed that KK-ex4 and DIO-ex4 reduced cardiac steatosis. Echo-cardiography revealed that systolic function of DIO-v was suppressed (-13.8% vs control), which was restored in DIO-ex4 with reduced LVdpw (-11.1% vs DIO-v). Mitochondria-specific dyes (MitoTracker) revealed diffuse mitochondrial Cx43 expression in heart failure. Mitochondria-specific dyes (MitoTracker) revealed diffuse mitochondria in the hearts of STZ-induced diabetic rats were swollen and the structure of cristae was collapsed; however, these changes were attenuated by the treatment with KN-93 and apocynin. This observation indicates that activation of CaMII followed by NADPH oxidase-derived ROS increase contributes to mitochondrial dysfunction which may lead to cell death.

Conclusion: Increase in NADPH oxidase by activating CaMII is a mechanism of ROS increase in the heart of diabetes mellitus. Up-regulation of ROS production facilitates mitochondrial malfunction and may result in cardiac dysfunction in diabetic patients.

Figure 1. Typical mitochondria images by TEM

Conclusion: GLP-1R activation protects cardiac remodeling induced by steatosis through the restoring mitochondrial oxidative damage mediated by the activation of cAMP/PKA-dependent mechanisms.

Expression and physiological role of the novel adipokine nestatin-1 in cardiomyocytes

S. Feijoo-Bandi, D. Rodriguez-Penas, V. Garcia-Rua, M.F. Otero, A. Mosquera-Leal, J.R. Gonzalez-Juarety, M.F. Lago. IDIS, University Clinical Hospital. Santiago de Compostela, Spain

Purpose: Nestatin-1 is a novel adipokine involved in the control of food intake and energy metabolism which shows anti-inflammatory properties. The role of this adipokine in cardiovascular physiology is unknown. In previous studies we determined that nestatin-1 is expressed in human, rat and mouse heart. Our aim now is to study the effect of this adipokine in cardiomyocytes and the possible regulation of nestatin-1 cardiac synthesis by diet and inflammatory mediators.

Methods: Real-time PCR was used to determine nestatin-1 mRNA levels in cultured neonatal cardiomyocytes of Sprague Dawley rats treated with TNF-α, dexamethasone and insulin. In heart tissue of rats fed with high fat diet for 16 weeks, we used real-time PCR to determine nestatin-1 cardiac mRNA levels and an ELISA to determine nestatin-1 plasma levels. Cardiomyocytes were treated with nestatin-1 and confocal microscopy was used to study the glucose transporter Glut-4 mobilization. Finally, western blot was used to identify possible transduction signalling molecules (Erk 1/2, AMPK and AKT) after nestatin-1 treatment in cardiomyocytes.

Results: Cardiomyocytes treatment with 0.1-20 ng/ml TNF-α for 6-48 h induces an increase of nestatin-1 mRNA levels with a maximum stimulatory effect at 20 ng/ml for 24 h (p<0.0159; Fold-Change (FC)=1.16, n=5). Treatment with 0.1-100 nM dexamethasone for 6-48 h also increases of nestatin-1 mRNA levels with a maximum stimulatory effect at 100 nM for 24 h (p=0.0079; FC=2.457, n=5).
The metabolic kick to heart failure / Non pharmacological treatment in hypertension

247 Adherence to the Mediterranean diet and albuminuria in adolescents: Emerging data from the Lyceum Leoncio Albuminuria (3L) Study

K. Dimitriadis, C. Tsolous, D. Tsachnis, A. Kasiakogias, T. Paspoulou, V. Tzamou, A. Mazaraki, I. Andrikou, C. Pitsavos, C. Stefanidis. First Cardiology Clinic, University of Athens Hippokration Hospital, Athens, Greece

Purpose: Mediterranean diet has favorable effects on the cardiovascular system, while albuminuria is associated with atherosclerosis progression. The aim of the study was to investigate the relationship of dietary habits with urinary albumin excretion, expressed as the albumin to creatinine ratio (ACR), in a cohort of adolescents.

Methods: A total of 365 adolescents 12-17 years of age (212 males, aged 13.9 years, office blood pressure (BP)=115/67 mmHg) that were included in the Lyceum Leoncio Albuminuria (3L) study were considered for analysis. All participants were determined in a morning spot urine and for each adolescent a questionnaire was completed on lifestyle and socio-economic characteristics.

Results: The Mediterranean Diet Quality Index for children and adolescents (KIDMED) was estimated and accordingly subjects were divided into those with optimal (≥7), average (4-7) and low (<4) score.

Conclusion: In adolescents there is an inverse relation of KIDMED score with urinary albumin excretion, expressed as the albumin to creatinine ratio (ACR), in a cohort of adolescents.

NON PHARMACOLOGICAL TREATMENT IN HYPERTENSION

249 Dietary omega-3 acid esters enhance omega-3 index, attenuate myocardial arrhythmogenic substrate and protect from malignant arrhythmias in a model of human essential hypertension

N. Tribulova1, B. Baczova1, J. Radoszinska1, T. Berova1, V. Knez1, E. Goncalvesova1, J. Slezak1,2,3. 1Slovak Academy of Sciences, Institute for Heart Research, Bratislava, Slovak Republic; 2Comenius University, Faculty of Medicine, Bratislava, Slovak Republic; 3Slovak Academy of Sciences, Institute of Experimental Pharmacology & Toxicology, Bratislava, Slovak Republic; 4National Institute of Cardiovascular Diseases (NIVDI), Bratislava, Slovak Republic

Background: Hypertension-induced myocardial remodeling is known to be associated with increased propensity to malignant arrhythmias that can be attributed to impairment of cell-to-cell synchronization due to alterations in electrical coupling protein, connexin-43 (Cx43). Omega-3 fatty acids (omega-3) exert cardioprotective and antiarrhythmic effects in both experimental and clinical setting. We tested our hypothesis that dietary omega-3 intake can protect of hypertensive rats from malignant arrhythmias via protection of intercellular communication ensured by Cx43 channels.

Design and Methods: Experiments were conducted on male spontaneously hypertensive rats (SHR) at early (3 month) and late (12 month) stage of diseases as well as age-matched normotensive Wistar rats. Untreated rats were compared with animals supplemented by omega-3 (EPA+DHA ethyl esters, Vesterlanes, Norway, 30 mg/day) for two month. Blood pressure, body weight and body weight were monitored. Plasma and red blood cells (RBC) fatty acids profile (omega-3 index) was estimated by gas chromatography. Left ventricular tissues were taken for examination of Cx43 distribution (using immunostaining and electron microscopy) and expression (using immunoblotting). Expression of protein kinase C-isoforms (PKC) (phosphorylated Cx43 was examined as well. Langendorff-isolated hearts were compared according to Cx43 distribution in SHRs and Cx43 expression (using immunoblotting).

Key results: Comparing to healthy rats the omega-3 index was lower in old SHR (0.7 vs 2.5%) and increased due to omega-3 intake in both groups to 2.3% and 8%. Young SHR hearts exhibited with enhanced distribution of Cx43 on lateral surfaces of the cardiomyocytes, while old SHR exhibited both lateralization and severely disordered distribution of Cx43 at the area of fibrosis. Cx43 expression was more pronounced in young and decreased in old SHR. Young SHR hearts but phosphorylated (functional) forms of Cx43 were suppressed in both SHR groups. In contrast, omega-3 intake diminished arrhythmogenic substrate, i.e. abnormal Cx43 distribution and attenuated significantly abnormal Cx43 expression and phosphorylation. The latter was linked with enhanced PKCε expression. Consequently, omega-3-treated SHR were less prone to inducible VF compared to untreated rats.

Conclusion: Results indicate that hypertensive rats benefit from omega-3 fatty acids supplementation due to an increase of omega-3 index, alleviation of Cx43-related arrhythmogenic substrate and suppression of malignant arrhythmias. This work was supported by VEGA 2/0046/12 grant.

248 Influence of potassium intake on blood pressure of subjects with different levels of sodium consumption

J.G. Mill1, S.L. Rodrigues1, M.P. Baldi1, P. Magalhaes1.
1Federal University of Espirito Santo, Vitoria, Brazil; 2Faculty of Medicine, University Agostinho Neto, Luanda, Angola

Background: Increase of potassium (K) intake has been recommended as a non pharmacologic strategy to reduce blood pressure (BP) levels and hypertension incidence. However, the benefits of such strategy in subjects with different patterns of sodium (Na) intake have not been evaluated. In this study we investigated in a population-based study the influence of the K intake on BP of individuals consuming low (<6 g/day) or high (>6 g/day) salt diets.

Methods: A random sample (n=1,661) of the adult (25-64 population) of Vitoria, Brazil, was recruited to investigate cardiovascular risk factors. BP, anthropometry and biochemical variables (fasting blood) were obtained according to standard methods during a programmed visit to the University Hospital. Urine was collected overnight (10 pm to 7 am) in the urine samples collected in the morning spot urine to assess Na, K and creatinine excretion. Individuals with inadequate urine collection (n=54), plasma creatinine >1.4 mg/dL (n=52) or under use of any hypertensive medication, including diuretics (n=270) were excluded from the present analysis.

Results: Data refer to 1,285 subjects (613 men, age = 43±10 y). Hypertension (blood pressure >140/90 mmHg) was found in 31%, obesity (BMI>30 kg/m2) in 15.5% and diabetes (fasting glycemia >125 mg/dL) in 5.3%. Mean urinary Na and K excretion was 112±57 mmol/24 h and 23±15 mmol/24, giving a mean daily consumption of 211 meq Na and 78 meq K. Higher K intake was associated with individuals older and with higher BMI and urinary Na excretion. Systolic and diastolic BP mean levels were stable along quartiles of urinary K excretion. However, significant (P<0.001) decrease was observed for the systolic and diastolic BP adjusted for age, BMI and 12h Na and creatinine excretion. Interestingly, the association between K excretion (as surrogate of K intake) was lost in the subgroup of subjects (N=182) consuming <6 g salt/day (-1.20 g Na/12h urine). In subjects consuming >6 g salt/day, the adjusted systolic and diastolic BP were, respectively, 7 mmHg and 3 mmol/lower in those in the upper urinary K excretion quartile (>28 g/day) as compared to those in the lowest one (<14 g/day).

Conclusion: Our data confirm based in data obtained in the general population that increasing the K intake may partially inhibit the hypertensive effects of high salt diet. This strategy seems to be more effective in high salt consumers.

250 AT1 receptor blockade attenuates insulin resistance and myocardial remodeling in rats with diet-induced obesity

S.A. Oliveira Jr1, M.P. Okoshi1, P.F. Martinez1, D.M. Guizoli1, B.P. Torres2, M. Dal Pai-Silva2, K.O. Okoshi1, A.C. Cicogna1, C.R. Padovas2, A.P. Lima-Leopoldo1,3. 1Sao Paulo State University, Botucatu Medical School, Department of Internal Medicine, Botucatu, Brazil; 2Univ. Estadual Paulista (UNESP), Botucatu Biosciences Institute, Botucatu, Brazil; 3Federal University of Espirito Santo, Vitoria, Brazil

Interactions between angiotensin II type 1 (AT1) receptor and insulin has classically resulted in insulin resistance and cardiac remodeling in obesity. This study evaluated the influence of AT1 receptor blockers losartan on insulin receptor/phosphotyrosin 3-kinase (PI3-kinase) pathway and myocardial remodeling in rats with diet-induced obesity.
Methods: Male Wistar-Kyoto rats (n=40) were subjected to a standard rat chow (C; 3.2Kcal/g) or a hypercaloric diet (OB; 4.6Kcal/g) for 30 weeks and then allocated into four groups: C, CL, OB, and OBL. The groups were randomized and divided in 2 groups. Study group of 204 patients treated with music therapy and Control group of 202 patients with no music therapy. Each patient in study group underwent two sessions of medical therapy (12 minutes) in a day. Both groups were similar in baseline, post AMI characteristics and post AMI medical therapy.

Results: Comparing parameters of Study and Control group of patients in 12- year follow-up period. Statistic analysis remained unchanged between OBL and CL (p=0.9412 NS). Myocyte cross-sectional area and collagen interstitial fractional volume were compared between OBL and CL. OBL (n=7) 0.78 ±0.35; OB (n=7) 1.00 ±0.20; C (n=7) 0.89 ±0.61; OBL (n=7) 1.46 ±0.73% was significantly higher in OBL than C. Western blot results are shown in the Table.

Conclusion: This study provides support for the use of music therapy in patients with HT and AMI to reduce blood pressure, heart rate and new coronary events expression. These effects of music therapy are probably because of decreasing in sympathetic nervous system activity.

NEW INSIGHTS IN MICRO AND MACROVASCULAR CORONARY ARTERY DISEASE

269 Plasma endothelin and adrenomedullin are associated with coronary conduit and microvascular function

A. Alfadfi1, N. Uddin1, D.J. Clark2, M. Freeman1, A. Wilson3, L.M. Burrell1, O. Farouque1

1Austin Health, Department of Cardiology, Melbourne, Australia; 2The University of Melbourne, Melbourne, Australia; 3Austin Health, Department of Cardiology, Melbourne, Australia

Purpose: Endothelin (ET-1) and adrenomedullin (ADM) are potent vasoactive peptides. ET-1 is a vasoconstrictor and an elevated level is associated with cardiovascular disease (CVD). ADM is a vasorelaxant and may result in protection from atherosclerosis in experimental studies. We sought to determine the relationship of ET-1 and ADM with coronary conduit and microvascular resistance.

Methods: Patients with chest pain syndromes having coronary angiography were recruited (n=32). Plasma ET-1 and ADM level were measured. Coronary flow mediated dilatation (FMD) was defined as percentage increase in coronary diameter during maximal hyperaemia as assessed by quantitative coronary angiography (QCA). Index of microcirculatory resistance (IMR) and coronary flow reserve (CFR) were measured by coronary pressure guidewire. Pearson’s correlation and linear regression analysis were used to determine the relationship between plasma biomarkers and coronary measures.

Results: Mean age was 66±8 year-old with 68% male. The sample included patients with hypertension (75%), dyslipidaemia (84%), diabetes (34%) and current smokers (13%). Mean BMI was 33.6±6 kg/m² and 66% had prior coronary artery disease. The correlation between plasma biomarkers and coronary function is displayed in the table below.

For each 1pmol/L increase in ET-1, IMR increased by 7 units (95%CI 2.8, 10.5; p=0.01). For each 1pmol/L increase in ADM, CFR increased by 0.20 (95%CI 0.10, 0.30; p=0.04) and FMD increased by 0.92% (95%CI 0.29, 1.55; p=0.001). After adjustment for age, gender, mean blood pressure, hypertension, diabetes, dyslipidaemia,BMI, and serum glucose and cholesterol, the relationship between AD and FMD and CFR remained significant. The association between ET-1 and IMR (r=0.57;95%CI 1.4, 10.0; p=0.01), and between ADM and FMD (r=0.79;95%CI 0.45,1.13; p=0.01) remained significant.

270 Coronary microvascular dysfunction induced by primary hyperparathyroidism is restored after parathyroidectomy

E. Osto1, F. Fallo1, M.R. Pelizzo2, A. Maddalozzo1, F. Cortesi1, R. Montisci1, R. Belli2, T. Luscher2, S. Riccio1, F. Tona1

1University of Padua Polyclinic, Padua, Italy; 2University of Cagliari, Cardiology Clinic, Cagliari, Italy; 3Department of Cardiology, University Hospital and Cardiovascular Research, Institute of Physiology, University of Zurich, Switzerland

Purpose: Symptomatic primary hyperparathyroidism (PHPT) is associated with increased cardiovascular mortality. However, data on the association between asymptomatic PHPT and cardiovascular risk are lacking. We assessed coronary flow reserve (CFR), as a marker of coronary microvascular function, in asymptomatic PHPT of recent onset.

Methods: We studied 100 PHPT patients (pts) (80 F, aged 58±12 years) without cardiovascular disease, and 50 controls matched for age and gender. CFR in the left anterior descending coronary artery (LAD) was detected by transthoracic
Doppler echocardiography (TDE), at rest and during adenosine infusion. CFR was the ratio of hyperemic diastolic flow velocity (DFV) to resting DFV.

Results: In PHPT, CFR was lower than in controls (3.0 ± 0.6 vs 3.8 ± 0.7, p < 0.001). CFR was abnormal (≤2.5) in 27 (27%) pts compared with controls (4%) (p < 0.001). CFR was inversely related to parathyroid hormone (PTH) levels (r = 0.3, p < 0.004). In pts with CFR ≤2.5 PTH was higher (28.4 [16-37] vs 18 [13-26] pmol/L, p < 0.007) whereas calcium levels were similar (2.9 ± 0.1 vs 2.8 ± 0.3 mmol/L, p = 0.2). At multivariable linear regression analysis, PTH and age were the only determinants of CFR (p = 0.03 and p = 0.01 respectively). At multiple logistic regression analysis only PTH increased the probability of CFR ≤2.5 (p < 0.001).

In all 27 PHPT pts with CFR ≤2.5, parathyroidectomy normalized CFR (3.3 ± 0.7 vs 2.1 ± 0.5, p < 0.0001).

Conclusions: PHTP pts have coronary microvascular dysfunction which is completely restored after parathyroidectomy. PTH independently correlates with the coronary microvascular impairment, suggesting a crucial role of the hormone to explain the increased cardiovascular risk in PHPT.

### Relationship between leukocyte and subtype counts, low-grade inflammation and slow coronary flow

#### Background:

Slow coronary flow (SCF) is an angiographic finding characterized by decreased perfusion of epicardial coronary arteries in the absence of obstructive coronary disease. We aimed to investigate whether there is a positive correlation between leukocyte counts, high-sensitive C-reactive protein (hsCRP) and CFR determined by frame rates.

#### Methods:

Forty-seven patients with NCA and SCA in all three coronary vessels and 3D sex and age matched control participants with NCA but without SCA were investigated. The quantification of the coronary flow was assessed by the thrombolysis in myocardial infarction (TIMI) frame count (TFC) in all coronary arteries.

#### Results:

hsCRP was significantly positively correlated with mean TFC (r=0.52, p<0.001). Besides, leukocytes, neutrophils and monocytes were significantly positively related to mean TFC (r=0.353, p=0.002; r=0.298, p=0.009 and r=0.511, p<0.0001). In multivariate analyses, only hsCRP (beta: 0.324, p=0.003) and monocyte count (beta: 0.350, p=0.003) were related to SFC determined by TFC.

#### Table 1. The independent effects of hsCRP and monocytes on slow coronary flow phenomenon

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean TFC (Dependent variable)</th>
<th>SFC (Dependent variable)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p value*</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>0.1 ± 0.1</td>
<td>0.96 (0.94−1.00)</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>0.3 ± 0.1</td>
<td>0.53 (0.42−0.67)</td>
</tr>
<tr>
<td>Gentler (male)</td>
<td>0.3 ± 0.1</td>
<td>0.53 (0.42−0.67)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.2 ± 0.1</td>
<td>0.91 (0.83−0.99)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.3 ± 0.1</td>
<td>0.53 (0.42−0.67)</td>
</tr>
<tr>
<td>Smoking, +</td>
<td>-0.2 ± 0.1</td>
<td>0.80 (0.73−0.88)</td>
</tr>
<tr>
<td>Hypertension+Diab+</td>
<td>-2.3 ± 0.1</td>
<td>0.10 (0.03−0.31)</td>
</tr>
<tr>
<td>HS-CRP (mg/L)</td>
<td>0.6 ± 0.1</td>
<td>1.00 (1.00−1.01)</td>
</tr>
<tr>
<td>Monocyte (10^9/L)</td>
<td>0.3 ± 0.1</td>
<td>0.53 (0.42−0.67)</td>
</tr>
<tr>
<td>Neutrophil (10^9/L)</td>
<td>0.3 ± 0.1</td>
<td>0.53 (0.42−0.67)</td>
</tr>
</tbody>
</table>

#### Conclusion:

Our results showed that circulating monocytes and low-grade inflammation positively related to mean TFC and negatively related to CFR. hsCRP is an independent determinant of SFC.

### Increased levels of circulating endothelial microparticles and erythrocytes degradation products in microvascular angina

#### Background:

Microvascular angina (MVA) is a rare condition associated with myocardial ischemia and no evidence of epicardial coronary artery obstructive lesions. Although MVA is related to endothelial dysfunction, its precise pathophysiology still remains partially unknown. Enhanced hemolysis and free heme release can impair endothelial function, through direct endothelial injury and nitric oxide scavenging. We sought to investigate if MVA was associated increased hemolysis phenomenon that could lead to endothelial injury.

#### Methods:

Patients without acute coronary syndromes who underwent a coronary angiography in our institution were screened for inclusion. Patients were classified in 3 groups, according to their clinical presentation and angiographic features: patients with stable CAD, patients with MVA (as defined by the Lanza criteria) and subjects with cardiovascular risk factors (CRF) and no evidence of ischemia on non invasive medical test. Levels of endothelial (CD144+ and CD31+/41-) EMPs, erythrocytes (CD235+) RBCMPs, platelets (CD41+ PMPs) and leukocytes-derived microparticles (CD11+ LMPs) were measured by flow cytometry methods on free platelets plasma samples. Levels of circulating free heme (CFH) were analyzed by absorption spectrophotometry methods.

#### Results:

A total of n= 104 subjects (62.6 ± 1.2% vs 75% male gender) were included in the study (n=9 MVA patients, n=71 CAD patients and n=24 CRF patients). Patients with MVA displayed significantly higher levels of circulating RBCMPs (146±63 ev/L) compared to CAD (94±41 ev/L) and CRF patients (266±72 ev/L, p<0.01 ANOVA). Moreover, we also observed a significant increase in CFH levels in MVA patients (0.79±0.19 Units/L) compared to the others (0.44±0.03 and 0.66±0.1 Units/L, p<0.01 for all), suggesting an endothelial injury in these patients. No significant difference was observed for LMPs and PMPs levels between groups.

#### Conclusions:

Patients with MVA have evidences of enhanced hemolysis with increases in circulating free heme and erythrocytes derived MP's levels as well as increased endothelial injury circulating biomarkers.
BIOMARKERS AND MECHANISMS IN HEART FAILURE

Paradoxical preservation of NO signalling in Takotsubo cardiomyopathy

T.H. Nguyen1, C. Neill1, A. Svolo1, D. Ngo1, W. Chan1, Y. Chirkov2, D. Takase1, M. Frenneaux1, J. Horrow1. 1University of Adelaide, Queen Elizabeth Hospital, Adelaide, Australia; 2Institute of Clinical Pharmacology, Hannover, Germany; 3Aberdeen Royal Infirmary, Aberdeen, United Kingdom.

Introduction: Takotsubo cardiomyopathy (TTC) is characterized by the sudden development of segmental (usually periapical) left ventricular systolic dysfunction, usually in post-menopausal women and often after acute severe stress. To date, little information is available concerning the mechanism(s) underlying this presumably ‘chemical’ asymmetric myocardial process, other than evidence of associated catecholamine secretion. We tested the hypothesis that TTC might also be associated with impairment of nitric oxide (NO)-based signalling.

Methods: In 56 patients with TTC, we utilized (1) platelet responsiveness to NO and (2) plasma levels of asymmetric dimethylarginine (ADMA) as indices of potential NO effect. Additionally, endothelial progenitor cell (PEC) counts, which are partially NO-dependent, were evaluated. We sought correlations between these parameters, measured at the time of diagnosis and 3 months thereafter, and (1) severity of TTC episodes and (2) extent of recovery after 3 months. An aging female population sample (n = 110) was used for control purposes.

Results: Surprisingly, platelet NO responsiveness was substantially elevated (p < 0.005) and ADMA concentrations lowered (p < 0.05) in TTC vs. control subjects both acutely and after 3 months (Figure 1). Furthermore, extent of platelet NO responsiveness correlated directly with several markers of severity of TTC attacks. However, ADMA levels were predictive of markers of incomplete recovery at 3 months (p < 0.001).

Conclusions: In conclusion, (1) TTC is associated with ‘paradoxical’ integrity of NO signalling and (2) there is a direct relationship between tissue NO responsiveness and severity of TTC episodes. Acute NO generation may both contribute to the extent of acute myocardial injury and to subsequent rapid recovery in TTC.

Coronary flow reserve versus CT scan study to differentiate non-ischemic from ischemic dilated cardiomyopathy

F. Rigo1, N. Galbazi2, E. Grolla1, C. Reverberi1, G. Ossena3. 1dell’Angelo Hospital Department of Cardiology, Mestre-Venice, Italy; 2Hospital Parma, Department of Cardiology, Parma, Italy; 3Hospital dell’Angelo, Department of Cardiology, Mestre-Venice, Italy.

Background: Discriminating the underlying mechanism of dilated cardiomyopathy represents a key for proper management and therapy with significant impact for patient outcome.

Aim: To compare the diagnostic value of an integrated study based on coronary flow reserve on left anterior descending coronary artery (CFR-LAD) and multidetector CT (CTA) scan in patients with unknown dilated cardiomyopathy (DCM).

Methods: Since 2009, we have prospectively enrolled 131 consecutive patients with DCM (95 males, mean age 69 ± 16 years) who underwent dipyridamole (up to 0.84 mg/kg per 6’ stress echo with combined assessment of CFR-LAD by transthoracic Doppler). A value of CFR < 2.0 was taken as abnormal. Within 7 days, a multidetector coronary CT, for both CaS and CTA assessment, was performed. Each patient underwent coronary angiography (CAG) within 30 days and a quantitatively assessed vessel stenosis ≥ 50% was considered significant.

Results: CFR-LAD (<1.6) had an AUC = 0.90, CaS (<90) had an AUC = 0.86 and the finding of at least 1 obstructive coronary stenosis (≥ 50%) with CTA had an AUC = 0.96 in order to predict obstructive coronary artery disease (CAD) at coronary angiography, configuring an ischemic DCM.

Conclusions: Conventional risk factors for coronary disease were fairly useful in predicting DCM due to coronary disease (global chi square = 42.0). By progressively adding CaS, CFR-LAD and finally CTA, we provided increasingly accurate information (p < 0.001 for all sequential comparisons) for predicting the underlying cause of DCM correctly.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>Hemodynamic response to transient hypoxia</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>SBP slope</td>
<td>HR slope</td>
<td>SVR slope</td>
</tr>
<tr>
<td>CHF high chemosensitivity</td>
<td>1.11 ± 0.32</td>
<td>1.17 ± 0.71</td>
<td>0.71 ± 0.32</td>
</tr>
<tr>
<td>CHF high chemosensitivity</td>
<td>1.11 ± 0.32</td>
<td>1.17 ± 0.71</td>
<td>0.71 ± 0.32</td>
</tr>
<tr>
<td>Control</td>
<td>0.22 ± 0.25</td>
<td>0.41 ± 0.29</td>
<td>0.36 ± 0.23</td>
</tr>
</tbody>
</table>

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790 by guest on 11 March 2019
Selective heart rate reduction with ivabradine unloads the left ventricle in heart failure patients

J.-C. Reil1, J.-C. Tardif2, I. Ford3, S.M. Lloyd4, E. O’Meara4, M. Komajda1, J. Borre5, L. Tavazzi6, K. Swedberg7, M. Boeim1

1Montreal Heart Institute, Montreal, Canada; 2University of Glasgow, Glasgow, United Kingdom; 3University Pierre & Marie Curie (UPMC), Paris, France; 4Howard Gilman Institute for Heart Valve Diseases, New York, United States of America; 5Maria Cecilia Hospital-GVM Care and Research, Catignola, Italy; 6Shahgloreska Academy, University of Gothenburg, Department of Emergency and Cardiovascular Medicine, Gothenburg, Sweden

Purpose: The effective arterial elastance (Ea) represents resistive and pulsatile afterload of the heart derived from the pressure volume (PV) diagram. Heart rate modulates Ea, and, therefore, afterload burden. It was the aim of this study to investigate whether selective heart rate reduction with ivabradine reduces afterload of patients with systolic heart failure included in the echocardiographic substudy of the SHIFT trial.

Methods and results: 275 patients with systolic heart failure (EF < 35%) treated either with placebo (n=132) or ivabradine (up to 7.5 mg bid; n=143) were included. Ea, vascular compliance (VC) and end-systolic elastance (Ees) were assessed at baseline and after 8 months of treatment. Blood pressure was measured by an oscillometric 7.5 mmHg device. IVC, tricuspid and left ventricular end-diastolic volume (EDV) were evaluated by echocardiography. At baseline Ea, VC, heart rate and Ees did not differ significantly between groups treated with placebo or ivabradine. After 8 months of treatment heart rate was significantly reduced in the ivabradine group (p<0.001) and was accompanied by marked reduction in Ea (p<0.001) and improved VC (p=0.048). Because Ees remained unchanged (p=0.59), ventricular-arterial coupling was markedly improved (p=0.0003) resulting in a higher stroke volume (p<0.001), and a decrease EDV (p=0.0002) in the ivabradine treated patients.

Conclusion: Selective heart rate reduction by ivabradine improved vascular compliance and help to explain the good hemodynamic tolerability of the lower heart rate.

Serum tenascin-c levels might be a candidate biomarker for myocardial noncompaction

H.B. Eren1, T. Guven2, A. Kemik3, S. Altay4, N. Sayar5, D. Oz1, A. Ekmeck1, A. Zenirci1, S. Kull1, M. Eren1, S. Yasar1. 1Siyami Ersek Thoracic and Cardiovascular Surgery Center, Department of Cardiology, Istanbul, Turkey; 2University of Kafkas, School of Medicine, Department of Cardiology, Kars, Turkey; 3Istanbul University, Cerrahpasaa Faculty of Medicine, Department of Biochemistry, Istanbul, Turkey; 4BaskerTEM University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey

Background & Purpose: Myocardial noncompaction (MN) is a rare form of congenital cardiomyopathy which is assumed to occur secondary to interruption of the normal myocardial morphogenesis. Tenascin-C (TN-C), an extracellular matrix glycoprotein that appears in several important steps of embryonic development such as the initial differentiation of cardiomyocytes or coronary vasculogenesis, but it is not detected in a normal adult myocardium. The clinical significance of TN-C levels has not yet been studied in patients with MN. The aim of this study is to elucidate whether serum TN-C levels might be a useful biomarker for MN.

Methods: Serum TN-C levels were measured by ELISA in 50 MN patients both with/without systolic dysfunction and 23 normal controls. Systolic dysfunction was defined as EF < 40. Mann-Whitney U test and ROC curve analysis were done. Results: Of 51 MN patients, 24 MN (47%) patients had systolic dysfunction (mean age 38±18) and 27 MN patients (53%) had normal systolic function (mean age 36±16). The mean age of controls was compatible with the patients (mean age 37±16). The mean levels of serum TN-C were significantly higher than that of controls, while stroke volume and MN patients with systolic dysfunction and without systolic dysfunction (26±10 ng/ml and 26±8 ng/ml, respectively, p < 0.001). No significant was observed between two groups of MN patients regarding TN-C levels (p=0.8). ROC curve analysis revealed that TN-C value of 11.7 ng/ml was related to MN with 100% sensitivity and specificity and the results were compatible for all MN patients whether they had systolic dysfunction or not.

Conclusion: TN-C might be a candidate biomarker for MN patients and seems not to be affected by systolic function.

Measurement of anti beta1-adrenoreceptor auto-antibodies in heart failure by a cellular ELISA assay

H.P. Holthinr1, S. Zeitlig1, V. Boivin-Jahn2, M.J. Lohse2, S. Kaeber2, S. Claus2, R. Jahr2, G. Muench2, M. Untergerg et al.

1Coninurn GmbH, Martinsried, Germany; 2Institute of Pharmacology and Toxicology and Rudolf-Virchow-Center, University of Wurzburg, Wurzburg, Germany; 3-Ludwig-Maximilians University, Medical Clinic and Polocinio I, Clinic Grosshadern, Munich, Germany

Background: Auto-antibodies directed against the second extracellular loop of the cardiac beta1-adrenergic receptor (β1-AR) contribute to the pathogenesis of heart failure, such as dilated cardiomyopathy (DCM) and Chagas disease. Various assays have been used to detect these autoantibodies, and the reported prevalence of positive patients varied depending on the assay method.

Methods: We analysed sera from 164 patients with DCM (ejection fraction < 45%) and from 110 healthy volunteers with an existing method, and compared it to a novel cellular ELISA using the full transgene for the human β1-AR. This novel assay was designed in strong analogy to the most reliable anti-TSH receptor antibody ELISA used in Graves’ disease diagnostics (“third generation assay”), and also uses a competition with a mononclonal anti-receptor antibody which specifically recognizes the relevant epitope of the β1AR.

Results: The assay was validated and showed high reproducibility; clear cut-off values were determined. Anti-β1-AR antibody titers (determined as inhibition of mononclonal antibody binding) were markedly reduced in sera of patients compared to sera of healthy controls. Analysis of the β1-AR transgene of a patient with DCM treated with immunosuppression revealed that sera were depleted from antibodies by protein G column purification.

In contrast, a previously used ELISA conducted with a 26-meric peptide derived from the uncleaved, extracellular loop of the β1-AR protein failed to recognize the epitope. The specificity of the novel assay is markedly superior to existing assays. The assay was validated according to “good laboratory practice” (GLP), and now serves as a companion bio-diagnostic assay to develop and control individualized therapies in antibody-positive patients.

DIAGNOSIS AND PROGNOSIS IN ACUTE PULMONARY EMBOLISM

P. Henrichsson1, E. Westerlund1, L. Brandö2, O. Hoivata3, A. Ekom2, Karolinska Institutet, Department of Clinical Sciences, Danderyd Hospital, Stockholm, Sweden; 2Karolinska Institutet, Department of Medicine, Clinical Epidemiology Unit, Stockholm, Sweden; 3Karolinska Institutet, Department of Clinical Science, Intervention and Technology, Stockholm, Sweden

Objective: To estimate the risk of pulmonary embolism (PE) and venous thromboembolism (VTE) in pregnancy after in vitro fertilization (IVF).

Design: A cross-sectional study in Sweden of all women who had given birth within 1 year to a child after IVF between 1990 and 2008 and prospectively compared to 2,510,000 (n=2591) in a national registry. The main outcome measure was maternal mortality and a condition where clinical suspicion is critical to diagnosis, VTE in women during the first part of the pregnancy. As PE is a leading cause of maternal mortality and a condition where clinical suspicion is critical to diagnosis, the knowledge and an awareness of this risk of IVF is important to all practicing physicians.

Participants: 23,498 women who had given birth to a child after IVF between 1990 and 2008 and 116,960 individually matched women.

Main outcome measures: Risk of PE and VTE during the trimesters of pregnancy.

Results: The proportion of pregnancies complicated by VTE was 4.2/1000 (n=99) in exposed as compared to 2.5/1000 (n=2591) in unexposed women (odds ratio, 4.7, 95% CI, 3.00 to 7.47). The proportion of women suffering PE during the first trimester was 3.0/1000 as compared to 0.4/1000 in controls (odds ratio, 6.98; 95% CI 2.22 to 21.98).

Conclusions: IVF is associated with a substantially increased risk of PE and VTE in women during the first part of the pregnancy. As PE is a leading cause of maternal mortality and a condition where clinical suspicion is critical to diagnosis, the knowledge and an awareness of this risk of IVF is important to all practicing physicians.
Short term prognosis in acute pulmonary embolism: external validation of the European Society of Cardiology prognostic model

C. Becattini1, F. Casazzata1, A. Bongarzoni2, C. Forgione3, C. Cuccia4, L. Ronconi4, F. Porrone5, L. Pignataro5, G. Aghetti2, 1University of Perugia, Perugia, Italy; 2San Carlo Borromeo Hospital, Milan, Italy; 3Foundation Policlinico - Institute Hospital, Brescia, Italy; 4Santa Maria della Misericordia Hospital, Padova, Italy; 5Foundation IRCCS Ca' Granda Polyclinic, Milan, Italy

Purpose: The aim of this study is to externally validate the prognostic model proposed by the European Society of Cardiology (ESC) in patients with acute pulmonary embolism (PE) included in the Italian Pulmonary Embolism Registry (IPER).

Methods: IPER is a web-based registry including patients with acute PE hospitalised in Cardiology, Emergency or Internal Medicine Departments in Italy. 1716 consecutive patients with confirmed acute PE were enrolled in IPER. Hemodynamic impairment was the main independent predictor for in-hospital death (HR 6.4, 95% CI 4.3 to 9.6, p < 0.001), along with age > 75 and bed-rest. Echocardiography and troponin were obtained in 869 of 1561 hemodynamically stable patients (55.3%). In-hospital death or clinical deterioration occurred in 8.6% (95% CI 5.9 to 11.7%) patients with both RVD and elevated troponin levels, in 4.7% (95% CI 2.4 to 7.0) patients with RVD or elevated troponin in 0.6% (95% CI 0.9 to 1.6) of the patients with no RVD and normal troponin levels. Among hemodynamically stable patients, the risk for in-hospital death or clinical deterioration was higher in those with both RVD and elevated troponin (adjusted HR 7.2; 95% CI 1.3-37.6; p = 0.001) and in those with RVD or elevated troponin (adjusted HR 4.3; 95% CI 1.1-18.7; p = 0.05) as compared with those without these markers (Figure). The risk for in-hospital death was higher in patients with both RVD and elevated troponin (HR 2.5; 95% CI 1.2-5.2; p = 0.01), than in patients with RVD or elevated troponin. None of the patients with no RVD and normal troponin died.

Conclusions: The ESC prognostic model can be used for risk stratification of hemodynamically stable patients with acute PE.

Inconsistencies in the use of cardiac biomarkers or echocardiography in patients with acute non-massive pulmonary embolism

D. Spirk1, T. Baldi2, T. Willenberg3, D. Ajuszek4, M. Husmann5, D. Hayoz5, A. Brugger1, B. Annan-Verst1, I. Baumbargner4, N. Kucher4, 1Sanofi-Aventis (Suisse) SA, Meyrin, Switzerland; 2University Hospital Basel, Basel, Switzerland; 3Imperial College London, London, United Kingdom; 4Berner University Hospital, Bern, Switzerland; 5University Hospital Zurich, Zurich, Switzerland; 6Cantonal Hospital, Fribourg, Switzerland

Background: Cardiac biomarkers and echocardiography for assessing right ventricular function are recommended to risk stratify patients with acute non-massive pulmonary embolism (PE) but their use and effect on the management and clinical outcomes in daily practice remains unclear.

Methods and Results: Overall, 587 patients with acute non-massive PE from 18 hospitals were enrolled in the Swiss Venous Thromboembolism Registry (SWISHERT): 178 (30%) neither had a biomarker test nor an echocardiographic evaluation. Among the 409 (70%) patients with biomarkers or echocardiography, 164 (41.1%) had biomarker test only, and 47 (11%) had echocardiographic evaluation only: 210 (51%) had at least one positive test and 67 (16%) had positive biomarkers and right ventricular dysfunction. Syncope (OR 3.49, 95% CI 1.07-10.15; p = 0.022), heart rate > 110 beats/min (OR 2.31, 95%CI 1.37-3.91; p = 0.002), and increasing age per year (OR 1.02; 95%CI 1.01-1.04; p = 0.001) were independently associated with testing of cardiac risk; outpatient status at the time of PE diagnosis (OR 2.24, 95%CI 1.49-3.36; p = 0.001), cancer (OR 1.81, 95%CI 1.17-2.79; p = 0.008), and provoked PE (OR 1.58, 95%CI 1.05-2.40; p = 0.029) were associated with its absence. The hospitalization rates were 59% with vs. 80% without testing (p = 0.001), and the ICU admission rates were 6% vs 5%, respectively (p = 0.78). Thrombolysis or embolectomy were performed in 4.9% with vs. 2.8% without testing (p = 0.29). In comparison to risk-stratified patients without any positive test, there was more frequent use of thrombolysis or embolectomy in patients with at least one positive test (7.1% vs. 2.5%; p = 0.038) and in patients with positive biomarkers and right ventricular dysfunction (14.9% vs. 2.5%; p = 0.001). The 30-day rates of mortality or PE recurrence were 3.2% with vs. 7.4% without testing (p = 0.001).

Conclusions: In hemodynamically stable patients with acute PE, biomarker testing and echocardiographic evaluation are currently used inconsistently and rarely in combination. With such lack of systematic use, their utility in guiding PE management is extremely low.

Prognostic significance of tricuspid annular displacement in normotensive patients with acute symptomatic pulmonary embolism

D. Jimenez1, J.L. Lobato2, A. Holley2, V. Tapon2, L. Moores3, M. Orbie3, M. Barron2, R. Otero1, D. Nazarian4, R.D. Yusen5 on behalf of PROTECT investigators. 1University Hospital Ramon y Cajal, Madrid, Spain; 2Hospital Txagorritxu, Vitoria, Spain; 3Edward Hébert School of Medicine, Bethesda, United States of America; 4Duke University Medical Center, Durham, United States of America; 5Hospital Galdacano, Galdacano, Spain; 6Hospital San Pedro, Logroño, Spain; 7University Hospital of Vigin del Rocio, Seville, Spain; 8Hospital La Fe, Valencia, Spain; 9Washington University in St. Louis, School of Medicine, St. Louis, United States of America

Background: The tricuspid plane systolic excursion (TAPSE) is an emerging prognostic indicator in patients with acute symptomatic pulmonary embolism (PE). However, outcome implications of TAPSE have not been analyzed in the context of routine clinical practice and in a multicenter study.

Methods and Results: We prospectively examined 782 normotensive patients with acute PE enrolled in the PROTECT study (NCT00860737); of those, 35 patients died (4.5%; 95% confidence interval [CI] 3.0% to 5.9%), and 56 (7.0%; 95% CI, 5.2% to 8.8%) suffered a complicated course within the 30-days of follow-up. Compared with patients with a TAPSE greater than 1.6 cm, those with a TAPSE less than 1.6 cm or less had significantly higher systolic pulmonary artery pressure (3.7 + 16.7 mm Hg vs. 40.0 + 15.5 mm Hg, P < 0.001), right ventricle end-diastolic diameter (3.5 + 0.8 cm vs. 3.0 + 0.6 cm, P < 0.001), and right ventricle to left ventricle end-diastolic diameter (1.0 + 0.3 vs. 0.8 + 0.2, P < 0.001). Patients with a TAPSE of 1.6 cm or less had a higher prevalence of right ventricular free wall hypokinesis (68% vs. 11%, P < 0.001). Patients with a TAPSE of 1.6 cm or less at the time of acute PE diagnosis were significantly more likely to die from any cause during follow-up (hazard ratio [HR] 2.3; 95% CI 1.2 to 4.7; P = 0.02). A TAPSE of 1.6 cm or less at the time of presentation was also independently, significantly associated with PE-related death (HR 4.4; 95% CI 1.3 to 15.3; P = 0.02).

Conclusions: In normotensive patients with acute symptomatic PE, TAPSE powerfully reflects right ventricular function. For these patients, TAPSE is independently predictive of survival.

Pulmonary embolism in Sweden, a national cohort and survival analysis

T.A. Andersson1, F. Larsen2, B. Carlberg3, S. Soderberg1, 1Umea University Hospital, Heart Centre, Department of Cardiology, Umea, Sweden; 2Karolinska Institute, Stockholm, Sweden; 3Department of public health and clinical medicine, medicine, Umea, Sweden

Background: Ranging from asymptomatic and incidentally discovered to massive embolism with rightheart failure and death, acute pulmonary embolism (PE) is a diagnosis associated with difficulties in respect to diagnosis, treatment and follow-up. The clinical course of pulmonary embolism is associated with serious co-morbidities such as malignancies and ischemic heart disease, and complicated byrecurrences and the development of chronic thromboembolic pulmonary hypertension (CTEPH).

Purpose: To determine incidence, demographic characteristics, prognosis, and co-morbidities of acute pulmonary embolism in Sweden.

Methods: Records of 5793 patients diagnosed with acute PE during 2005 were retrieved from the Swedish National Board of Health and Welfare In-Patient Register, and an age, sex and zip code matched control group was designed for studies of short- and long-term survival. All cases of hospital care preceding the PE (1998-2005) and the corresponding ICO-10 codes were identified and collected. Mortality data was collected until 2009.

Results: The national incidence rate of PE was 0.61/1000 person years. Mean age (±SD) was 70.5 (±15.1). 30 061 episodes of in-hospital care were registered between 1986 until the index PE in 2005. Persons with PE had higher mortality than the matched control group during follow-up (p < 0.001). This excess mortality seen in the PE group remained after 12 and 24 months (p < 0.001). Common comorbidities were ischemic heart disease (21%), heartfailure (18%), and malignancies (28%). Notably, only 3% had had prosthesisurgery within 6 months before the PE.

Conclusion: After surviving the acute phase of a PE, an excess mortality remains even 2 years after the acute episode compared to the control group. These findings insinuate the need for further investigation of the possible sequelae of acute pulmonary embolism and of the appropriate follow-up for these patients.
342 Plasma MR-proADM is superior to NT-proBNP for all-cause short term mortality prediction in acute pulmonary embolism

J. Pedewska-Wloszek, M. Kostrubeck, A. Labyk, S. Pacho, O. Dzikowska, B. Birmas, B. Lichodziejewska, P. Palczewski, M. Cizirzyns, P. Pruszczyk, Medical University of Warsaw, Warsaw, Poland

Objective: NT-proBNP reflects RV dysfunction and according to ESC guidelines can be used for risk stratification in APE. Proadrenomedullin, secreted by failing heart, was proposed to be a predictor of short-term mortality in acute heart failure and adds prognostic value to NT-proBNP for diagnosis and prognosis in APE. We hypothesized that MR-proADM plasma levels are related to the severity of APE and predicts short term mortality in APE. We also compared prognostic values of MR-proADM and NT-proBNP for prediction of early mortality in APE.

Material and methods: We studied 98 consecutive pts (51F/47M, 59.6±18.4 yr) with confirmed by spiral CT APE. On admission, echocardiography was performed and blood samples were collected for MR-proADM (Thermo Fisher Scientific, BRAINTMS Henriques, Germany) and NT-proBNP (bioMerieux I'Etolle, France). MR-proADM concentrations were also measured for 40 healthy individuals (36F/4M).

Results: Our study group included 5 pts with high-risk APE, 66 pts with intermediate-risk APE and 27 pts with low-risk APE. Median of MR-proADM and NT-proBNP concentrations shows table 1. Six pts died during hospital stay observation. MR-proADM was higher in non-survivors than in survivors (2.12±0.3 vs. 0.99±0.4, p<0.0001, and vs. control group 0.65±0.3 vs. 0.39±0.2, p<0.0001). The AUC of the MR-proADM and NT-proBNP ROC curve for predicting all-cause mortality was 0.935 (95% CI 0.86-0.98) and 0.844 (95% CI 0.75-0.91), respectively. Cut-off value for MR-proADM 1.4nmol/L showed sensitivity of 100%, specificity 89%, PPV 35.2%, and NPV 100% for all-cause mortality. MR-proADM and NT-proBNP plasma levels were predictors of 30-day all-cause mortality in univariable Cox's proportional hazard regression analysis HR 1.65 (95% CI 1.21-2.25, p=0.01) and HR 1.0 (95% CI 1.00-1.02, p=0.09), respectively. In multiparametric model MR-proADM but not NT-proBNP was significant prognostic predictor of all-cause mortality HR 61.47 (95% CI 6.65-576.30, p<0.0008).

Conclusion: NT-proBNP and MR-proADM are important risk markers in APE. However, MR-proADM is superior to NT-proBNP for all-cause short term mortality prediction in APE.

351 Echocardiographic determinants of maximal exercise capacity in asymptomatic patients with primary mitral regurgitation

J. Magne1, H. Mahjoub2, J-C. Bologna1, R. Dulguer1, L. A. Pierard1, P. Pibart1, R. Lancellotti1, University of Liege - Sart Tilman, Liege, Belgium; 2Quebec Heart Institute, Quebec, Canada

Background: Despite a symptom-based management recommended by both EAE and ESC guidelines in patients with primary mitral regurgitation (MR), the assessment of maximal exercise capacity (MEC) is rarely performed and its determinants remain unknown. We sought to assess MEC and to identify its determinants in asymptomatic patients with primary MR.

Method and results: We prospectively studied 63 asymptomatic patients (60±13 years, 52% of male) with at least moderate MR (regurgitant volume (RgV) >30mL and preserved left ventricular (LV) systolic function (LV ejection fraction >60%), LV end-systolic diameter <45mm) in whom comprehensive resting and exercise echocardiography and cardiopulmonary exercise test were performed. MEC was assessed using peak exercise VO2 and varied extensively among the patients (mean: 23.6±7.7; median: 22.7; range: 19.2-42.4 mL/kg/min).

According to the median of peak VO2, patients with reduced MEC were significantly older (p=0.005) and were more frequently women (p=0.02). There was no other significant difference between the 2 groups (reduced vs. preserved MEC) regarding demographic and clinical data and medication. However, patients with reduced MEC had significantly (all p<0.05) lower exercise LV stroke volume and higher resting E/A ratio, exercise left atrial (LA) volume and exercise systolic pulmonary arterial pressure (SPAP). With regards to resting parameters, peak exercise VO2 correlated only with resting E/A ratio (r=-0.47, p=0.0003) and LA volume (r=-0.32, p=0.02). With regards to exercise parameters, peak VO2 correlated significantly with exercise LV stroke volume (r=-0.33, p=0.002), exercise SPAP (r=0.52, p<0.0001), and exercise LA volume (r=-0.59, p<0.0001). In addition, there was a trend for significant correlation with exercise RegV and effective regurgitant orifice area (r=-0.35, p=0.05 and r=-0.3, p=0.07, respectively).

In multiple regression analysis (model R2=0.67), after adjustment for exercise LV stroke volume and resting E/A, age (β=0.17±0.07, p=0.02), female gender (β=3.1±0.8, p=0.0006), exercise LA volume (β=-0.12±0.03, p=0.02) and exercise SPAP (β=-0.15±0.06, p=0.0003) were identified as the independent predictors of peak exercise VO2.

Conclusion: MEC may vary considerably in asymptomatic patients with primary MR and preserved LV systolic function. The main independent determinants of MEC are related to MR consequences on LA and SPAP, in particular during exercise. Furthermore, these results suggest that patients with reduced MEC are probably at higher risk of poor outcome.

352 Interaction of cardiac valve calcification and C-reactive protein improves the predicting of mortality in end-stage renal disease patients at starting hemodialysis therapy

H. Takahashi1, H. Ishii2, Y. Kumada1, T. Aoyama1, D. Kamoi1, M. Tanaka2, T. Muraoka1, 1Nagoya Kyoritsu Hospital, Nagoya, Japan; 2Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Purpose: Cardiac valve calcification is frequently seen in patients with end-stage renal disease (ESRD) and may potentially reflect systemic atherosclerosis. Serum C-reactive protein (CRP) is also reported to predict future cardiovascular (CV) events. We investigated whether the interaction of cardiac valve calcification and CRP improves the prediction of mortality in ESRD patients.

Methods: A total of 1,290 consecutive ESRD patients who electrically started HD therapy were screened by echocardiography. Patients were divided into 3 groups; those without valve calcification (group 0, n=548), those with calcification in a single (aortic or mitral valve) (group 1, n=393) and those with both calcified valves (group 2, n=355). They were also divided into tertiles (T) according to serum CRP levels. They were followed up for about 10 years.

Results: Mortality rates were independent associated to valve calcification (OR 1.12, 95%CI 1.05-1.19, p=0.0009). Adjusted HR of valve calcification was 2.64 (95%CI 1.53-4.56, p=0.0023 for group 2 vs. 0) for CV mortality and 1.86 (95%CI 1.30-2.67, p<0.0001 for group 2 vs. 0) for all-cause mortality, respectively. Similarly, adjusted HR of elevated CRP levels was 3.09 (95%CI 1.54-6.16, p=0.0050 for T3 vs. T1) for CV mortality and 2.44 (95%CI 1.64-3.64, p<0.0001 for T3 vs. T1) for all-cause mortality, respectively. Regarding the combination of valve calcification and CRP, the risk of CV and all-cause mortality was 6.35-fold (p=0.0073) and 3.59-fold (p<0.0001) in the group 2 with T3 of CRP compared with the group 0 with T1 of CRP, respectively. C-index for such endpoints was 0.84 for the established risk model and 0.85 for the model with valve calcification and CRP (Table).

Conclusion: Valve calcification and elevated CRP levels were closely linked, and the interaction of valve calcification and CRP improves the prediction of mortality in ESRD patients who started HD therapy.

353 Anterior leaflet tethering: the importance in predicting recurrence of ischemic mitral regurgitation after restrictive anoplasty

F. Luca1, L.A.F.M. Van Garosse1, E. Cheriex1, C.M. Rao2, G. Gennini2, J. Maessen2, S. Gelsomino2, 1Cardiovascular Research Institute Maastricht (CARIM), Maastricht, Netherlands; 2CAREG University Hospital, Florence, Italy

Objective: We hypothesized that a specific leaflet configuration with anterior mitral leaflet (AML) tethering predominance is related to higher postoperative MR recurrence. Relationships between AML tethering and recurrent mitral regurgitation were investigated.

Methods: In 434 patients underwent surgical anoplasty for chronic ischemic mitral regurgitation and 100 controls, posterior and lateral placement of papillary muscles (PMLs), the AML and posterior mitral leaflet (PML) tethering angles and their ratio, coaptation length and anterior mitral leaflet (AML) tethering angle were measured and followed up (median [Interquartile range] 44.7 months (25.9-66.4)). Patients were divided in 5 Groups on the basis of the preoperative AML tethering angle α: Group 1, normal/small (< 27.2°); Group 2, mild (27.2°-32.1°); AML tethering angle (β): Group 2, normal/small (< 39.5°); Group 3, moderate/severe (≥ 39.5°); Group 4, moderate-severe (36.0°-39.5°) AML tethering (γ): Group 5, severe (≥ 39.5°) AML tethering (γ) was excluded.

Results: Subjects with AML tethering α:moderate-severe had preoperatively a more symmetric tethering (p<0.001), a more accentuated anterior papillary muscle displacement (p<0.001) and a larger anterior local remodeling (p=0.001). Pre-reurrence of MR was significantly higher in patients with moderate-severe/severe AML tethering (p<0.001). Postoperatively, tethering of posterior leaflet increased (p<0.001) and it was predominant without difference between groups, resulting in a more asymmetric tethering in most of patients with recurrent MR (p<0.001).
At multivariable logistic regression the AML tethering angle α was the primary determinant of MR recurrence after adjustment of known risk factors (p = 0.001).

Conclusions: The grade of preoperative AML tethering was strongly associated with recurrence of MR. Assessment of leaflet tethering and PMs displacement by 2-D echocardiography should be incorporated into clinical risk assessment and prediction models.

354

Tricuspid annulus systolic velocity as a parameter for opened right ventricular function for predicting clinical outcome after MitraClip implantation

M. Schöpp, T. Schau, M. Neuss, C. Butter. Heart Center Bernau, Bernau bei Berlin, Germany

Background: Interventional implantation of MitraClip is increasingly used as an alternative therapeutic option for patients with severe mitral valve regurgitation and high intraoperative risk. The purpose of this study was the evaluation of right ventricular function on clinical outcome after MitraClip implantation.

Methods: Right ventricular function was evaluated by echocardiography before and after MitraClip implantation from March 2009 to April 2011 in 68 consecutive patients (age 73±16ys.; LVEF 35.8%; NT-proBNP 6705±8908pg/ml; 60% c/). The indication for MitraClip-implantation was a functional mitral valve regurgitation grade 2 or severe mitral valve prolaps with high surgical risk (mean log Euroscore 34). All patients were followed up at our centre regularly. A combined endpoint (overall mortality, LVAD, surgery of mitral valve, futile implantation) was evaluated by Kaplan-Meier-analysis.

Results: Overall there were 29 combined endpoint events. Patients with reduced tricuspid annulus systolic velocity (TASV < 10cm/s) had significantly more events as patients with higher TASV (univariate Cox-model HR 2.3 [95% CI: 1.0-5.5]). In patients with AR were LV ejection fraction (LVEF) 35.8 ± 16ys.; LVEF 35.8%; NT-proBNP 6705 ± 8908pg/ml; 60% c/). In contrast TAPSE, right ventricular diameter and graduated tricuspid valve regurgitation showed no significance.

Conclusion: An impaired right ventricular function is a significant predictor for a poorer medium term outcome in patients with high-grade mitral valve regurgitation after MitraClip implantation. The evaluation of the TASV by echocardiography before intervention is recommended.

355

Left ventricular shape and mass impact apical rotation in patients with aortic regurgitation. A speckle-tracking echocardiography study

R. Enache1, D. Muraru2, R. Piazza3, B.A. Popescu4, F. Pircu2, A. Calin2, G.C. Beladan4, M. Rosca2, G.L. Nicolosi2, C. Giningha2,1 Institute of Cardiovascular Diseases "Prof. Dr. CC Iliuca," Bucharest, Romania; 2 University of Padua, Department of Cardiac, Thoracic and Vascular Sciences, Padua, Italy; 3 Cardiology S.Maria degli Angeli Hospital, Pordenone, Italy; 4 University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

Background: Apical rotation, an essential determinant of left ventricular (LV) twist and twist over a wide range of loading conditions, is considered an effective noninvasive index of global LV function. Chronic aortic regurgitation is a condition associated with a unique pattern of LV overloading, both in volume and pressure, leading to LV remodeling.

Purpose: To study the impact of LV shape and mass on systolic and diastolic LV apical rotation assessed by speckle-tracking echocardiography (STE) in patients with chronic AR.

Methods: We prospectively enrolled 42 consecutive patients (47±17.6 yrs, 33 men) with moderate-severe and chronic severe AR and 30 age- and gender-matched normal subjects (48±18.0 yrs, 21 men). Exclusion criteria for the patients with AR were LV ejection fraction (LVEF) ≤ 50%, significant coronary artery disease, more than mild mitral regurgitation, non-sinus rhythm. A comprehensive echocardiogram was performed in all patients. Systolic apical rotation and rotation rate and diastolic apical rotation rate were measured from two-dimensional greyscale LV parasternal apical short-axis images by STE using a dedicated software (2D strain, EchoPac, GE Healthcare). Global LV geometry was assessed using a sphericity index defined as LV end-diastolic volume divided by the volume of a sphere with the same diameter as the LV end-diastolic longitudinal length, as previously described.

Results: Left ventricular EF was similar in both groups (60–4% in AR group vs 61±3% in control group, p=0.27). Patients in AR group had significantly higher LV diameters and volumes and LV mass (all p < 0.001). Peak systolic apical rotation was significantly lower in the AR group as compared to normal subjects (13.1±7.6 vs 17.6±6.3°, p<0.007). Peak diastolic apical rotation rate was also significantly lower in the AR group (-81.2±38.2 vs -107.7±34.8°/s, p<0.004). Peak systolic apical rotation had an inverse correlation with LV sphericity index (r= -0.41, p<0.007) and did not correlate with LV mass index (r=-0.18, p=0.26). Peak diastolic apical rotation rate correlated significantly both with LV sphericity index (r=0.44, p=0.000) and LV mass index (r=0.45, p=0.000).

Conclusions: The shape and mass of a remodeled LV have an impact on systolic and diastolic apical rotation in patients with significant chronic AR and normal LVEF. These parameters of LV rotation could identify early LV dysfunction (before EF declines) and may be used for monitoring asymptomatic patients with severe AR.

356

The impairment of endocardial radial strain is related to aortic stenosis severity in patients with aortic stenosis and preserved left ventricular ejection fraction using two-dimensional speckle tracking

Y. Ohara, Y. Fujioka, I. Tabuchi, S. Sahara, S. Hosoghi, M. Nishimoto, K. Yamamoto. Kachi Health Sciences Center, Kochi, Japan

Background: Myocardial function is heterogeneous in different myocardial layers. Recently, 2-dimensional speckle-tracking echocardiography has been used to define myocardial deformation parameters of the left ventricular (LV) segment. This study aimed to investigate strain in subendocardial and subepicardial layers in patients with aortic stenosis (AS) and preserved LV ejection fraction (LVEF) using speckle-tracking echocardiography.

Methods: Parasternal short-axis and apical long-axis views of the left ventricle were acquired at the mid-papillary level in 35 control subjects and 32 patients with AS and preserved LVEF. Radial, circumferential strain in subendocardial and subepicardial layers at the posterior and antero-septal segments were calculated.

Results: There was no significant difference in circumferential strain in subendocardial and subepicardial layers between the control subjects and the patients with AS. Similarly, there was no significant difference in epicardial radial strain at the posterior and antero-septal segments between the control subjects and the patients with AS. AS patients had significantly decreased values of endocardial radial strain compared with those in controls (antero-septal: 18±11.2 vs. 34.5±14.8, p<0.005; posterior: 25.2±14.8 vs. 32.6±12.6, p<0.05). In the AS group, endocardial radial strain in the posterior and antero-septal segments was significantly correlated with the aortic valve area (posterior: r=0.41, p<0.05; antero-septal: r=0.33, p<0.05).

Conclusion: Patients with AS and preserved LVEF have impaired longitudinal strain and endocardial radial strain, although circumferential strain and epicardial radial strain are preserved. Despite preserved LVEF, endocardial radial strain gradually decreased as increasing AS severity.

373

Role of the cardiovascular magnetic resonance in patients with ventricular arrhythmia of unknown cause and non-diagnostic echocardiography


Introduction: Significant ventricular arrhythmia (here defined as > 1000 ectopies per 24 hours, or ventricular tachycardia) may itself have adverse consequences and/or may point to an underlying structural heart disease. In patients with significant ventricular arrhythmia and normal or non-diagnostic echocardiography, we hypothesized that cardiovascular magnetic resonance (CMR) may detect significant, previously unrecognized structural heart disease.
Methods: We performed a cardiomyopathy contrast CMR protocol in 42 consecutive patients with 1) frequent premature ventricular complexes defined as >1000 premature ventricular beats in 24 hours, (n=38) or 2) life threatening ventricular arrhythmia as sustained ventricular tachycardia, ventricular fibrillation or resuscitated sudden death (n=4) and 3) normal systolic ventricular function and absence of significant valve disease or left ventricular hypertrophy by echocardiography.

Results: CMR detected significant abnormalities in 54.7% patients (n=23). These were (number, percent); late gadolinium enhancement compatible with myocardial infarction (6, 27.3%), non-compaction cardiomyopathy (3, 13.1%), left ventricular enlargement (3, 13.1%); left ventricular hypertrophy (3, 13.1%); right ventricle dilatation (3, 13.1%); myocardial infarction (2, 8.7%); mild left ventricular dysfunction (2, 8.7%) and/or one case (13.1%) each of the following: chagasic cardiomyopathy, right ventricular arrhythmogenic dysplasia and right ventricle dysfunction.

Conclusions: In patients with significant ventricular arrhythmia, the search for structural heart disease should not stop at non contrast echocardiography and the diagnostic yield of significant ventricular pathology using CMR is greater than 50%.

P374 Silent cerebral embolism after PVAC and irrigated-tip ablation for atrial fibrillation: incidence and clinical implications

M.G. Comper1, E.F. Bruggemann2, M.A. Van Buchem3, H.A.M. Middelkoop4, K. Van Der Heide4, K. Zeppenfeld5, M.J. Schuit1, S.A. Trines6, L. Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 1Leiden University Medical Center, Department of Cardiothoracic Surgery, Leiden, Netherlands; 1Leiden University Medical Center, Department of Radiology, Leiden, Netherlands; 4Leiden University Medical Center, Department of Radiology, Leiden, Netherlands; 5Leiden University Medical Center, Department of Neurology, Leiden, Netherlands; 6Leiden University Medical Center, Department of Thorrograms and Hemostasis, Leiden, Netherlands

Purpose: Catheter ablation is an effective treatment for atrial fibrillation (AF). Silent thromboembolism occurs more frequently than clinical strokes. The aim of this pilot was to study silent cerebral embolism during ablation with an irrigated-tip catheter (Thermocool) and a non-cooled, decapolar duty-cycled catheter (PVAC).

Methods: 15 Patients undergoing a first ablation of paroxysmal AF were prospecively randomized in a 2:1 fashion to PVAC or Thermocool, respectively. A diffusion-weighted cerebral MRI was performed 1 day before and after the procedure. Blood samples were obtained before, during and after ablation for determination of endothelial damage and coagulation factors. Development of microembolic signals (MES) during the procedure was evaluated by Transcranial Doppler ultrasound. Endo-epicardial mapping performance was tested 1 day before and 1 day after the ablation. If a new lesion was observed on MRI after ablation, a 3-month follow-up scan was performed.

Results: Baseline characteristics including sex, age, left atrial size, CHADS2-VASc and INR were comparable between both groups. In the Thermocool-group, no new MRI lesions were detected. In the PVAC-group, 2 patients developed a new microembolus (~5 mm) and 1 patient showed a microbleed after ablation, all located in the cerebellum. At 3 months follow-up, MRI showed remainder lesion-size in all 3 patients with microembolism. Patient performance on psychometric tests decreased after PVAC-afiblation (mean score reduced from 32.8 to 32.7), while it increased after Thermocool (from 33.6 to 36.8, p=0.02). The total duration of MES was significantly higher during ablation with PVAC (98.5±59 sec) as compared to Thermocool ablation (38±13 sec, p=0.016). Finally, Willebrand factor antigen increased (1.05 to 1.3 IU/ml) and Prothrombin time decreased (from 41.2 to 37.2 sec after PVAC p=0.05), while they remained stable after Thermocool.

Conclusions: Ablation with PVAC led to a 30% incidence of new lesions on MRI, all located in the cerebellum. It also showed significantly longer duration of MES during ablation and increased endothelial damage, potentially indicating increased risk for cerebral embolism. Patients showed decreased psychometric functioning after PVAC-afiblation, which may correlate with the lesions being located in the cerebellum. Altogether, the thromboembolic risk of the PVAC catheter is increased compared to the irrigated tip catheter. Expanding the amount of included patients will be necessary to confirm these findings and further assess clinical implications.

P375 Accuracy of scar identification on contrast enhancement cardiac magnetic resonance to predict the site of origin of ventricular tachycardias?

D. Andreu1, A. Beruezo1, J.T. Ortiz2, E. Gusach3, J. Fernandez-Armenta1, D. Perez1, T.M. De Carvalho1, T. Boushy1, L. Mont1, J. Brugada1, Arhythmia Section, Cardiology Dept. Thorax Institute. Hospital Clinic, Universitat de Barcelona, Barcelona, Spain; 2Cardiology Department. Thorax Institute. Hospital Clinic, Universitat de Barcelona, Barcelona, Spain; 3Image Diagnostic Centre. Hospital Clinic, Universitat de Barcelona, Barcelona, Spain

Purpose: The decision to perform an epicardial access for VT ablation could be based on pre-procedural contrast enhanced-Cardiac Magnetic Resonance (ce-CMR), to avoid possible complications if the access is needed after anticoagulation.

Methods: A ce-CMR study was performed in 80 patients with a clinical documented sustained VT and structural heart disease (SHD) before the ablation procedure. Sequential short axis slices from base to apex were analyzed by an independent cardiologist(blinked to clinical and EP data) who assigned the presence on hyperenhancement (HE) according to the 17-segment model as absent, subendocardial, epicardial, transmural or mid-myocardial. Additionally, an electrophysiologist determined the LV segment and the true endocardial or epicardial origin of the VT according to the location and approach needed for VT ablation.

Results: A total of 37 patients (46.3%) had ischemic heart disease and 43 (53.7%) non-hypokinetic cardiomyopathy. Sixty-two (77.5%) patients were found to have HE on ce-CMR. In segments with successful ablation, HE was found to be absent in 22.5%, subendocardial in 22.5%, transmural in 33.8%, mid-myocardial in 10% and epicardial in 11.2%. The presence and distribution of the HE on the ce-CMR had a sensitivity of 64.7% (44/68) and a specificity of 97.8% (44/45) to predict an endocardial origin of the VTs and a sensitivity of 75% (9/12) and specificity of 100% (9/9) in predicting an epicardial origin of the VTs. In ischemic patients the values increased to a 100% (34/34) sensitivity and 92.3% (34/37) specificity to predict an endocardial origin while in non-ischemic patients the values changed to a 60% (8/13) sensitivity and 100% (8/8) specificity to predict an epicardial origin of the VTs.

Conclusions: Ce-CMR might be helpful to plan the approach needed, epicardial or endocardial, before the procedure, as well as as target the VT ablation.
Methods: Prospective observational study of patients referred to AF catheter ablation. Before the procedure, CMR with LA angiography was performed, in order to characterize LA anatomy, volume and ejection fraction. Atrial fibrillation was analyzed in post-processing with clinical data: bland qualitative (presence of late enhancement in each atrial wall and in the peri-ostial regions) and quantitative (mass of fibrotic tissue) evaluation was performed.

Results: Twenty-eight patients were enrolled (82% male; age 59±15 years) affected by either idiopathic VA (19 RVOT, 3 LVOT, 1 Aortic Cusp, 1 Fascicular VT) or structural heart diseases (HD) (1 ARVD, 1 dilated idiopathic cardiomyopathy and 9 post-MI cardiopathy) were submitted to ablation of VA using a 3D mapping system providing image-integration with echo data. The ICE probe with a location sensor tracked by the mapping system was positioned in the right chambers. The endocardial contours traced on gated images of the RV and LV were used to generate a 3D anatomy, then mapping and ablation were performed using the standard techniques. Procedural and Fluoroscopy time in both groups were compared with gender and age matched control groups who underwent a standard EA mapping procedure.

Results: Fourty procedures (including 5 Redo) were performed. Mean time required to create 3D echo maps of both ventricles was 20.5±5 min. Ablation procedure was acutely successful in 34/35 patients. No ICE related complication was observed. Major complication were observed in 2 cases: cardiac tamponade (1) and complete AV block (1). When compared with EA mapping alone, the ICE-EA mapping induced a significant reduction of the fluoro time in both groups (see table).

Conclusions: ICE imaging combined with EA mapping is safe and feasible during VA ablation. The use of ICE image integration mapping allowed easier navigation and reduced fluoroscopy and procedural time.

### Table 1: Results

<table>
<thead>
<tr>
<th>Description</th>
<th>Controls (n=18)</th>
<th>BS pts (n=48)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVOT shortening</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RV free wall Long S</td>
<td>-33.5±6.8</td>
<td>-20.7±4.2</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>RV free wall TPS</td>
<td>-32.1±4.9</td>
<td>-26.8±4.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S wave of TA</td>
<td>350.9±39.1</td>
<td>380.1±35.2</td>
<td>0.04</td>
</tr>
<tr>
<td>TTL (ms)</td>
<td>15.9±3.0</td>
<td>14.1±2.5</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Point of note:** RVOT shortening was more significant in BS pts compared with controls.

### Figure 1

**Image:** RVOT shortening by ST

Conclusions: BS pts have significantly impaired Long S and RVOT shortening as well as delayed activation of RV wall. A type 1 ECG pattern is associated with
poorer RVOT shortening. Further studies are warranted to identify echocardiographic predictors of high risk.

HEART FAILURE: FROM BENCH TO BEDSIDE

**P381** Left ventricular dyssynchrony predicts limited exercise capacity in heart failure irrespective of ejection fraction

G. Bajrami1, A. Batali1, A. Ponku1, A. Ahmeti1, R. Olloni1, V. Hiro1, Z. Vela2, B. Morina1, R. Tosaki1, M.Y. Heniez1

1University Clinical Centre of Kosovo (UCC), Service of Cardiology, Pristina, Kosovo, Republic of; 2Heart Centre and Department of Public Health and Clinical Medicine, Umeå University, Umeå, Sweden

**Aim:** The aim of this study was to prospectively examine functional echocardiographic parameters that correlate and predict 6 minute walk test (6-MWT) results in patients with heart failure (HF).

**Methods:** In 147 HF patients (mean age 61 ± 11 years, 50.3% male), a 6-MWT and an echo-Doppler study were performed in the same day. Global LV dysynchrony was indirectly assessed by total isovolumic time - 6MT [in s/min; calculated as: 60 – (total ejection time – total filling time)]; and Tei index (6-MT+Tei) 6MT+Tei time divided into two groups based on the 6-MWT distance (Group I: ≤300m; Group II: >300m).

**Results:** The 6-MWT correlated with 6-MT+Tei (r=0.49, p<0.001) and Tei index (r=0.33, p<0.01) but not with isovolumic contraction time (r=0.003), isovolumic relaxation time (r=0.003) and longer t-IVT (p=0.03), compared with Group II patients. In multivariable analysis, only 6-MWT+Tei (r=0.27, p=0.005) ELA index (0.947 [0.903-0.993], p<0.02), and E/A ratio (0.533 [0.315-0.972], p=0.04) independently predicted poor 6-MWT performance (>300m) in the group as a whole. No predictors for exercise tolerance were detected for HF-PEF.

**Conclusion:** In patients with HF, the limited exercise capacity, assessed by 6-MWT, is related mostly to severity of global LV dysynchrony, more than EF or raised filling pressures.

**P382** Health-related quality of life in patients with systolic chronic heart failure in Spain: is gender important?

J. Comín-Colell1, M. Anguita2, M. Crespo-Leiro3, F. Formiga4, L. Almena4, L. Manzano5, J. Chaves1, T. De Fruutos1 on behalf of VIDA IC investigators; 1Cardiology, Hospital del Mar, IMIM, Barcelona, Spain; 2Cardiology, Hospital Universitari de Bellvitge, Barcelona, Spain; 3Cardiology, Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain; 4Cardiology, Hospital Universitario de Fuenlabrada, Madrid, Spain

**Purpose:** Several studies have reported the impact of chronic heart failure upon quality of life within community samples. Further, evidence of gender differences in HRQoL has been mainly provided by studies conducted in North America and may not be available in the south of Europe. Whether these differences may be extrapolated to the geographical and socio-cultural context is not known. The aim of this study was to describe the HRQoL in ambulatory patients with systolic CHF in Spain and to explore the self-perceived health status according to gender.

**Methods:** The VIDA-IC was designed to include 1200 consecutive patients with systolic HF seen in 120 hospitals in Spain in 2011. HRQoL was assessed at inclusion using the Kansas City Cardiomyopathy Questionnaire (KCCQ - specific for HF) and the generic EQ-5D questionnaire that includes the Visual Analogue Scale (VAS). The 6-MWT correlated with 6-MT+Tei (r=0.49, p<0.001) and Tei index (r=0.33, p<0.01) but not with isovolumic contraction time (r=0.003), isovolumic relaxation time (r=0.003) and longer t-IVT (p=0.03), compared with Group II patients. In multivariable analysis, only 6-MWT+Tei (r=0.27, p=0.005) ELA index (0.947 [0.903-0.993], p<0.02), and E/A ratio (0.533 [0.315-0.972], p=0.04) independently predicted poor 6-MWT performance (>300m) in the group as a whole. No predictors for exercise tolerance were detected for HF-PEF.

**Conclusion:** In patients with HF, the limited exercise capacity, assessed by 6-MWT, is related mostly to severity of global LV dysynchrony, more than EF or raised filling pressures.

**P383** Diastolic function is the most valuable predictive marker for perioperative acute heart failure in noncardiac surgery

H. Maeba, Y. Miyasaka, S. Tsujimoto, Y. Suwa, T. Iwasaka. Kansai Medical University, Hikariga City, Japan

**Background:** Although perioperative risk stratification for non-cardiac surgery is essential, the predictive factors are still uncertain. We investigated herein the predictive factors for perioperative acute decompenesated heart failure (ADHF) in patients with non-cardiac surgery.

**Methods:** A total of 129 patients divided into GroupA (19 patients with perioperative ADHF) and GroupB (110 patients without perioperative ADHF). All patients were risk-stratified by ACC/AHA Guidelines for Perioperative Cardiovascular Evaluation. Transcardiac echocardiography and tissue doppler echocardiography were performed to evaluate the left ventricular (LV) systolic-diastolic function.

**Results:** The perioperative risk stratification evaluated by ACC/AHA guidelines was identical in the two groups. Although the systolic function was identical in both groups, the LV diastolic function showed that the degree of diastolic dysfunction was significantly greater in GroupA than in GroupB (0.51 ± 0.53 vs. 0.46 ± 0.44; p=0.004, 31.9/7.8 mm vs. 27.9/5.4 mm; P=0.02, 9.8/2.2 mm vs. 9.0/1.4 mm; P=0.04, 7.9/1.2 mm vs. 8.7/1.2 mm; P=0.02, 46.5/19.2 mm² vs. 34.9/13.5 mm²; P=0.002, 16.7/9.1 mm² vs. 12.2/5.2 mm²; P=0.002, 26.6/5.9 mm² vs. P=0.02, respectively). Multivariate analysis revealed that E/e' was the only valuable predictive factor for development of perioperative ADHF in the two groups (P<0.05).

**Conclusion:** The ratio of E/e' is an excellent predictive factor for development of perioperative acute heart failure in non-cardiac surgery.

**P384** Progress of neurohumoral activation and diastolic function in patients with preserved left ventricular function in one-year-follow-up

A. Duvignaig1, I. Roesser1, R. Staherberg1, H.-D. Duengen2, B. Hasenbusch1, B. Pieske1, H. Lassen1, E. Stienen3, R. Edelmann1, 1Georg-August-University, UMG, Department of Cardiology, Göttingen, Germany; 2Chaire - Centre Vircow-Klinikum, Department of Cardiology, Berlin, Germany; 3Medical University of Graz, Department of Cardiology, Graz, Austria; 4Georg-August-University, UMG, Department of Psychosomatic Medicine, Göttingen, Germany

**Background:** There is limited knowledge about the development and the correlation of neurohumoral activation and diastolic function in patients with and without diastolic dysfunction and diastolic heart failure. This study therefore investigated the progress and the association of neurohumoral activation as well as parameters of diastolic function in long term follow-up.

**Methods:** In the DIASH-FAC observational study n=1937 patients (±50years) with risk factors for heart failure or previously confirmed diagnosis of heart failure were prospectively included, of them n= 1036 with normal systolic function (LVEF ≥50years) and completed 1 year follow up were analysed. All patients underwent standardized blood sampling, detailed echocardiography and 6-minute-walking-test (6-MWT). According to their diastolic function at baseline (BL) all patients were classified as having E/e'<9, E/e' 9-15 and E/e' ≥15. Data are shown as mean ±SD. (E/e' ± E/e' 9-15 / E/e' ≥15).

**Results: At BL n=364 (35.1%) had E/e'<9, n=570 (55.5%) had E/e' 9-15 and n=102 (9.9%) had E/e' ≥15.** Age (64.2±7.7/67.6±7.3/69.1±6.1), female gender (43,5/53,3/68,6%), LVEF (61.2±5.9/61.6±6.2/61.0±6.4%), 6-MWT (551±86.9/525±95.4/548.5±96.1, mT), NT-proBNP (116,3/145,0/272,3pmol/l), MR-proADM (0,57/0,63/0,65 nmol/l) and MR-proANP (88,6/104,4/125,4 pmol/l) significantly between the three groups (all p<0.001). Also LAVI 23.1±24.5/28.4±28.4 m²/m² (p<0.001) and LVM 114.0±117,4/122.2±16.1 g/m² (p<0.006) was different across the groups, whereas LVEF did not differ between the three. In theivariate correlation the levels of neurohormonal activation (NT-proBNP, MR-proADM, MR-proANP) were significantly correlated with the progress of diastolic function (E/e' after one year (p=0.007/0.002<0.001). However, the multiple regression analyses revealed that only logMRproANP vs. logMRproANP (p=0.004) and logMRproANP (p=0.001) were independently associated with changes in E/e' after one year.

**Conclusion:** In patients with cardiovascular risk factors levels of NT-proBNP, MR-proADM and MR-proANP were increased with changes in diastolic function. However, this suggests that neurohumoral activation is linked to the severity of diastolic dysfunction and also has the potential to reflect changes of diastolic function during long term follow up.
**P385**

Long-term therapy with capadenoson, a partial adenosine A1-receptor agonist, prevents calcium-overload and improves mitochondrial function in left ventricular myocardium of dogs with heart failure

R.C. Gupta,1 M. Wang,1 S. Rastogi,1 K. Zhang1, P.M. Mohy1.2, B. Albrecht-Kupper2, H.N. Sabbah1.1, Henry Ford Hospital, Detroit, United States of America.2Bay Healthcare, Cardiology Research, Wuppertal, Germany

**Background:** Calcium overload and mitochondrial (MTO) dysfunction are hallmark features of failing left ventricular (LV) myocardium. The former occurs partly due to reduced sarcoplasmic reticulum (SR). SERCA-2a activity and expression and the latter, partly due to reduced expression of MTO uncoupling proteins (UCPs) responsible for maintaining MTO membrane potential and, consequently, ATP synthesis. We previously showed that capadenoson (CAP), a partial adenosine A1-receptor agonist, improves LV systolic function in dogs with chronic heart failure (HF). This study examined the effects of CAP on SERCA-2a activity and expression and on expression of UCP2 and UCP3 in LV myocardium of dogs with HF.

**Methods:** Studies were performed in 12 HF dogs randomized to 3 months oral monotherapy with CAP (7.5 mg twice daily, n=6) or to no therapy at all (Control, n=6). Thapsigargin-sensitive SERCA-2a activity and affinity (Ka) were determined in LV tissue homogenate. SERCA-2a protein level normalized to calmodulin (CM) and UCP2 and UCP3 protein levels, normalized to porin, a MTO protein that is unchanged in HF, were also measured in LV homogenate using Western blotting. LV tissue from 6 normal (NL) dogs was used for comparison.

**Results:** Data shown in the table, SERCA-2a activity and expression were reduced significantly in Control dogs compared to NL. In CAP-treated HF dogs, SERCA-2a activity and expression were significantly increased compared to Controls. Reactivation of a fetal gene program, including atrial (ANP) and brain natriuretic peptides (BNP), is a hallmark of cardiac hypertrophy and failure. Although the mechanisms of ANP and BNP reactivation are incompletely understood, epigenetic modifications may play an important role. Histone acetylation and methylation affect the conformation of chromatin, which in turn governs the accessibility of DNA for transcription factors. Here, we characterized histone modifications in the promoter regions of ANP and BNP in human failing myocardium and analyzed the underlying mechanisms of epigenetic modifications.

**Material and Methods:** Healthy C57BL6/J-mice (n=40) received a continuous infusion of Angiotensin II (AngII, 0.5 μg/kg min) and a control group (NL) (n=6). Thapsigargin-sensitive SERCA-2a activity and affinity (Ka) were determined in LV tissue homogenate. The latter, partly due to reduced expression of MTO uncoupling proteins (UCPs) responsible for maintaining MTO membrane potential and, consequently, ATP synthesis. We previously showed that capadenoson (CAP), a partial adenosine A1-receptor agonist, improves LV systolic function in dogs with chronic heart failure (HF). This study examined the effects of CAP on SERCA-2a activity and expression and on expression of UCP2 and UCP3 in LV myocardium of dogs with HF.

**Results:** In dogs with HF, long-term therapy with CAP attenuates calcium overload by up-regulating SERCA-2a activity and expression and improves protein levels of UCP2 and UCP3. These finding explain, in part, the improvement of LV function seen with long-term CAP therapy in dogs with HF.

**Conclusions:** Long-term therapy with capadenoson, a partial adenosine A1-receptor agonist, prevents calcium-overload and improves mitochondrial function in left ventricular myocardium of dogs with heart failure.

---

**P386**

G-CSF leads to a normalization of diastolic function in a mouse model of diastolic heart failure


**Background:** Nearly half of all patients with heart failure have a preserved ejection fraction (HFrEF). The treatment of these patients represents a daily clinical challenge because contemporary therapeutical approaches failed to improve diastolic function. Fibrosis is a major point in the pathogenesis of HFpEF. As recently shown, granulocyte colony-stimulating factor (G-CSF) modulates inflammatory reactions in a mouse model of pressure overload and subsequent unloading, thereby leading to the regression of cardiac fibrosis and a significant improvement of functional parameters. The aim of the present study was to investigate whether osteopontin is associated with lysyl oxidase (LOX)-mediated collagen cross-linking and stiffness in the hypertensive failing human heart.

**Methods:** Twenty-one patients with hypertensive heart disease and HF were included. Biopsies from the interventricular septum were obtained. Cardiac morphology and matrix density were assessed by echocardiography and confocal microscopy. Myocardial expression of osteopontin and LOX was measured by immunohistochemistry and western blot. Collagen cross-linking (i.e. the relationship between insoluble and soluble collagen) was assessed by in vitro samples from 10 subjects who died for non-cardiovascular causes were used as a control group to establish reference values. In vitro experiments were performed with cultured cardiac fibroblasts with osteopontin-induced collagen cross-linking in human dermal fibroblasts.

**Results:** Whereas osteopontin and LOX expression was very sparse in normal hearts, it was high in failing hearts. Collagen cross-linking was increased (P<0.001) in HF patients compared with normal hearts. Osteopontin expression was directly correlated with LOX (r=0.466, P<0.05), collagen cross-linking (r=0.517, P<0.05), LV chamber stiffness (r=0.458, P<0.05), and pulmonary capillary wedge pressure (r=0.558, P<0.01) in all HF patients. Along with LV LOX and collagen cross-linking were strongly correlated with each other (r=0.759, P<0.005) and directly correlated with LV chamber stiffness (r=0.459, P<0.05 and r=0.716, P<0.05, respectively) and pulmonary capillary wedge pressure (r=0.588, P<0.01 and r=0.711, P<0.01, respectively). These correlations remained significant after adjusting for potential confounding factors (age, gender, systolic and diastolic blood pressure and LV mass index). Interestingly, stimulation of human cardiac fibroblasts with osteopontin induced an increase in LOX expression both at the mRNA (P<0.01) and protein (P<0.05) levels.

**Conclusions:** Osteopontin is associated with increased LOX and collagen cross-linking in the hypertensive failing human heart. In addition, osteopontin and LOX may be involved in the development of LV stiffness and increased left-sided filling pressures in these patients, suggesting that the osteopontin/LOX axis might facilitate the deposition of stiff collagen and the subsequent alteration of LV diastolic mechanical properties in the hypertensive failing heart.

---

**P387**

Association of osteopontin with cardiac fibrosis and diastolic dysfunction in heart failure of hypertensive origin: A role for lysyl oxidase

B. Lopez Salazar1, A. Gonzalez Miquelo1, R. Querejeta Inaola2, J. Beaumont Ezcurra1, S. Ravassa Albeniz1, J. Diez Martinez1.

1CIMA, University of Navarra, Pamplona, Spain; 2Donostia University Hospital, San Sebastian, Spain

**Purpose:** The matricellular protein osteopontin is involved in the development of myocardial fibrosis which, in turn, plays a role in the onset of left ventricular (LV) dysfunction and heart failure (HF). The aim of this study was to investigate whether osteopontin is associated with lysyl oxidase (LOX)-mediated collagen cross-linking and stiffness in the hypertensive failing human heart.

**Methods:** Studies of all patients with hypertensive heart disease and HF were included. Biopsies from the interventricular septum were obtained. Cardiac morphology and matrix density were assessed by echocardiography and confocal microscopy. Myocardial expression of osteopontin and LOX was measured by immunohistochemistry and western blot. Collagen cross-linking (i.e. the relationship between insoluble and soluble collagen) was assessed by in vitro samples from 10 subjects who died for non-cardiovascular causes were used as a control group to establish reference values. In vitro experiments were performed with cultured cardiac fibroblasts with osteopontin-induced collagen cross-linking in human dermal fibroblasts.

**Results:** Whereas osteopontin and LOX expression was very sparse in normal hearts, it was high in failing hearts. Collagen cross-linking was increased (P<0.001) in HF patients compared with normal hearts. Osteopontin expression was directly correlated with LOX (r=0.466, P<0.05), collagen cross-linking (r=0.517, P<0.05), LV chamber stiffness (r=0.458, P<0.05) and pulmonary capillary wedge pressure (r=0.558, P<0.01) in all HF patients. Along with LV LOX and collagen cross-linking were strongly correlated with each other (r=0.759, P<0.005) and directly correlated with LV chamber stiffness (r=0.459, P<0.05 and r=0.716, P<0.05, respectively) and pulmonary capillary wedge pressure (r=0.588, P<0.01 and r=0.711, P<0.01, respectively). These correlations remained significant after adjusting for potential confounding factors (age, gender, systolic and diastolic blood pressure and LV mass index). Interestingly, stimulation of human cardiac fibroblasts with osteopontin induced an increase in LOX expression both at the mRNA (P<0.01) and protein (P<0.05) levels.

**Conclusions:** Osteopontin is associated with increased LOX and collagen cross-linking in the hypertensive failing human heart. In addition, osteopontin and LOX may be involved in the development of LV stiffness and increased left-sided filling pressures in these patients, suggesting that the osteopontin/LOX axis might facilitate the deposition of stiff collagen and the subsequent alteration of LV diastolic mechanical properties in the hypertensive failing heart.

---

**P388**

Uregulation of JmC-domain containing histone demethylases contributes to ANP and BNP gene activation in human heart failure

M. Wagner, M. Hohi, M. Tauchnitz, A.M. Zimmer, M. Boehm, C. Maack. Staatland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany

**Background:** Reactivation of a fetal gene program, including atrial (ANP) and brain natriuretic peptides (BNP), is a hallmark of cardiac hypertrophy and failure. The mechanisms of ANP and BNP reactivation are incompletely understood, but epigenetic modifications may play an important role. Histone acetylation and methylation affect the conformation of chromatin, which in turn governs the accessibility of DNA for transcription factors. Here, we characterized histone modifications in the promoter regions of ANP and BNP in human failing myocardium and analyzed the underlying mechanisms of epigenetic modifications.

**Methods and Results:** In human failing myocardium (n=16), ANP and BNP expression and function7 decreased and correlated with histone H3K9 methylation (r=0.66, 0.70 and 0.70; P<0.01), respectively, and with demethylation of histone 3 lysine 9 (H3K9) in ANP and BNP promoter regions, as analyzed by chromatin immunoprecipitation (ChiP). In contrast, H3K4 and H3K27 methylation as well as H3 acetylation were unchanged. Methylated H3K9 silences genes by recruit-
50% in neonatal cardiac myocytes increased HKII methylation (~3-4 fold) at the ANP promoter and reduced ANP and BNP expression by 13±2% and 15±1%, respectively. In contrast, siRNA of either Jmjd1a or Jmjd2a alone did not affect ANP or BNP expression.

Conclusions: Jmjd1a and Jmjd2a control ANP and BNP expression via demethylation of HKII and dissociation of HP-1 from the promoter regions of ANP and BNP. In conclusion, downregulation of these Jmjd genes results in increased demethylation of ANP and BNP promoters, which may be mediated by HP-1 binding.

Understanding lipid metabolism and designing future therapies for dyslipidemia

Large scale reverse siRNA-transfection: a novel tool to dissect regulators of lipid metabolism in human macrophages

G. Domschke1, P. Blattmann2, G. Rupp1, A. Helmer1, F. Linden1, M. Eide1, H.A. Katus1, H. Erle1, H. Runz1, C.A. Gleisner1, 1University Hospital of Heidelberg, Department of Cardiology, Heidelberg, Germany; 2European Molecular Biology Laboratory (EMBL), Cell Biology and Biophysics Unit, Heidelberg, Germany; 3University of Heidelberg, BioQuant, Heidelberg, Germany; 4University of Heidelberg, Institute of Human Genetics, Heidelberg, Germany

Objective: Reverse siRNA-transfection has previously been used as a high-throughput screening tool in immortalized cell lines such as HeLa cells. In order to identify new regulators of macrophage lipid metabolism with possible relevance for cardiovascular disease, we sought to apply this technology to primary human monocyte-derived macrophages isolated from human blood and differentiated macrophages.

Methods and Results: Human blood-derived monocytes were obtained from blood by negative bead isolation and seeded onto 96- and 384-well plates pre-coated with siRNA for reverse transfection. Macrophage differentiation was induced by stimulation with 100ng/ml M-CSF for three days. To detect changes in lipid metabolism we then used four different assays: cellular uptake of fluorescent labeled (17) native or (22) oxidized lipoproteins (DLiQvLDL), (3) intracellular free cholesterol by staining with Filipin and (4) lipid droplet formation upon exposure of cells to lipids by Oil red O staining. Image data were systematically acquired on an automated widefield epifluorescence microscopy platform and fluorescence signal intensities were measured from individual cells using a tailored image analysis software. Using Cy3-tagged control siRNA we show that human monocyte-derived macrophages can be efficiently reverse transfected with siRNAs in a 96- and 384-well format. Upon transfection with siRNAs targeting genes relevant for macrophage lipid metabolism we were able to detect marked changes in the uptake of Oil-labeled LDL and oxLDL, Oil red O staining and free cholesterol levels.

Conclusions: For the first time, these data suggest that reverse siRNA-transfection represents a valuable new screening tool for dissecting the mechanisms of uptake and foam cell formation in primary human monocyte-derived macrophages. This establishes reverse siRNA-transfection as a novel high throughput platform, which may bring insights into macrophage foam cell formation, a process crucial for atherogenesis.

High-density lipoprotein (HDL) elevation by cholesteryl ester transfer protein inhibition promotes insulin secretion in humans

B.A. Kingwell1, A.S. Siebel1, A.K. Nato1, F. Yap1, A.L. Carey2, D. Sviridov1, C.I. Kiu Weber2, G. Meneses-Lorente2, C. Maugeais2, B.A. Kingwell1, A.S. Siebel1, A.K. Nato1, F.Yap1, A.L. Carey1, V. Fuster4, J.H.F. Rudd5, M.E. Farkouh6, D. Rader7, Z.A. Faday2, J.M. Forbes1, 1Baker IDI Heart and Diabetes Institute, Melbourne, Australia; 2European Molecular Biology Laboratory (EMBL), Cell Biology and Biophysics Unit, Heidelberg, Germany; 3University of Heidelberg, BiocQuant, Heidelberg, Germany; 4University of Heidelberg, Institute of Human Genetics, Heidelberg, Germany

Purpose: For the first time, these data suggest that reverse siRNA-transfection represents a valuable new screening tool for dissecting the mechanisms of uptake and foam cell formation in primary human monocyte-derived macrophages. This establishes reverse siRNA-transfection as a novel high throughput platform, which may bring insights into macrophage foam cell formation, a process crucial for atherogenesis.

Conclusion: Our large prospective study showed for the first time in MI patients that reduced HDL was associated with increased levels of ADMA, but not of SDMA levels. Our data suggest that increased CV risk associated with low HDL-cholesterol could be partly mediated through ADMA-related effects.
Dysfunctional high density lipoprotein (HDL) from patients with chronic kidney disease (CKD) increases arterial blood pressure: role of TLR-2 and endothelial NO synthase

T. Speer1, L. Rohrer2, N. Kraenkel1, K. Kuschnerus1, A. Akhmedov1, A. Von Eckardstein2, D. Fliser1, T. Luescher1, F.H. Bahnmann3, U. Landmesser1

1Cardiovascular Research, Physiology Institute, University of Zurich, Zurich, Switzerland; 2Medizinische Hochschule Hannover, Hannover, Germany; 3Saarland University Hospital, Department of Internal Medicine IV, Nephrology and Hypertension, Homburg, Germany

Background: Patients with chronic kidney disease (CKD) exhibit a high cardiovascular morbidity and mortality, even in the early stages, and frequently develop hypertension. Patients with advanced CKD have an uremic dyslipidemia, characterized by low levels of total cholesterol, low density lipoprotein and HDL cholesterol. In addition to its role in reverse cholesterol transport, HDL from healthy subjects (HS) exerts several potential vasoprotective effects. Thus, we compared endothelial effects of HDL from CKD patients and HS and potential consequences for blood pressure response.

Methods: HDL-IV was isolated from patients with CKD (K/DOQI stage II, IV, each n=15) and healthy subjects (n=15) by sequential ultracentrifugation. The effect of HDL on endothelial nitric oxide production (NO) was assessed by electron spin resonance (ESR) spectroscopy. To evaluate the effect of HDL on systolic blood pressure (SBP) in vivo, HDL was injected into wild-type and eNOS-deficient mice. The expression of VCAM-1 and endothelial mononuclear cell (MNC) adhesion was assessed to quantify HDL’s anti-inflammatory capacity. Moreover, the endothelial repair capacity of HDL was assessed in vitro and vivo, using a gap closure assay and carotid injury model in nude mice.

Results: HDL from HS stimulated endothelial NO production; whereas HDL from CKD patients markedly inhibited endothelial NO production (~70% by HDL of these patients; P<0.05), even in incipient CKD. TRL2, but not TLR4 inhibition, prevented the inhibitory effects of HDL-CKD on endothelial NO production. In vivo, HDL-IV reduced the influx of monocytes (~20% vs 111 mmol/L; P<0.05), while healthy HDL reduced SLP (~113±57.7 μmol/L; P<0.05). Notably, HDL from patients with CKD induced basal endothelial VCAM-1 expression and promoted endothelial MNC adhesion, whereas HDL from healthy subjects did not suggest a change to a proinflammatory phenotype. In vitro gap closure and in vivo reendothelialization after carotid injury were suppressed by HDL of CKD patients.

Conclusion: Our data demonstrate for the first time that endothelial-protective effects of HDL are considerably impaired in patients with CKD independently of the severity of CKD. Furthermore, HDL may be involved in initiation and aggravation of hypertension in these patients. This reveals a new potentially important pathomechanism of cardiovascular disease in patients with incipient CKD.

Efficacy, safety and tolerability of 150 mg Q2W dose of the anti-PCSK9 mAb, REGN727/SAR236553: data from 3 phase 2 studies

M. Koren1, E. Stein2, E. Roth3, J.M. Mckinney4, D. Gipe4, C. Hanotin5, A.-C. Ferrand6, R. Wu4, R. Dutou7, J. Jacksonville Center For Clinical Research, Jacksonville, United States of America; 2Metabolic & Atherosclerosis Research Center, Cincinnati, United States of America; 3Sterling Research Group, Cincinnati, United States of America; 4Virginia Commonwealth University School of Medicine and National Clinical Research, Richmond, United States of America; 5Regeneron Pharmaceuticals, Inc, Tarrytown, New York, United States of America; 6Sanofi, Paris, France; 7Institut de recherches cliniques de Montreal, Montreal, Canada

Purpose: Proprotein convertase subtilisin/kexin type 9 serine protease (PCSK9) plays a pivotal role in LDL receptor (LDLR) degradation. Gain-of-function mutations of PCSK9 in humans result in hypercholesterolemia, while loss-of-function mutations are associated with low LDL-cholesterol (LDL-C) and significantly reduced coronary heart disease risk. REGN727/SAR236553, a fully human monoclonal antibody targeted to PCSK9, has been evaluated in 3 recently completed phase 2 studies, DFI11565 (NCT01284443), DFI11566 (NCT01284649), and R727-CL-1003 (NCT01266876). We present a combined analysis from these 3 studies to assess the efficacy and safety profile of REGN727.

Methods: A total of 352 patients with primary hypercholesterolemia (heterozygous familial hypercholesterolemia [FH] or non-FH) and LDL-C ≥ 100 mg/dL on background lipid-lowering therapies which included a statin, were enrolled in 3 double-blind, randomized, placebo-controlled phase 2 studies of 8- to 12-week treatment durations. At randomization, 77 patients were administered placebo, 167 received any other regimen of REGN727 and 108 received 150 mg REGN727 every 2 weeks (Q2W; 31 patients from DF11565, 61 from DF11566 and 16 from R727-CL-1003). The 150 mg Q2W dose was selected for analysis as it was common to all 3 studies.

Results: REGN727 150 mg Q2W resulted in robust reductions in LDL-C with mean percent reductions from baseline ranging from -66.2% to -71.8% as compared to placebo (-5.7% to -8.9%) by week 12 in studies DF11565 and R727-CL-1003. In study DF11566, mean percent reductions from baseline ranged from -66.7% to -72.3% as compared to 17.7% for placebo by week 8. We also observed similar reductions at earlier time points and reductions in other apoB-containing lipoprotein parameters. Additionally, modest increases in HDL-C and apoA1, along with reductions in Lp(a) were observed. REGN727 150 mg Q2W was well tolerated and exhibited no clear adverse event signal compared to placebo. Among those patients who received at least one dose of REGN727 150 mg Q2W (safety population; n=108), adverse events occurring in >10% of patients included dizziness, nausea, headache, diarrhea, and injection-site reactions. In this treatment group, there were 0 deaths, 1 SAE and 2 discontinuations as compared to 0 deaths, 2 SAEs and 4 discontinuations for patients on placebo (safety population; n=77).

Conclusion: In Phase 2 studies, REGN727 150 mg Q2W provides robust reductions in LDL-C and other atherogenic lipoproteins while providing a good safety and tolerability profile.

Ambulatory blood pressure measurement-mandatory for blood pressure monitoring in treated hypertensive patients?

M.V. Lehmann1, U. Zeymer2, R. Dechend3, S. Hupfer4, E. Deep5, J. Senges5, R.E. Schmidt1. 1University Hospital, Department of Nephrology and Hypertension, Erlangen, Germany; 2Medical Clinic B, Hospital of the City of Ludwigshafen, Ludwigshafen, Germany; 3Charité University Hospital, Department of Molecular and Clinical Cardiology, Berlin, Germany; 4Novartis Pharma, Clinical and Regulatory Affairs, Nuremberg, Germany; 5Research Institute for Heart Attack Ludwigshafen (IFH), Ludwigshafen, Germany

Purpose: In epidemiological and clinical studies 24-hour ambulatory blood pressure monitoring (ABPM) for hypertension management has been shown to be superior in predicting cardiovascular events to office blood pressure (BP) readings and recent guidelines recommend ABPM in the diagnostic set up (in NICE now routinely mandatory). But the usefulness of ABPM has only been scarcely examined in cohorts of treated hypertensive patients.

Methods: In this non-interventional study conducted in Germany (3A-Registry) in 999 general practitioners’ offices, office BP and ambulatory blood pressure (ABP) was measured in 3826 hypertensive patients, enrolled for 1 year in the registry, with ≥140/90 mmHg, for ABP 24 hour ≥140/90 mmHg, independently of BP 24 hour: ABP ≥140/90 mmHg groups, according to ESC-ESH 2009 guidelines. 50.5% of the patients had controlled office BP values, and with ABPM 23.7% had controlled ABPM values. Percentage of patients on office BP values ≥140/90 mmHg and ABP values ≥140/90 mmHg was 32.9%, indicating masked hypertensive disease. In this cohort, only 6.1% of the patients with ABP values ≥140/90 mmHg had office BP ≥140/90 mmHg indicating some white coat hypertension.
Ambulatory blood pressure and dipping-pattern after diurnal activity (dSD), and during the hours of nocturnal rest (nSD). The independent deviation of all measurements during 24-hours (24SD), during the hours of between hours of diurnal activity and nocturnal rest divided by average BP obtained "n-point forward moving average" method has been used to derive 24-hour CSP (BPro). 24-hour peripheral blood pressure (BP) was measured using Space-and "n-point forward moving average" method has been used to derive 24-hour average, daytime and nighttime SBP and DBP as well as maximum SBP/DBP was reduced by 8.6/4.5 mmHg (p=0.019/0.025) and 11.5/6.5 mmHg (p<0.05) in hypertensives whereas in no such association was found in normotensives. Nocturnal CSP fall was not related to any of these parameters. IMT was related to CSP variability (24SD -0.40 ± 0.14; p=0.01; dSD - 0.35 ± 0.13; p<0.05; nSD 0.25 ± 0.13; p<0.05) in hypertensives only. IMT was not related to PSP variability. Microalbuminuria was not associated with nocturnal BP fall or with BP variability. Conclusion: Central systolic pressure variability is related to carotid IMT whereas nocturnal CSP fall is related to LVM and LV geometry in untreated hypertensives.

The value of non-invasive ambulatory blood pressure variability parameters for the determination of increased arterial stiffness in untreated hypertensive subjects


Purpose: Increased evidence supports the association of blood pressure (BP) variability with cardiovascular risk in patients with essential hypertension. Our purpose was to investigate the relationship between BP variability parameters and arterial stiffness in untreated patients with essential hypertension.

Methods: We estimated 24-h ambulatory blood pressure variability (systolic, diastolic, mean, pulse pressure) in 254 untreated hypertensive patients with essential hypertension (mean age 51.7±11.33 years, 148 men). Variability was assessed as the standard deviation (SD) of the mean out of 24-hour, awake and asleep BP recordings done at 15-minute intervals during daytime and 30-minute intervals at nighttime. Cardiac to femoral wave velocity (PWV) was assessed as an index of arterial stiffness.

Results: In a univariate analysis, variability of all blood pressure (BP) parameters (systolic, diastolic and pulse pressure) was significantly and inversely related with increased PWV (p<0.01). In a multiple linear regression analysis, after adjustment for age, sex, BMI, smoking habit, dyslipidemia, diastolic pressure, 24 mean systolic BP, 24 mean diastolic BP and 24 mean pulse pressure, variability of each one BP parameter was independently related to PWV (systolicSD: b=-0.150, diastolicSD: b=-0.211 and pulse pressureSD: b=-0.283, p<0.05). Furthermore, in another model including the above confounding factors, the addition of respective SD value (systolic, diastolic, pulse pressure) was further increase significantly the value of model for the prediction of PWV by 24h mean systolic BP, 24h mean diastolic BP and 24h mean pulse pressure, variability of each one BP parameter was independently related to PWV (systolicSD: r2 change from 0.280 to 0.312, for diastolicSD: r2 change from 0.224 to 0.271 and for pulse pressureSD: r2 change from 0.342 to 0.403 respectively, p<0.01).

Conclusions: In untreated patients with newly diagnosed essential hypertension reduced blood pressure variability (systolic, diastolic, pulse pressure), estimated by non-invasive ambulatory BP measurement, is an independent and additive determinant of increased arterial stiffness.

Out-of-office blood pressure measurement

K. Harada, A. Toba, A. Tanaka, M. Sugie, R. Aoyama, H. Yokota, T. Ishiyama, K. Takeya, T. Tsukubou, H. Fujimoto. Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

Background: B-type natriuretic peptide (BNP) is a marker of elevated left ventricular (LV) filling pressure or myocardial stretch, as well as a risk marker of cardiovascular diseases. However, increased BNP levels in treated hypertensives, in association with out-of-office blood pressure (out-of-OBP) and LV geometry remain to be examined.

Methods: 245 elderly hypertensive patients (mean age, 74 years; men: 38%) underwent ambulatory BP measurement (ABPM) (30-min intervals), trans-thoracic echocardiography, and measurement of plasma BNP concentration.

Results: Logarithmically transformed BNP concentration (LnBNP) correlated with age, Body mass index, eGFR, 24-hour systolic BP, night-time BP, respectively, but not OBP of grade 2 hypertension. It also correlated with left atrial dimension, relative wall thickness, but not with LV mass index (LVM). In the multiple linear regression analysis, night-time BP and eGFR independently predicted LnBNP after adjusting age, sex, LVMI, and relative wall thickness. 24-hour systolic BP and not with LnBNP concentration also determinants of LnBNP. Plasma BNP concentration increased both with concentric and eccentric LV remodelling. The former affected BNP concentration more than the latter. In the logistic regression analysis, the hazard of non-dipper status after adjusting age and sex was 1.55 (95%CI:1.02-2.36; p=0.05) for the patients with BNP=42 pg/ml versus those with BNP=42 pg/ml.

Conclusions: Nighttime BP predicted plasma BNP concentrations independent of LV geometry and hypertension. Increased BNP in patients with treated hyper-

Central blood pressure variability is related to carotid intima-media thickness whereas nocturnal central blood pressure fall is related to left ventricular mass in untreated hypertensives

A. Bednarek1, P. Jankowski1, A. Olszanecka1, A. Windyk1, K. Kawecka-Jaszcz1, C. Ukena1, A. Spiess1, B. Cremers1, I. Kindermann1, M. Lenski1, M. Schlach1, B. Scheller1, U. Laufs1, M. Boehm1, I. Kindermann1, A. Spiess1, B. Cremers1, C. Ukena1, F. Mahfoud1, C. Ukena1, A. Spieks1, B. Cremers1, I. Kindermann1, M. Lenski1, M. Schlach1, B. Scheller1, U. Laufs1, M. Boehm1,

Background: Catheter-based renal sympathetic denervation (RDN) in patients with resistant hypertension has been shown to reduce sympathetic drive and office blood pressure. Ambulatory blood pressure monitoring (ABPM) is mandatory in every patient with uncontrolled hypertension. Nighttime blood pressure and non-dipping is associated with cardiovascular morbidity and mortality. The influence of RDN on ambulatory blood pressure (ABPM) and dipping pattern has not been studied in details.

Methods and Results: Eighty patients with resistant hypertension were included in the study. Systolic and diastolic blood pressure (SBP/DBP) as well as ABPM (SBP/DBP, standard deviation variability (SDV) and blood pressure variability (BV) were measured prior to, and at 3 and 6 months follow-up. RD reduced office SBP and DBP at 3 and 6 months by 20.9/7.1 mmHg (p=0.001/0.001), respectively. After 3 and 6 months 24-hour average SBP/DBP was reduced by 8.6/4.5 mmHg (p=0.001/0.005) and 11.6/5.5 mmHg (p=0.018/0.022), respectively. Average SBP/DBP were lowered at 3 and 6 months follow-up at daytime by 9.2/5.4 mmHg (p=0.001/0.001) and 11.9/7.1 mmHg (p=0.001/0.001) and at nighttime by 6.2/5.1 mmHg (p=0.002/0.004) and 10.25/1mmHg (p=0.001/0.001), respectively. Renal denervation also reduced maximum SBP by -12.8 mmHg at 3 months and by -14.7 mmHg at 6 months follow-up (p=0.009 and 0.003) whereas maximum DBP was unchanged. Six months after RD 21 patients had an improvement in their dipping-pattern.

Conclusion: Beside significant reductions in office SBP and DBP, RD also reduced the difference, daytime and nighttime SBP and DBP as well as maximum SBP after 3 and 6 months. RD has the impact to improve dipping-pattern in at least some patients.

Ambulatory blood pressure and dipping-pattern after catheter-based renal sympathetic denervation in patients with resistant hypertension

F. Mahfoud1, C. Ukena1, A. Spieks1, B. Cremers1, I. Kindermann1, M. Lenski1, M. Schlach1, B. Scheller1, U. Laufs1, M. Boehm1, I. Saarland University Hospital, Department of Internal Medicine III, Cardiology, Hospital, Germany; 2Baker ID Heart and Diabetes Institute, Melbourne, Australia

Out-of-office blood pressure measurement

K. Harada, A. Toba, A. Tanaka, M. Sugie, R. Aoyama, H. Yokota, T. Ishiyama, K. Takeya, T. Tsukubou, H. Fujimoto. Tokyo Metropolitan Geriatric Hospital, Tokyo, Japan

Background: B-type natriuretic peptide (BNP) is a marker of elevated left ventricular (LV) filling pressure or myocardial stretch, as well as a risk marker of cardiovascular diseases. However, increased BNP levels in treated hypertensives, in association with out-of-office blood pressure (out-of-OBP) and LV geometry remain to be examined.

Methods: 245 elderly hypertensive patients (mean age, 74 years; men: 38%) underwent ambulatory BP measurement (ABPM) (30-min intervals), trans-thoracic echocardiography, and measurement of plasma BNP concentration.

Results: Logarithmically transformed BNP concentration (LnBNP) correlated with age, Body mass index, eGFR, 24-hour systolic BP, night-time BP, respectively, but not OBP of grade 2 hypertension. It also correlated with left atrial dimension, relative wall thickness, but not with LV mass index (LVM). In the multiple linear regression analysis, night-time BP and eGFR independently predicted LnBNP after adjusting age, sex, LVMI, and relative wall thickness. 24-hour systolic BP and not with LnBNP concentration also determinants of LnBNP. Plasma BNP concentration increased both with concentric and eccentric LV remodelling. The former affected BNP concentration more than the latter. In the logistic regression analysis, the hazard of non-dipper status after adjusting age and sex was 1.55 (95%CI:1.02-2.36; p=0.05) for the patients with BNP=42 pg/ml versus those with BNP=42 pg/ml.

Conclusions: Nighttime BP predicted plasma BNP concentrations independent of LV geometry and hypertension. Increased BNP in patients with treated hyper-
tension were not associated with office hypertension, but with nighttime hypertension, therefore, hypertensives with elevated BNP might be classified as stage-B heart failure.

**Regional cerebral blood flow and circadian blood pressure profile in patients with metabolic syndrome: effect of combined antihypertensive therapy**

I. Efimova, T. Kalashnikova, Y.U. Lishmanov. Institute of Cardiology. Tomsk, Russian Federation

**Purpose:** Study of regional cerebral blood flow (rCBF) in patients with metabolic syndrome (MetS), revealing of interrelation between parameters of blood pressure monitoring and the results of brain perfusion single photon emission computed tomography (SPECT), as well as estimation of combined antihypertensive therapy on cerebral perfusion.

**Methods:** Twenty-four patients with MetS were investigated by brain SPECT with 99mTc-HMPAO and blood pressure monitoring before and after 6 months of antihypertensive therapy, sustained-release verapamil in combination with indapamide sustained release or enalapril. Regional cerebral blood flow (rCBF) (ml/100g/min) was calculated. All patients had no focal neurological symptoms. Fifteen patients of similar age without angiographic signs of carotid atherosclerosis, cardiac and renal disease, coronary artery disease and arterial hypertension, neurological and psychiatric disorders were investigated as control group.

**Results:** All patients with MetS showed a decrease rCBF in all regions of the brain compared with the control group. The most pronounced decrease in perfusion in all subjects was found in the temporal, occipital and upper frontal regions (p<0.001). Antihypertensive therapy with verapamil and indapamide for 24 weeks led to the reduction of rCBF by 7% in the left temporal region (p<0.009). The combination of verapamil and enalapril improved CBF over a larger range of study areas. Thus, the increase in CBF we observed in the right lower frontal (p<0.007), temporal (p<0.001), upper frontal (p<0.01), anterior parietal and in the posterior parietal lobes on both sides (p<0.009 and p<0.003, respectively). There was a direct correlation between the degree of nocturnal diastolic blood pressure reduction and values of rCBF in the right temporal region (R= -0.5, p<0.04), which confirms the danger of excessive loss of blood pressure in hypertensive patients during sleep.

**Conclusions:** Our results suggest that patients with MetS even without focal neurological symptoms may have marked signs of CBF disorders. Combination antihypertensive therapy has a positive effect on cerebral perfusion.

**CARDIOVASCULAR RISK ASSESSMENT IN CLINICAL APPLICATION**

**Association of heart rate on all-cause and cardiovascular mortality in the general population during long-term follow-up**

F.P.J. Brouwers1, N. Verweij1, F.W. Asselbergs2, P. Van Der Harst1, R.A. De Boer1, H.L. Hillege1, W.H. Van Gilst1. 1University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; 2University Medical Center Utrecht, Department of Cardiology, Utrecht, Netherlands

**Purpose:** Increased resting heart rate (HR) has been proposed as a risk factor for all-cause (AC) mortality. The effect of an increased HR on cardiovascular (CV) mortality is not equivocal. We hypothesize that monitoring the change in HR over a four years period could be an independent risk factor for AC and CV mortality in the general population.

**Methods:** From the Prevention of Renal and Vascular End Stage Disease (PREVEND) cohort (N=8592), 7189 subjects had no previous history of CV disease and were not on beta-blocker therapy on both HR measurements. Between 1997 and 2001, two standardized HR measurements were recorded after 10 minutes rest. Baseline HR was divided into: low (<5th percentile), medium (5th to 95th) and high (>95th percentile). Change in HR was defined in the same manner: decreased (>5th percentile), unchanged (5th to 95th) and increased (>95th). After the second HR measurement, median follow-up was 6.3 years (range 5.8-6.9). Multivariable Cox proportional hazard analyses were performed, adjusting HR for age, gender, smoking, systolic blood pressure, cholesterol and the biomarkers C-reactive protein, high-sensitive Troponin-T and N-terminal pro-B-type natriuretic peptide.

**Results:** At baseline, mean age was 48±12 years and 49% of subjects were male. Mean HR was 70±10bpm and mean change in HR was 0.2±7.5bpm (p=0.045 vs. baseline). There were 472 deaths (6.6%), of which 89 (18.9%) of CV origin. Using Cox-proportional hazard analyses, high baseline resting HR was associated with CV mortality (1.5 fold increase, CI: 1.0-2.2%; p=0.036, compared to low resting HR), but not with CV mortality (p=0.763). Over 4 years, 1238 subjects decreased in HR, 3377 subjects remained unchanged and 1137 subjects had an increased HR (mean change -1.0 -1.0 and 10.1 bpm, respectively). Subjects with an increased HR had two-fold increased risk for AC (2.9 CI: 1.0-4.4; p=0.047) and six-fold increased risk for CV mortality (6.0, CI: 1.8-19.9; p=0.004), both compared to subjects with decreased HR.

**Conclusions:** In a middle aged general population, a single measurement of increased resting HR is associated with increased AC mortality, but not with increased CV mortality. In contrast, a change in HR of >5bpm over 4 years, was associated with a major, six-fold increased risk for CV mortality, whereas risk for AC mortality was only two-fold increased during further follow-up. Serial HR measurements may be more informative with regard to mortality risk, especially of CV origin.
Elevated resting heart rate is a risk factor for mortality independent of physical fitness (VO2max)

M.T. Jøensen,1,2 P. Suadanni,2 H.O. Heim,1 F. Gintzler2 1Copenhagen University Hospital Gentofte, Copenhagen, Denmark; 2Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark

Purpose: Elevated resting heart rate has been shown to be associated with mortality. However, it is still uncertain whether resting heart rate is merely a marker of physical fitness or an independent risk factor. We studied the relationship between resting heart rate, physical fitness (VO2max), and mortality.

Methods: A prospective study of middle-aged employed men without known cardiovascular disease.

Resting heart rate was assessed from the ECG, physical fitness (VO2max) was determined by the Åstrand bicycle ergometer test. Only subjects with sinus rhythm were included. Subjects were classified according to quintiles of resting heart rate.

Associations were studied in multivariate Cox models adjusted for physical fitness and conventional cardiovascular risk factors.

Results: 2964 subjects were followed for 16 years. 1180 deaths occurred. Resting heart rate was inversely related to physical fitness (p<0.001). Resting heart rate in the highest vs lowest quintile predicted mortality after adjusting for age alone, age + physical fitness, and age + physical fitness + cardiovascular risk factors (HR: 1.31 (1.08-1.58)) (all p<0.01).

Conclusion: Elevated resting heart rate is a risk factor for mortality independent of physical fitness. These findings suggest that resting heart rate is an independent risk factor and not merely a marker of physical fitness.

445 Atrial fibrillation is a strong independent risk factor for ischemic heart disease mortality

M. Igarashi1, T. Sairenchi1, F. Ine1, N. Murakoshi1, D.Z. Xu1, J. Gunji1, T. Tomizawa1, I. Yamaguchi2, H. Ota1, K. Aonuma1 1University of Tsukuba, Ibaraki, Japan; 2Dokkyo Medical University, Mibu, Japan

Purpose: Atrial fibrillation (AF) is a common sustained arrhythmia and is well known as a major risk factor for thrombo-embolic stroke and heart failure. However, the association of AF and ischemic heart disease (IHD) remains controversial. Although it has been reported that AF is a predictor of death and coronary artery events in patients with coronary artery disease in some small clinical studies, the information about an association between AF and IHD mortality is not enough. The aim of this study was to evaluate the association between AF and risk of IHD mortality among general population.

Methods: A total of 30,693 male and 59,884 female aged 40-79 years without history of heart diseases and who completed health checkups in Ibaraki prefecture, Japan, in 1993, enrolled into this study and were followed-up through 2006. The hazard ratios (HR) and 95% confidence intervals (95%CI) of AF for cause-specific mortality by using a multivariable Cox proportional hazards regression model were analyzed.

Results: AF was significantly associated with excess risk of total death (HR [95%CI]: 1.93 [1.59-2.33]), all-cause vascular mortality (3.87 [2.99-5.02]), CI mortality (5.38 [3.58-8.06]) and IHD mortality (4.93 [2.95-7.44]) in all age groups. Furthermore, AF was the strongest predictor for IHD mortality among conventional risk factors including hypertension (1.56 [1.33-1.84]), diabetes mellitus (1.81 [1.36-2.40]), dyslipidemia (1.06 [0.86-1.31]) or smoking (2.05 [1.62-2.59]) (See the Figure).

Conclusion: In this large-scale community-based cohort study, AF was strongly associated with increased risk of IHD mortality as well as risk of CI mortality.

446 Premature atrial contractions in the general population: prevalence and risk factors

D. Conen1, M. Adam2, J.C. Barthélémy1, M. Imboden1, N. Kundu2, A. Von Eckardsten3, T. Rocha1, J.M. Gaspoz1, N. Probst-Hensch2, D. Cattano4 on behalf of SAPALDIA Study Group. 1University Hospital Basel, Basel, Switzerland; 2Swiss Tropical and Public Health Institute - University of Basel, Basel, Switzerland; 3University Hospital of Saint-Etienne - Hospital Nord, Saint-Etienne, France; 4University Hospital Zürich, Institute of Clinical Chemistry, Zurich, Switzerland; 5University Hospital of Geneva, Geneva, Switzerland; 6University Hospital of Geneva, Department of Cardiology, Geneva, Switzerland

Purpose: The occurrence of premature atrial contractions (PACs) is an independent predictor of incident atrial fibrillation and other adverse outcomes, including stroke and death. However, little is known about PAC prevalence in the general population and risk factors for PAC occurrence.

Methods: We performed a cross-sectional analysis among participants of the population-based Swiss cohort study on Air Pollution and Lung Diseases in Adults (SAPALDIA). At the SAPALDIA follow-up visit in 2002/2004, holter electrocardiograms were performed in 5,428 after exclusion of participants. PACs were identified by a coupling interval to the preceding QRS complex <80% of the mean RR interval before the event, and a QRS duration of <0.12 seconds unless aberration was suspected. Stepwise multivariable linear regression models were constructed to determine independent correlates for the number of PACs per hour (log-transformed).

Results: The median number (interquartile range) of PACs per hour was 0.8 (0.4-1.8), 1.1 (0.5-2.4), 1.4 (0.7-4.6), 2.3 (0.8-6.9) and 2.6 (1.9-6.2) among participants aged 50-55, 55-60, 60-65, 65-70 and 70+ years, respectively (p for trend <0.0001). Only 18 of 1742 (1.0%) participants did not have at least 1 PAC on Holter monitoring. Sex was not associated with PAC occurrence (p=0.27). In stepwise linear regression models, significant predictors for PAC occurrence were age (β per year 0.05, 95% confidence interval (CI) 0.04-0.07, p<0.0001), height (β per cm -0.02, 95% CI 0.01-0.03, p<0.0001), log-transformed potassium (β per mmol/l -0.02, 95% CI -0.04-0.00, p<0.0001), log-transformed B-type natriuretic peptides (β per log-unit 0.44, 95% CI 0.34-0.54, p<0.0001), elevated high sensitivity troponin levels >0.014 μg/l (β compared to reference level -0.003 μg/l, 95% CI -0.05-0.02, p<0.002) and low HDL cholesterol (β per mmol/l 0.22, 95% CI 0.03-0.40, p<0.02). Elevated blood pressure, body mass index and a history of cardiovascular disease were not significantly related to PAC occurrence.

Conclusions: To our knowledge, this is the first study of risk factors for PAC occurrence in a representative sample of the general population aged 50 years or older. PAC occurrence is common and independently associated with age, height, natriuretic peptide levels, troponin levels and HDL cholesterol. The underlying mechanisms of these relationships need to be addressed in future studies.

GENETIC TESTING FOR PLATELET INHIBITION: WHY ARE WE NOT DOING IT?

458 Global high on-treatment platelet reactivity identifies patients at high risk of ischemic events: data from RECLOSE 2-ACS study

R. Marcucci1, A.M. Gorli2, R. Valenti3, R. Paniccia3, G. Parodi3, B. Giusti2, A. Migliorini2, G.F. Gensini2, D. Antonucci1, R. Abbate2, 1Careggi University Hospital, Florence, Italy; 2Careggi University Hospital - Thrombosis Centre, Department of Heart and Vessels, Florence, Italy; 3Department of heart and vessel, Florence, Italy

Objectives: This study sought to determine the impact of a global platelet hyperreactivity – both to arachidonic acid and ADP – as the possible prognostic marker of per-ACS long-term thrombotic events in patients with acute coronary syndromes (ACS) undergoing an invasive procedure.

Background: High-on-clopidogrel platelet reactivity has been found to be associated with high risk of ischemic events after percutaneous coronary interventions (PCI). Some data have found that the real adverse prognostic marker is the presence of a global high on-treatment platelet hyperreactivity (GHPH) identified by the measurement of platelet function induced by both arachidonic acid and aspirin.

Methods: Prospective, observational, referral center cohort study of 1772 consecutive patients with ACS undergoing PCI from April 2005 to April 2009 at the Division of Cardiology of Careggi Hospital, Florence, Italy, who were consultant to investigate the global high on-treatment platelet hyperreactivity (GHPH) by identified the measurement of platelet function induced by both arachidonic acid and aspirin.

Results: GHPH was documented in 152/1772 (8.6%); isolated HPR by ADP was found in 96/1772 (5.5%) and isolated HPR by AA in 21/1772 (1.1%). The pri-
Personalized antiplatelet treatment after percutaneous coronary intervention: the MADONNA study

J.M. Siller-Matula, M. Francesconi, C. Dechant, B. Jalma, G. Maurer, G. Delle-Karth, G. Gouya, K. Ruzicka, A. Podczeck-Schweighof, G. Christ, Medical University of Vienna, Vienna, Austria; *Kaiser Franz Joseph Hospital, Vienna, Austria.

Background: Clopidogrel nonresponsiveness is associated with adverse clinical outcome.

Objectives: We aimed to investigate whether individualized antiplatelet treatment is an effective and safe strategy.

Methods: This was a prospective controlled study with a follow-up of 1-month. Responsiveness to clopidogrel was assessed by multiple electrode aggregometry (MEA) in 798 patients with coronary artery disease undergoing percutaneous coronary intervention (PCI). In the guided group (n=403) clopidogrel nonresponders received repeated loading doses of clopidogrel (up to 4 loading doses of 600mg) or prasugrel (60mg), in the non-guided group (n=395) clopidogrel nonresponders did not undergo any change of treatment.

Results: Twenty six percent of patients (n=106) were classified as nonresponders in the guided group. Of them 56 received a prasugrel loading dose of 60mg and were re-loaded with 600mg of clopidogrel. All prasugrel treated patients reached a sufficient level of platelet inhibition whereas 14% (n=7) of clopidogrel nonresponders remained non-responders after the addition of 400mg of clopidogrel in the guided group and 6% (n=3) of them remained non-responders in the non-guided group. The 5 clopidogrel non-responders receiving a third clopidogrel loading dose of 600mg and 60% (n=3) of them remained non-responders. The 5 clopidogrel non-responders receiving a fourth clopidogrel loading dose of 600mg and 60% (n=3) of them remained non-responders. The two non-responders receiving a prasugrel loading dose of 60mg. One of them responded sufficiently, another one remained a non-responder. In summary, two patients of 403 (0.5%) did not reach a sufficient platelet inhibition despite reloading with clopidogrel or prasugrel. Stent thrombosis occurred significantly less often in the guided group than in the non-guided group (0.2% vs. 1.9%, p=0.027).

Multivariate Cox regression analysis showed that patients in the non-guided group were at a 7.9-fold higher risk to develop stent thrombosis compared to patients in the guided group (OR: 7.9; 95%CI: 1.09-69.2; p=0.048). In line, acute coronary syndromes occurred significantly less often in the guided group than in the non-guided group (0% vs. 2.5%; p=0.001) whereas there was no difference in the event rates of cardiac death (2% vs. 1.3%; p=0.42) or major bleedings (1% vs. 0.3%; p=0.16).

Conclusion: Personalized antiplatelet treatment according to the platelet function testing with MEA resulted in an improved efficacy with an equal safety compared to the standard treatment.

457 Ticagrelor vs prasugrel in patients with ST elevation myocardial infarction undergoing primary percutaneous coronary intervention

I. Xanthopoulou, K.F. Theodoropoulou, G. Kassionis, V. Gizas, P. Tzagkas, N. Koutougiannis, P. Pavloures, J. Chiladakis, D. Alexopoulos. Patras University Hospital, Cardiology Department, Patras, Greece.

Purpose: Few data exist about the onset of action and the extent of platelet inhibition after ticagrelor or prasugrel loading dose (LD) in patients with ST elevation myocardial infarction (STEMI). We aimed to compare the antiplatelet effect of ticagrelor versus prasugrel in STEMI patients undergoing primary percutaneous coronary intervention (PCI).

Methods: This was a prospective, randomized, single-center study of parallel design. Antiplatelet-naive STEMI patients, undergoing PCI were randomized in a 1:1 ratio to either: ticagrelor 60mg LD/10mg maintenance dose-MD or prasugrel 180mg LD/90mg MD. Platelet reactivity (PR) was assessed at Oripree regression analysis, 1, 2, 6, 24 hours and at day 5 with the VerifyNow assay (in PR units-PRU, with a value<230 indicating high on-treatment platelet reactivity-HTPR).

Results: Thirty eight patients were randomized (76.3% men, age 60±2.1±3 years). There was no difference in patients’ characteristics between ticagrelor (N=18) and prasugrel (N=20) group. The primary end point of PR at hour 1 did not differ significantly between groups. There was a trend towards lower PR with prasugrel compared to ticagrelor at hour 2 (Table 1). HTPR rate remained high in both groups at hour 1 (72.2% for ticagrelor vs 70.0% for prasugrel, p=1.0). There was a trend towards lower HTPR rate with prasugrel compared to ticagrelor at hour 2 (31.6% vs 56.2% respectively, p=0.2). Beyond hour 6 both agents effectively reduced PR.

Conclusion: Point-of-care assessment showed a more potent P2Y12 inhibition with prasugrel than ticagrelor early after treatment with either prasugrel or ticagrelor. Apart from a trend towards better platelet inhibition with prasugrel compared to ticagrelor 2 hours post LD, both agents effectively treated HTPR thereafter.

CYP2C19*2 and *17 alleles have a significant impact on the platelet response and bleeding risk in patients treated with prasugrel after acute coronary syndrome

T. Cuisset, P.M. Morange, J.Q. Quilici, P.J.M. Moro, J.L.B. Bonnet, M.C.A. Alessi. AP-HM - Hospital La Timone, Marseille, France.

Background: Clopidogrel and Prasugrel are thiopryridine which need transformation to active metabolite via the cytochrome P450. CYP2C19*2 “loss of function” allele and CYP2C19*17 “gain of function” allele have been linked with re-
sponse to clopidogrel and clinical outcomes. While previous data did not show significant influence of these alleles on response to loading dose of prasugrel, the effect on chronic response to prasugrel and bleeding risk has not been well investigated. We therefore designed the present study to answer this question.

**Methods and Results:** 213 patients undergoing successful coronary stenting for acute coronary syndrome and discharged with prasugrel 10 mg daily were prospectively included. Prasugrel Response was assessed at one month with the PRI VASP and High on-treatment Platelet reactivity (HTPR) defined as PRI VASP >50% and “hyper response” as PRI VASP >8% (95th percentile). Platelet reactivity was assessed by ADP-induced aggregation. CYP2C19*2 and CYP2C19*17 genotyping were performed. At one month, carriers of “loss of function” 2 alleles had significantly higher PRI VASP than non carriers (33±15 vs. 27±14, p=0.03) and higher rate of HTPR (16% vs. 4%, p=0.01). Conversely, carriers of “17 gain of function” allele had significantly lower PRI VASP than non carriers (25±13 vs. 31±15, p=0.03, p=0.02), lower rate of HTPR (1% vs. 10%, p=0.02), higher rate of “hyper response” (11% vs. 3%, p=0.02) and higher rate of bleeding complications than non carriers: 22% vs. 11% (OR 95%CI: 2.5 [1.2-5.4]; p=0.02).

**Conclusion:** The present study shows a significant influence of CYP2C19*2 and *17 allele on response to chronic treatment by prasugrel 10 mg daily and occurrence of bleeding complications.

### Differential effects of platelet transfusion on correction of the bleeding time in prasugrel and ticagrelor treated rats

Y. Tomizawa1, N. Kasauni1, K. Ohno1, J.A. Jakubowski2, A. Sugidachi1, 1Biological Research Laboratories, Daiichi Sankyo, Co., Ltd., Tokyo, Japan; 2Lilly Research Laboratories, Eli Lilly and Company, Indianapolis, United States of America

**Purpose:** Clinical trials have shown that dual antiplatelet therapy, aspirin plus novel P2Y12 inhibitors, result in superior efficacy regarding major adverse cardiovascular events in patients with acute coronary syndrome. However, an increased number of bleeding events in certain patient groups has also been reported. Platelet transfusion is a treatment option in such patients. In the present study, effects of platelet transfusion on bleeding time were compared in rats treated with prasugrel, ticagrelor and clopidogrel.

**Methods:** Vehicle, or doses of prasugrel (10 mg/kg, p.o.) and ticagrelor (30 mg/kg, p.o.) that resulted in similar levels of platelet inhibition were administered to rats 4 hr before bleeding time measurements. Fresh, washed platelets (10 billion platelets/ml) were prepared and suspended in Hank’s balanced salt solution. Platelets (10 billion platelets/rat) were transfused via the jugular vein to rats 1 hr before the bleeding time measurements. For bleeding time measurements, a 21 G needle was advanced 1 cm into the tail vein at a 3 cm point from the tail end and immediately withdrawn. Insulating blood was babbled every 5 sec with a filter paper and the bleeding time was determined. Red blood cells and platelets in whole blood were measured just before platelet transfusion and after bleeding time measurements.

**Results:** Both prasugrel and ticagrelor significantly prolonged the bleeding time compared to vehicle-treated control groups (p<0.001 and p<0.01, respectively, both n=14). Platelet transfusion resulted in similar significant increases in blood platelet numbers in both prasugrel- and ticagrelor-treated animals. In contrast, red blood cell numbers were not changed by platelet transfusion in all groups tested. In the prasugrel-treated group, platelet transfusion caused significant shortening of bleeding time (p<0.05, n=13). In the ticagrelor-treated group, by contrast, platelet transfusion showed no influence on bleeding time (p>0.05, n=14).

**Conclusion:** The present results indicate that the prolongation of bleeding time by high-dose prasugrel was significantly reversed by platelet transfusion. However, bleeding time prolongation associated with ticagrelor was not lessened under the experimental conditions employed. The disparity in finding between prasugrel- and ticagrelor-treated animals may reflect the different reactivity profiles of the two agents.

### Long-acting loop diuretic azosemide is superior to short-acting furosemide in treatment of congestive heart failure: the J-MELDICO study

T. Tsujino1, T. Masuyama1, H. Orihara2, K. Yamamoto1, T. Akasaka1, Y. Hirano1, N. Ohte1, T. Dainon1, S. Nakatani1, H. Kato2 on behalf of J-MELDICO Investigators, 1Hyogo University of Health Sciences, Kobe, Japan; 2Hyogo College of Medicine, Nishinomiya, Japan; 3Toyama University Graduate School, Toyama, Japan; 4Tottori University, Yonago, Japan; 5Wakayama Medical University, Wakayama, Japan; 6Kinki University, School of Medicine, Osaka, Japan; 7Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan; 8Osaka University, Graduate School of Medicine, Osaka, Japan; 9Akita University Graduate School of Medicine, Akita, Japan

**Purpose:** It is unknown what kind of loop diuretics is optimal for the treatment of patients with chronic heart failure (CHF). A previous animal study reported that the administration of azosemide, a long-acting loop diuretic, improved mortality rate in a hypertensive heart failure model compared to furosemide, a short-acting one. We conducted J-MELDICO (Japan - Long-acting short-acting Diuretics in Congestive Heart Failure) to compare therapeutic effects of furosemide and azosemide in patients with CHF.

**Methods:** In this multicenter, prospective, randomized, open, blinded endpoint trial, we compared effects of azosemide and furosemide in patients with CHF with New York Heart Association class II or III symptoms. 320 patients (160 patients in each group; mean age 71 years) were followed up for a maximum of 2 years. We considered 40 mg furosemide to be equivalent to 60 mg azosemide based on the result of a previous clinical pharmacology study. Electrocardiography, echocardiography, chest X-ray and blood sample were examined at the study entry and every 12 months after the randomization. The primary endpoint was a composite of cardiovascular death or unplanned admission to hospital for congestive heart failure.

**Results:** Etiologies of heart failure were ischemic heart disease (33%), dilated cardiomyopathy (22%), and others (45%). Median left ventricular ejection fraction (LVEF) was 51%. During a median follow-up of 35.2 months, the primary endpoint occurred in 23 patients in the azosemide group and 34 patients in the furosemide group (hazard ratio, 0.55, 95% confidence interval [CI], 0.32 to 0.95; P=0.03). Hazard ratio for the patients with LVEF <50% was tended to be lower than that for patients with LVEF ≥50% (0.42 [95%CI], 0.20-0.85) vs. 0.79 (0.36-1.21); P=0.25. Among the secondary endpoints, unplanned admission to hospital for congestive heart failure or a need for modification of the treatment for heart failure were also reduced in the azosemide group compared to the furosemide group (hazard ratio, 0.60; 95% CI, 0.36 to 0.99; P=0.046). Increase in plasma BNP concentration after 1 year randomization was tended to be lower in the azosemide group than in the furosemide group (3% vs. 25%, p=0.06). Changes in renoproteinine were not different between the 2 groups.

**Conclusion:** Azosemide, compared to furosemide, improved the prognosis of patients with CHF.

### Comparison of carvedilol, nebivolol and bisoprolol on cardiorespiratory function in moderate heart failure

M. Conti1, S. Paolillo1, A. Iorio1, E. Bertella1, A. Apostolo1, G. Cattadori1, S. Fa r i n a1, D. M a g r i1, P. G. A g o s t o n i2, 1Cardiology Center Monzino (IRCCS), Milan, Italy; 2University of Milan, Department of Cardiovascular Sciences, Milan, Italy

**Purpose:** Several β blockers are available for heart failure (HF) treatment but only a few comparative data among molecules are available. We compared Carvedilol (β1, β2, a blocker), Bisoprolol (β1 blocker), and Nebivolol (β1 blocker with NO releasing activity) (N).

**Methods:** We studied 61 moderate HF patients (age 61±9 years) in stable clinical conditions. Patients were randomized to receive, for 2 months, C, B, N in a blind, cross-over design. Averaghe daily dose were 25.6±12.5 mg for C, 0.5±4.8 mg for B and 0.4±3.5 mg for N. At the end of each period, patients underwent spirometry with lung diffusion measure (DLco and its subcomponents Dm, Vc, VE).

**Main results**

<table>
<thead>
<tr>
<th></th>
<th>C (mg/4 h)</th>
<th>B (mg/d)</th>
<th>N (mg/4 h)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dm (cm3/min/mmHg)</td>
<td>25.3±4.5</td>
<td>30.4±4.5</td>
<td>30.4±4.5 *</td>
</tr>
<tr>
<td>Vc (ml)</td>
<td>207±50</td>
<td>89±34</td>
<td>85±32    *</td>
</tr>
<tr>
<td>Peak VO2 (ml/kg/min)</td>
<td>15±3.6</td>
<td>16±9.4</td>
<td>16±9.4 *</td>
</tr>
<tr>
<td>VO2max slope</td>
<td>24.9±4.1</td>
<td>29.1±4.4</td>
<td>28.8±4.5 *</td>
</tr>
<tr>
<td>CBN (μg/min/mmHg)</td>
<td>2.65±1.21</td>
<td>3.06±1.31</td>
<td>2.85±1.25</td>
</tr>
<tr>
<td>CO2max CO2 (mM/L/mmHg)</td>
<td>0.06±0.03</td>
<td>0.07±0.03</td>
<td>0.06±0.03</td>
</tr>
</tbody>
</table>

**Conclusion**
Is there a relationship between adequacy of medical therapy for heart failure and results of imaging of sympathetic neuronal status using 123I-metaiodobenzylguanidine (mIBG)?

Methods: Medication data for 782 HF subjects (81% male; 82% NYHA class II, 18% class III; 65% ischemic, 35% non-ischemic) with left ventricular ejection fraction (LVEF) <35% (mean 27%) were reviewed. All subjects were enrolled in a US/Europe clinical trial which required subjects to be on a stable regimen of guidelines-based medical therapy. Based upon clinical trial results and HF guidelines, a panel of 3 cardiologists rated dosage for each medication category on a 0-3 scale: 0-none; 1-inadequate; 2-adequate; 3-maximum. Allowing a maximum score of 3 for ACE and ARB combined, total scores could range from 0 to 9. Cardiac 123I-mIBG uptake was quantified as the heart/mediastinum ratio (H/M) on 4-hour anterior planar images. The relationships between medication scores, H/M, and outcome events (composite of HF progression, arrhythmic events, and cardiac death) during median 17 months follow-up were examined using correlation and Cox proportional hazards methods.

Results: Total mean medication score was 4.7; most common scores were 4 and 5 (each n=142 (18%)). Only 123 subjects (16%) were judged to be receiving adequate doses (score ≥2) of all 3 medication categories. Mean H/M did not differ as a function of total medication score (range 1.41-1.47). However, for subjects with low (0-3), intermediate (4-6), and high scores (7-9), those who experienced events had significantly lower mean H/M (Table).

Conclusions: Regardless of the intensity of HF medical therapy, patients with poorer sympathetic innervation as determined using 123I-mIBG imaging are at increased risk for adverse outcomes. The optimal approach to use of 123I-mIBG uptake measurements as an indicator of adequacy of HF medication dosages remains to be defined.

Lung Impedance guided preemptive treatment of evolving pulmonary congestion-edema in course of acute myocardial infarction reduces use of furosemide

Methods: Patients sustaining an acute myocardial infarction (AMI) frequently develop pulmonary congestion-edema (PEd) during hospitalization. Treatment is initiated after the appearance signs of lung fluid content (LFC) increase. Ongoing monitoring of LFC may enable to predict impending PEd and prompt preemptive therapy. Late treatment beginning of PEd may require more diuretics.

Aims: We sought to find out whether non-invasive lung impedance (LI) guided preemptive treatment of evolving PEd may reduce the use of furosemide administered in comparison with common practice.

Methods: LI was measured by a method based on transversal distribution of electromagnetic energy through the chest which is more sensitive than current methods. We previously found that an LI decrease of 12-14% from baseline level, when patients are still asymptomatic, reflects the beginning of transition from interstitial to alveolar edema. In this study we evaluated the effect of preemptive LI-guided therapy on furosemide dosage required to treat evolving PEd.

Results: 222 AMI consecutive patients asymptomatic at admission in which an LI decrease of 12-14% from initial level was recorded during monitoring were randomized into two groups (2:1). Groups were well matched for demographic, laboratory parameters, reperfusion type and in-hospital therapy. Patients were monitored for 116±50 hours. Treatment for PEd was started in group 1 patients (common practice) only after symptom appearance (LI decrease 25±3.5% from initial) while group 2 patients diuretic preemptive therapy was begun at an asymptomatic stage when LI decreased by 12-14%.

All group 1 patients but only 11% of group 2 patients developed moderate to severe clinically and roentgenographically proven PEd (p<0.001). While admission group 1 patients were treated with more furosemide than group 2 patients (160 ±37 mg vs. 146 ±15 mg, p<0.001), from LI decrease 12-14% to initiation of therapy with furosemide was longer in group 1 by 545±339 minutes than in group 2 (p<0.001). Patients of group 1 and 2 required furosemide treatment and physical function score by +8.1 and -2.0 (p=0.004). In patients with initial Li decrease at baseline, the dosage of furosemide was 69% in group 1 and 41% in group 2 (p=0.004). In patients without LI decrease at baseline the reduction of furosemide dosing in group 1 was 96% in group 1 and 90% in group 2 (p=0.001).

Conclusions: Preemptive LI-guided therapy with furosemide in AMI patients is initiated earlier than in common practice and is effective in halting evolving PEd. Preemptive treatment translates into better clinical outcome and lower furosemide dosage.

Acute intravenous infusion of human stresscopin (JNU-39588146) improves left ventricular systolic function without increasing myocardial oxygen consumption in dogs with advanced heart failure

Methods: Studies were performed in 7 anesthetized dogs with intra coronary microembolization-induced HF. Each dog received both STG and volume matched vehicle control (Veh, 5 mM acetate/D2O) administered one week before the study. The left ventricle was monitored using transmural echocardiography (ME). End-diastolic fractional shortening (FS) and peak systolic velocity (S') were measured 5 mm in basal septal wall. Left ventricular end-diastolic pressure was followed using an indwelling catheter and right atrial pressure assessed using a balloon-tipped catheter. Left atrial pressure was measured by a pressure transducer in the left atrium connected to arespiratory pump. Heart rate was measured as the rate of QRS complexes. The STG was administered by a continuous infusion over 30 minutes (100 µg/kg/min). The study was performed in two groups of dogs: the first group (n=3) received STG and the second group (n=4) received vehicle control. Blood and ACEI/ARB was an principal HNC-goal. UC-patients received standard care, but up titration of drugs was recommended to general practitioners. Type and dosages of drugs, quality of life (Short Form Questionnaire 36 [SF-36] and NYHA class were assessed both at baseline [BL] and follow up (FU).

Results: At BL 80% (HNC: 81, UC 79%, NS) of patients received a BB and 88% (HNC: 89, UC 87%, NS) ACEI/ARB. The mean equivalent dosage for BB was 25% of the recommended maximum (p<0.05 for ACEI/ARB). 43% (HNC 44, UC 41, NS). 40% of patients were in NYHA class III (HNC 43, UC 36, NS), and mean SF-36 physical function score was 46 (HNC 48, UC 44, NS). ACEI/ARB patients had BB (p=0.06) and ARB (p=0.03) uptitration. Each arm -1% of patients were on ACEI/ARB (p=0.99). Mean equivalent dosages for BB increased by +8% in HNC and +4% in UC (p<0.001). For ACEI/ARB the changes were +9% and +2% (p=0.009). Overall, in HNC uptitration of BB and ACEI/ARB was achieved in 53, in UC in 43.5% (p<0.03). Here, NYHA-class changed by -0.43 and -0.11 (p<0.001), and physical function scores by +8.1 and -2.0 (p=0.004). In patients without uptitration NYHA-class changed by -0.29 in both arms (p=0.96) and physical function score by +3.3 (HNC) and +5.3 (UC) (p<0.05).

Conclusions: While BB and ACEI/ARB are often prescribed, dosing according to guidelines is not always possible. Even with personalised coaching full uptitration is feasible only in a minority of patients. However, compared with UC, uptitrated HNC-patients gained significantly more in quality of life and NYHA class, which suggests, that uptitration may require careful supervision to achieve maximum benefits for the patients.
apart in random order. STC was administered as a 60 min low dose (LD) infusion (2.2ng/kg/min), followed by a 60 min intermediate dose (ID) infusion (4.3ng/kg/min) and, finally, followed by a 60 min high dose (HD) infusion (7.3ng/kg/min). Hemodynamic and ventriculographic measurements were made at baseline, prior to drug administration, and at the end of each 60 min drug or vehicle infusion. Measurements included LV ejection fraction (EF), end-systolic volume (ESV), stroke volume (SV), LV end-diastolic pressure (EDP) and myocardial oxygen consumption (MVO2).

Results: Data are shown in the table. Neither STC nor Veh had any significant effect on heart rate or systolic blood pressure. Veh infusions had no effect on EF, ESV, SV, EDP or MVO2. In contrast, compared to Veh, STC significantly increased EF and significantly lowered ESV and EDP in a dose-dependent fashion without increasing MVO2. In addition, STC was safe and did not elicit de novo cardiac arrhythmias.

RISK STRATIFICATION FOR SUDDEN CARDIAC DEATH: A CONTINUUM PROCESS

053 A blood test for sudden death risk
S.C. Dudley, G. Gao, V. Brahmanandam, A. Shah, M. Raiču, A. Kutru, L. Gu, A. Schwartz, S. Neg, University of Illinois at Chicago, Chicago, United States of America

Background: Human heart failure (HF) is associated with decreased cardiac output and increased blood pressure. In this study, we evaluated whether white blood cell (WBC) sodium channel mRNA splicing varies as a function of the presence of HF or malignant arrhythmias as measured by appropriate implanted cardio-defibrillator (ICD) shock.

Methods and Results: One hundred eighty adult patients were recruited into this study, 45 controls without HF (Ejection Fraction (EF) > 60%) and 135 with HF (EF < 35%). Patients with congenital heart disease, infections, and inflammatory conditions were excluded. The splicing factor expression profile was investigated by gene array assay in circulating WBCs of HF patients. The mRNA abundances of SCN5A and SCN5A variants were determined by real-time PCR. The expressions of WBCs with SCN5A changes in paired heart tissues and WBCs were compared. There were no significant differences in the age, race, gender, NYHA class, coronary artery disease, QRS duration, ACE-inhibitor and antiarrhythmic use among the groups.

Conclusions: In dogs with advanced HF, acute intravenous administration of STC improved LV systolic function without increasing heart rate or MVO2 and significantly lowered ESV and EDP in a dose-dependent fashion without increasing systolic pressure. These findings support the continued development of STC for the treatment of patients with acute HF syndromes.

054 Early repolarization and prolonged filtered QRS duration associated with sudden cardiac death for a long term follow-up in patients with chronic heart failure
Y. Furukawa, T. Yamada, T. Morita, Y. Iwaseki, M. Kasawaki, T. Naito, T. Fujimoto, M. Fukumami, Osaka General Medical Center, Osaka, Japan

Background: Early repolarization pattern (ERP) is known to be associated with sudden cardiac death (SCD) in healthy subjects. Recently, it has been reported that ERP would be associated with SCD in patients with old myocardial infarction in the case-control study. However, there is no information available on the prognostic significance of ERP in chronic heart failure (CHF) patients, in relation to ventricular late potential (VLP) detection by signal-averaged electrocardiogram (SAE). We sought to prospectively investigate whether ERP would be associated with SCD in CHF patients, and whether the combination of ERP and VLP would improve the prediction of SCD.

Methods: The study population consisted of 129 consecutive outpatients with mild to moderate systolic heart failure with LVEF > 40%. All patients underwent the standard 12-lead electrocardiogram and SAE at enrollment, and we assessed the presence of ERP using the criteria of J-point elevation >0.1 mV in at least 2 inferior or lateral leads. The duration of filtered QRS (IQRs), the RMS voltage for the last 40 ms of filtered QRS (RMS40), and the late high amplitude signals <40 μV in the terminal portion of filtered QRS (LAS40) were measured on the vector magnitude of SAE. Abnormal values for these 3 parameters were set at enrollment as > 130 ms, RMS40 < 17 μV, and LAS40 < 40 μs. VLP was defined by the presence of 2 or more abnormal values. The primary endpoint of this study was SCD.

Conclusions: At the entry, 16 had ERP and 63 had VLP. During the follow up period of 6.7 (3.6) years, 26 patients had SCD. The incidence of SCD was significantly higher in patients with than without ERP (68% vs 14%, p<0.0001). Although patients with SCD trend to have VLP more frequently than those without SCD (24% vs 16%, p<0.01), IQRs was significantly longer in patients with ERP (24 ± 9 ms vs 13 ± 7 ms, p<0.002). A multivariate Cox analysis revealed that ERP (Hazard ratio (HR) 3.9, 95% CI 1.7 to 8.9, p=0.001) and abnormal IQRs (HR 3.1, 95% CI 1.1 to 8.6, p=0.03) were significantly associated with SCD. In Kaplan-Meier analysis, it was shown that patients with SCD was significantly often observed in patients with than without ERP (63 (10/16)% vs. 14 (6/11)% , p<0.001). HR of a combination of ERP and abnormal IQRs for prediction of SCD was 14.4 (95% CI 4.4 to 47.3), which was 3.7-fold of the HR of ERP only.

Conclusion: ERP would be associated with an increased risk of SCD in CHF patients. The combination of ERP and prolonged IQRs could improve the power to predict for SCD in patients with CHF.
Predictors, in-hospital, short and long term prognosis of cardiac arrest complicating first acute ST elevation myocardial infarction: analysis of national STEMI database

A.E. Alahmar1, K. Snee2, M.F. Yunyun1, M.D. Musameh1, A. Timmins1, J. Birkenhead, I. Squire, N.J. Samani1, 1University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom; 2British Heart Foundation, London, United Kingdom; 3Northampton General Hospital, Northampton, United Kingdom

Background: Cardiac arrest complicating first acute ST elevation myocardial infarction (STEMI) is known to associated with increased in-hospital mortality; however, any long-term impact is unclear especially in the setting of contemporary therapy for MI.

Aim: To assess the predictors and impact of cardiac arrest complicating first STEMI in the contemporary era of acute MI treatment in a large national database.

Methods: We analysed the UK Myocardial Ischaemia National Audit Project (MiNAP) which prospectively collects uniform data on all STEMI admissions into UK hospitals. All consecutive first STEMI entries from Jan 2008 until Mar 2010 were included. Firstly, using univariate and subsequently stepwise multivariate model we identified predictors of cardiac arrest. Then we used Cox regression model and Kaplan-Meier curves to compare in-hospital, 30 days, 1 year and longer-term mortality.

Results: Out of the 41,467 patients with first STEMI 4,240 had cardiac arrest (10%). Of these, 2,893 (68%) were in-hospital. In multivariate analysis, mortality [HR 1.01 p<0.001, female gender [HR 1.24 p<0.001], and chronic kidney disease[HR 1.23 p=0.05] were associated with increased risk of cardiac arrest whereas a previous episode of Hypertension[HR 0.73 p<0.001], family history of CAD[HR 0.73 p=0.001], previous use of beta blockers[HR 1.18 p<0.001] were associated with lower risk.

Excluding patients who died at the time of their initial arrest, cardiac arrest was the most significant independent predictor of in-hospital mortality [HR=6.93 95% CI (5.00-9.59)]. Furthermore, cardiac arrest was also the most significant predictor of 30 day mortality after hospital discharge [HR=2.32 CI (1.89-2.85), P<0.001]. Although in Kaplan-Meier curve the higher mortality rate in cardiac arrest patients extends to two years, in multivariate analysis excluding subjects who died in the first 30 days after discharge, there was no significant increase in hazard ratios in the cardiac arrest group beyond 30 days [HR=0.91 CI (0.77-1.08), P=0.27].

Conclusions: In this large, comprehensive and contemporary national database, cardiac arrest complicating a first STEMI was a strong independent predictor of in-hospital and 30 days post discharge mortality. However, beyond 30 days up to 3.5 years cardiac arrest at the time of the STEMI did not have any residual impact on mortality. Our findings suggest that special monitoring of these patients should be undertaken in the early period post-discharge.

Concomitant early repolarization increases the occurrence of sustained ventricular tachyarrhythmias and sudden death in the chronic phase of an acute myocardial infarction

Y. Naruse1, H. Tada1, Y. Hanamura2, M. Hayashi3, N. Takeyasu2, T. Hoshi1, A. Sato1, Y. Sekiguchi1, K. Aonuma1, 1University of Tsukuba, Graduate School of Comprehensive Human Sciences, Division of Cardiovascular, Tsukuba, Japan; 2Tsukuba Medical Center Hospital, Tsukuba, Japan; 3Ubaraki Prefectural Central Hospital, Department of Cardiology, Kama, Japan

Purpose: We recently demonstrated that the presence of early repolarization (ER) increased the risk of ventricular fibrillation (VF) occurrences in the early phase of acute myocardial infarctions (AMIs). However, it is unknown whether there is an association between ER and VF occurrences in the chronic phase of an AMI.

Methods: This study included 974 patients with AMIs (67±12 years; 742 male; 232 female) who underwent successful percutaneous coronary intervention. The primary endpoint was occurrence of sustained ventricular tachyarrhythmias (VT/VF) or sudden death after discharge from the AMI hospitalization. We evaluated the presence of ER from the ECGs recorded at pre-discharge. ER was electrocardiographically defined as a QRS-ST junction elevation of >0.1mV from baseline at least 2 inferior or lateral leads, manifested as QRS slurring or notch in the QRS. We also analyzed the localization (inferior or lateral leads), amplitude, morphology (notching or slurring), and ST segment characteristics (upsloping or horizontal/descending) of ER to evaluate the significance of the ER pattern.

Results: After a mean follow-up of 28.2±17.0 months, 15 (1.5%) patients experienced an episode of VT/VF or sudden death. There was no significant difference in the age, gender, Killip class on admission, medications, peak creatine kinase levels, or prevalence of cardiovascular risk factors between these 2 groups. However, the patients with VT/VF or sudden death had a greater prevalence of a left anterior descending culprit artery (73% vs. 45%; p<0.05) and lower left ventricular ejection fraction (39±11% vs. 54±11%; p<0.001) than those without. Furthermore, we analyzed the localization (inferior or lateral leads), amplitude, morphology, (notching or slurring), and ST segment characteristics (upsloping or horizontal/descending) of ER to evaluate the significance of the ER pattern.

Conclusions: In the context of STEMI, VF/HM is a tough and reproducible algorithm to quantitatively assess delayed hyperenhancement, greatly related to functional prognosis at 3 months follow-up.

Delayed CE-MRI quantification for predicting left ventricular remodelling after acute myocardial infarction

L. Biere1, V. Mateus2, S. Grah1, G. Clerford1, F. Pruinier1, S. Willoiteaux2, A. Furber1, 1University of Angers, UPRES 3860 (LPRM), Angers, France; 2University Hospital of Angers, Angers, France

Purpose: To aim the interest of quantitative versus qualitative assessment of myocardial hyperenhancement in the context of a first reproffered ST-elevation myocardial infarction (STEMI). Several methods were tested across their capacity to predict left ventricular (LV) remodelling at 3 months.

Methods: CE-MRI was performed on day 5 and after a period of 3 months in 92 patients with STEMI. LV scar and parameters were assessed visually (by using a four scale score) and quantitatively on day 5 and at 3 months. Dichotomous thresholds were defined first visually (VISUAL), then by 2, 5 and 6 standard deviations above remote myocardium, and by the full-width at half-maximum (FWHM) method.

Results: All infarct sizing methods showed great relation to LV remodelling at 3 months. The best predictor of an LVEF superior to 70 ml/m2 were: heart failure, CK peak and infarct size at day 5. FWHM was shown to be the best of all quantitative methods. An infarct size superior to 44 grams was related to LVEF>70% with a sensitivity of 0.9 and a specificity of 0.925. FWHM reproducibility was good (r=0.895 p<0.0001, Bland Altman bias of 0.8).

Treatment of decompensated left-sided heart failure lowers right ventricular pulsatile load and increases the pulmonary arterial time constant

M. Dupont1, W. Muller2, D.O. Taylor1, R.C. Starling1, W.H. Tang1, 1Cleveland Clinic, Department of Cardiovascular Medicine, Cleveland, United States of America; 2Hospital Osti-Limburg (ZON), Genk, Belgium

Background: Right ventricular (RV) failure frequently occurs in left-sided heart failure (HF) and independently prognosticates. We examined how decongestive treatment of left-sided HF influences the RV afterload components pulmonary vascular resistance (PVR) and pulmonary arterial capacitance (PAC) (stroke volume/pulmonary pulse pressure) which are supposed to have an inverse hyperbolic relationship in such way that their product (PVR×PAC, the pulmonary arterial time constant τ) forms a constant.

Methods: Changes in PVR, PAC and τ were analyzed in 75 patients in whom hemodynamically tailored treatment of acute decongested HF resulted in a decrease in pulmonary arterial capacitance (PAC) of 10 mmHg or more.

Results: In our patient cohort (age 57±13 years, EF 24±13%), decongestive treatment with diuretics (99%), nitroprusside (75%) and inotropes (41%) resulted in a decrease in PCWP (31±7 to 16±5 mmHg, p<0.001) and an increase in CI (1.84±0.64 to 2.67±0.83 mmHg;p<0.001). PVR decreased from 270±165 to 211±88 dynes sec cm⁻² (p=0.020±0.12 to 0.2±0.017 mmHg/sec; p=0.002) and PAC increased more obviously from 1.65±0.64 to 2.61±1.42 ml/mgm (p<0.0001) Fig. The product of PVR and PAC (time constant τ) increased from

THE HEART IN PULMONARY HYPERTENSION

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790/1934829 by guest on 11 March 2019
Right ventricular dyssynchrony impairs left ventricular performance in patients with pulmonary hypertension

M.L.A. Haek, U. Hoke, N. Ajmone Marsan, E.R. Holman, M.J. Schalij, U.J. Box, H.W. Vliegen, V. Delgado. Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands

Purpose: Pulmonary hypertension may cause right ventricular (RV) dyssynchrony and subsequently, through inter-ventricular interaction, left ventricular (LV) dyssynchrony. The aim of our study was to assess the influence of RV dyssynchrony on LV performance in patients with pulmonary hypertension.

Methods: Eighty-seven patients with pulmonary hypertension and LV ejection fraction (EF) ≥ 55% (age 65±15 years, SPAP 64±21 mmHg) were evaluated. Ventricular dyssynchrony was defined as the standard deviation of the time to peak longitudinal strain of 6 segments of the RV (RV-SD) and the LV (LV-SD) in the apical 4 chamber view as assessed with speckle tracking echocardiography.

Results: The patient population was divided according to the median RV-SD value of 54 ms. Pulmonary hypertension patients with RV-SD > 54 ms had significantly worse NYHA functional class (2.3±0.8 vs. 2.7±0.7, p<0.01), LV EF (50±8.6% vs. 65±6.8%, p<0.001), wider QRS duration (116±32 ms vs. 102±27 ms, p<0.04) and higher LV-SD (57±19 ms vs. 40±17 ms, p<0.001). A significant correlation between RV-SD and LV-SD (r=0.48, p<0.001) and between RV-SD and EF (r=0.34, p=0.001) was observed (figure 1 A and B). After multiple linear regression analysis, RV-SD was significantly associated with LV-SD (beta 0.3, 95% CI 0.16 – 0.45, p<0.001).

Conclusion: RV dyssynchrony is associated with LV dyssynchrony and impairment of LV performance in patients with pulmonary hypertension. This suggests that LV and RV function are interrelated in pulmonary hypertension.

Gas exchange measurements during exercise show early pulmonary arterial hypertension in scleroderma patients

O. Dumitrescu1, C. Seck1, P. Moimazadeh1, N. Hurzelmann3, S. Rosenkrantz1. 1Cologne University Hospital - Heart Center, Cologne, Germany; 2Cologne University Hospital - Department of Dermatology, Cologne, Germany; 3Cologne University Hospital - Department of Cardiology, Cologne, Germany

Background: Pulmonary arterial hypertension (PAH) is a well-known complication in patients (pts) with scleroderma (SSc), harboring a poor prognosis. Therefore, an early diagnosis of PAH in these pts is desirable. Here, we analyzed whether gas exchange parameters during maximal and submaximal exercise significantly differ in SSC pts without PAH vs pts with early and advanced PAH.

Methods: We analyzed 44 consecutive SSC pts with dyspnea. None of the pts had been diagnosed with PAH. Each patient underwent right heart catheterization (RHC) and cardiopulmonary exercise testing (CPET). PAH was diagnosed according to current guidelines. The pts were categorized into 3 groups: pts without PAH (group 1), pts with mild PAH elevation (25-35 mmHg, group 2) and pts with high PAH elevation (>35 mmHg, group 3). Gas exchange parameters were also compared to systolic PAP determined by RHC.

Results: PAH was diagnosed by RHC in 23 cases and could be ruled out in 21 cases. 9 of 23 pts with PAH had a mean PAP elevation of 25-35 mmHg. The detailed results are shown in table 1. The end-tidal CO2 partial pressure (PETCO2) at the anaerobic threshold (AT) showed the best ability to differentiate between pts without PAH and pts with mild PAH elevation.

Table 1. Resting echocardiography and gas exchange parameters in SSC pts without PAH and SSC pts in different stages of PAH

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Groups (1, 2, 3)</th>
<th>Significance (ANOVA)</th>
<th>p&lt;0.05</th>
<th>1 vs 2</th>
<th>1 vs 3</th>
<th>2 vs 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Systolic pressure gradient on echocardiography (mmHg)</td>
<td>Gr 1: 26.7±7.9, Gr 2: 36.8±15.1, Gr 3: 57.9±23.5</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>Peak oxygen consumption (ml/min/kg)</td>
<td>Gr 1: 11.5±3.1, Gr 2: 12.6±2.1, Gr 3: 14.3±2.9, Gr 4: 13.1±4.36, Gr 5: 24.1±1.8, Gr 6: 4.35±0.93</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
<td>yes</td>
<td>yes</td>
<td>no</td>
</tr>
<tr>
<td>VE/VC02 at the AT (no unit)</td>
<td>Gr 1: 13.8±1.40, Gr 2: 26.7±1.0, Gr 3: 3.25±7.64</td>
<td>yes</td>
<td>no</td>
<td>no</td>
<td>no</td>
<td>yes</td>
<td>no</td>
</tr>
</tbody>
</table>

Conclusion: Gas exchange measurements during exercise show significant differences between SSC pts with vs without PAH. However, only PETCO2 at the AT was able to show significant differences between pts without PAH, pts with mild PAH, and pts with severe PAH elevation. PETCO2 measured during exercise may be of additional value for the non-invasive screening algorithm.
Assessment of right ventriculo-pulmonary arterial coupling in patients with pulmonary hypertension

S. Fuke1, K.F. Kusuro2, S. Akagi2, M. Tanaka2, A. Ogawa1, S. Nagase2, K. Nakamura1, T. Sato1, H. Ito1. 1Japanese Red Cross Okayama Hospital, Okayama, Japan; 2Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences, Okayama, Japan

Purpose: Right ventricular (RV) failure is an important prognostic determinant in patients with pulmonary hypertension (PH). However, little is known about RV-pulmonary arterial (RA) coupling in PH patients. Accordingly we assessed PA effective elastance (Ea, index of arterial load), RV maximal end-systolic elastance (Ees, index of intrinsic contractility) and the time to peak-elastance to cycle length ratio (%Tpe) using single-beat estimation of RV pressure-volume relationship.

Method: Twenty-six patients with chronic PH (PH group; 49±20 years old, 16 females, and WHO class 2.4±0.5) and twenty-one patients with heart failure without PH (HF group; 71±12 years old, 6 females, and NYHA functional 2.3±0.5) were evaluated. All patients underwent pressure recording by PressureWire (St. Jude Medical, Inc., St. Paul, MN) via Swan-Ganz catheter. We estimated the maximal RV pressure of isovolumic beats (maxP) and %Tpe using by extrapolated sin curve fitted to RV pressure in isovolumic period and detected end-systolic pressure (Pes) using by second derivative curve of PA pressure. Ees was assessed as the slope of Pmax-derived end-systolic pressure-volume relationships, Eas as the slope of arterial distensibility to end-systolic relation, and coupling efficiency as the Ees-to-Ea ratio (Ees/Ea). We measured augmentation index (AI) of PA to assess pressure reflection.

Results: Mean PA pressure was higher in PH group than in HF group (46±15 mmHg vs. 39±6 mmHg, P<0.001) but cardiac index was comparable. Ees was higher in PH group than in HF group (74±0.54 mmHg/mL vs. 40±0.19 mmHg/mL, P<0.001) and Ea was also higher in PH group than in HF group (17±0.76 mmHg/mL vs. 33±3.18 mmHg/mL, P<0.001). Ees/Ea was significantly lower in PH group than in HF group (0.65±0.29 vs. 1.37±0.81, P=0.001). The AI was higher (20.0±11.2% vs. 4.3±13.9%, P<0.001) and %Tpe was longer in PH group than in HF group (20.7±4.2% vs. 26.2±4.1%, P=0.007). Ees showed significant correlation with Ees/Ea ratio (R=0.779, P<0.001). Ees showed positive correlation with the AI (R=0.295, P=0.044). Multivariate regression analysis revealed that logarithm of Ea was the independent predictor of %Tpe (R=0.54 mmHg/mL vs. 0.19 mmHg/mL, P=0.001).

Conclusions: 1) In PH group, pressure reflection augments the RV afterload. 2) Compared to HF group, PH group is associated with the worse right ventriculo-pulmonary arterial coupling and the longer RV systolic period that may result in reduced diastolic filling time.

Remarkable effectiveness of percutaneous transluminal pulmonary angioplasty for hemodynamics and long-term prognosis in patients with distal-type chronic thromboembolic pulmonary hypertension

K. Sugimura, Y. Fukumoto, K. Satoh, Y. Miura, K. Nochikoa, T. Aoki, S. Tatebe, S. Yamamoto, H. Shinomakaa, Tokoh University Graduate School of Medicine, Department of Cardiovascular Medicine, Sendai, Japan

Background: Pulmonary thromboendoarterectomy is an established treatment for chronic thromboembolic pulmonary hypertension (CTEPH), resulting in significant improvement in right ventricular hemodynamics. However, this surgical treatment is limited to the central-type CTEPH and is not feasible for distal-type CTEPH (dCTEPH). Indeed, dCTEPH still remains a serious condition with a poor prognosis due to the lack of effective treatment. Optical coherence tomography (OCT) is an interferometer-based imaging modality to produce a 2-D image of optical scattering from internal tissue microstructures. In the present study, in order to develop an effective and safe treatment for dCTEPH, we examined the effectiveness of our modified methods of percutaneous transluminal pulmonary angioplasty (PTPA) combined with OCT evaluation.

Methods: From July 2009 to February 2012, we prospectively enrolled 20 consecutive patients with dCTEPH, including 2 patients of post-thromboendoarterectomy with residual PH (5±17 SD) yrs, 19 females and one male, WHO-functional class III in 7, III in 8 and IV in 5). After stabilizing their condition with conventional vasodilator treatment and having defied proper treatment trials for its rarity and deadly outcome, we set out to analyze our experience of diagnosing, treatment and outcome of dCTEPH, although the procedure should be carefully performed in a step-wise manner to prevent major complications.

Conclusions: The yield of PTPA in GCM is significantly increased by repeat procedures. On combined immunosuppression two thirds of patients may reach a clinical remission.

Involvement of autoimmunity in arrhythmogenic right ventricular cardiomyopathy: serum anti- interleukin 6 receptor autoantibodies are associated with desmosomal gene mutations

A.L.P. Caforio1, E. Zachara2, F. Re3, P. Baratzia2, A. Schiavo3, G. Theiene2, S. Ilieco4, P. Syrits1, W.J. McKenna5. 1Cardiology/Dept Cardiological Thoracic and Vascular Sciences, Padua University, Padova, Italy; 2San Camillo Forlanini Hospital, Department of Cardiology, Rome, Italy; 3Special Pathological Anatomy, Dept Cardiological Thoracic and Vascular sciences, Padua University, Padova, Italy; 4University College London, Institute of Cardiovascular Science, London, United Kingdom

Purpose: Serum anti-heart autoantibodies (AHA) and anti-interleukin 6 receptor autoantibodies (AIA) are organ and disease-specific autoimmune markers in patients with inflammatory heart muscle disease and their relatives. Biopsy-proven myocarditis is frequently reported in arrhythmogenic right ventricular cardiomyopathy (ARVC) but its etiopathogenic significance remains undefined. It is also unknown whether AHA and AIA are autoimmune markers in ARVC with desmosomal gene mutations.

Methods: We assessed serum AHA and AIA in 164 ARVC patients (pts) or relatives (90 male, mean age 34±17 years, of whom 30 ARVC index pts, 110 affected relatives (AR) and 24 asymptomatic unaffected relatives (UR), ARVC pts, AR and UR met the 2010 revised ESC Task force diagnostic criteria. AHA and AIA were detected by indirect immunofluorescence on cryostat sections of the heart in pulmonary hypertension / Pathogenesis and treatment of myocarditis and inflammatory cardiomyopathies 47

Figure 1. Survival free of death or transplant
normal O blood group human myocardium and skeletal muscle, blindly from clinical and genetic diagnosis. Control groups for AHA and AHA included sera from patients with non-inflammatory cardiac disease (NICD) (n=160, 80 male, aged 37±12), with ischemic heart failure (n=141, 73 male, aged 51±12) and normal blood donors (n=270, 123 male, aged 35±11). Cascade mutation screening of five ARVC genes, e.g. plakoglobin (JUP), desmoplakin (DSP), plakophilin-2 (PKP-2), desmoglein-2 (DSG-2), desmocollin-2 (DSC-2) waslistened in 137 of the 164 pts.

Results: The frequencies of AHA and of AIDA were higher (31%; 15%) in ARVC, than in NICD (1%; 4%), ischemic heart failure (1%; 2%) or normal subjects (2.5%; 0%) (p<0.001; p<0.001 respectively). Of the 137 genotyped, 40 (29%) pts were associated with PKP-2 and DSP mutations were most frequent (19, 14% and 9, 6% respectively). Of the 137 genotyped, 40 (29%) pts were associated with PKP-2 (p=0.02), and DSP mutations (p=0.03), and with lower left ventricular ejection fraction (p=0.03).

Conclusions: The detection of serum AIDA suggests autoimmune involvement in the pathogenesis of desmosomal mutation associated ARVC.

517 Detailed histomorphologic and molecular analysis of myocarditis in the rat as an approach to identify novel molecular targets facilitating imaging of myocardial inflammation
P. Priyadarshini, X. Hellyer, Y. Ye, C. Zechmeister, K.H. Hiller, P. Jacob, M.J. Loehle, K. Klingel, R. Jahns, V. Bovin. 1. Institute of Pharmacology and Toxicology, Wuerzburg, Germany; 2. Department of Experimental Pathology, V. Wuerzburg, Germany; 3. Department of Molecular Pathology, University Hospital, Tuebingen, Germany; 4. Department of Internal Medicine I, Cardiology, Wuerzburg, Germany

Myocarditis is characterized by inflammation, myocyte necrosis/apoptosis and subsequent fibrotic replacement of heart muscle. In the human, about 30% of cases develop DCM. Because the clinical picture of myocarditis is multi-faceted, its diagnosis is difficult. We therefore screened for novel suitable tools for the detection of myocardial inflammation in acute myocarditis (EAM).

Methods: N=45 female Lewis rats were immunized with (pig) cardiac myosin (CM) emulsified in CFA and injected with heart killed B. Pertussis on days 0 and 3. Rats were boosted on days 7, 14, and 28. Myosin-antibody titers were followed by ELISA and cardiac function by echocardiography, respectively. On day 21 the animals underwent MRI (T2 or T2*/Flash sequences). Rats were sacrificed and consecutive heart sections were stained with Hematoxylin/Eosin (HE), Masson Goldner trichrome (MG), and compared with MRI findings. Mononuclear cells were detected with an anti CD-68 antibody. RNA isolated from apical cardiac tissues was screened for the expression of pro-inflammatory and pro-fibrotic markers including somatostatin and integrins alpha-v beta-3, and of genes involved in cardiac function.

Results: Sera from immunized rats strongly reacted against cardiac myosin. Echocardiography and MRI on days 18-21 revealed large pericardial effusion. MRI employing iron contrast agents (SPIO) as well as stained heart sections from immunized rats revealed massive cell infiltrates and severe fibrosis. Analysis of the time course of macrophage infiltration vs. fibrosis revealed that infiltration takes place from day 14 to 28. Disappearance of macrophages leads to replace-ment fibrosis in formerly invaded myocardial areas. This finding was confirmed by the time-dependent differential expression of cytokines in the myocardium; in particular, concordant M was found to be highly (±50-fold) up-regulated. Induced phenotypes could be categorized as an early or late phase of myocarditis. Histol-ogy correlated well with ex-vivo MRI images showing maximal infiltrates in same area and by MRI suggesting that iron particles are suitable for the detection of acute inflammation.

Conclusion: Cytokines like oncostatin M which are specifically expressed in the infiltrated heart might serve as molecular targets for the detection of acute myocarditis. Moreover, integrins alpha-v beta-3 and/or somatostatin may be labeled with nuclear tracers and detected by PET-scans. Thus, these molecular targets might serve to develop novel ligand-based MR and/or nuclear contrast agents to image myocardial inflammation in vivo.

518 Is improvement of the left ventricular systolic function in patients with new-onset dilated cardiomyopathy related to the presence of virus or inflammation in endomyocardial biopsy?
P. Kuchynka, T. Palecek, E. Nemec, T. Kovanrik, J. Hora, I. Vitkova, A. Linhart. Charles University in Prague, 1st Medical Faculty, Prague, Czech Republic

Background and aim of the study: The analysis of endomyocardial biopsy (EMB) is a useful tool in the diagnosis of myocarditis and it is currently performed as a part of the routine evaluation of patients with idiopathic dilated cardiomyopathy (DCM). However, it is the only technique that allows the identification of myocardial inflammation and infectious agents. The presence of macrophages, lymphocytes and multinucleated giant cells has been considered as a marker of myocardial inflammation. The presence of viral genome in the myocardium is associated with myocarditis. However, it is not clear whether myocardial inflammation is associated with virus persistence or with virus elimination. The aim of this study was to evaluate the presence of virus or inflammation in endomyocardial biopsy of patients with new-onset DCM.

Methods: In 35 consecutive patients (52±11 years; 28 women) with new-onset unexplained DCM (symptoms of heart failure lasting ≥ 12 months), EMB specimens were studied by immunohistochemistry and by PCR focused on detection of herpetic viruses, enteroviruses, adenoviruses, parvovirus B19 and Borella burgdorferi (Bb). LV ejection fraction (EF) was echocardiographically analyzed at baseline and after 6 months follow-up. All subjects with Bb positivity were specifically treated by ceftriaxone and not included in further analysis.

Results: Viral genome was found in 35 patients (37%) and Bb genome was present in 21 subjects (22%). Myocardial inflammation was detected in 35 pa-tients (37%), out of whom viral agent was present in 10 (11%) and Bb in 7 (7%) patients. Microbial agent and/or virus persistence were present in 30 patients with viral infection and/or myocardial inflammation and 33 subjects with negative EMB results were all treated only by conventional heart failure medical therapy. There was no significant difference between these 2 groups regarding LV EF at the time of diagnosis (EF: 28±6% vs. 29±8%; p=NS). During 6 months follow-up, LV EF significantly improved in both groups (44±10% and 42±12%, respectively; p<0.05). The degree of the LV EF improvement did not differ between the groups.

Conclusions: In more than half of the patients with new-onset DCM, myocardial inflammation and/or microbial agent persistence is present. Therefore, inflamma-tory DCM may represent a frequent cause of new-onset DCM. However, conven-tional heart failure therapy is associated with similar improvement in LV EF in patients with new-onset DCM regardless of the presence or absence of myocar-dial inflammation and/or virus persistence. This might be due to low impact of virus persistence and/or myocardial inflammation on prognosis of affected sub-jects or by underdiagnosing of inflammatory DCM by current techniques.

519 Beneficial actions of the natural triterpene oleanolic acid in an experimental model of myocarditis: a potential therapeutic role
R. Marlin, M. Hernandez2, C. Cordova2, J.C. Munoz2, J.A. Ram2, M.V. Calheiro1, M.L. Nieto Callej1, 1. University Hospital Valladolid, IClCOR, Valladolid, Spain; 2. Institute of Biology & Molecular Genetics, CSIC University of Valladolid, Valladolid, Spain; 2. University Hospital Rio Hortega, Cardiology Department, Valladolid, Spain; 3. Complutense University of Madrid, Department of Physiology, Madrid, Spain

Purpose: Myocarditis and dilated cardiomyopathy represent the acute and chronic phases of an inflammatory disease of the myocardium, for which no stan-dardized treatment is currently available. Oleanolic acid (OA), a natural triterpene widely distributed among higher plants, exhibits a variety of beneficial health prop-erties. OA is found in numerous products of the Mediterranean diet, including olive oil, and is the major component of many traditional medicinal herbs. Sev-eral experimental approaches have shown its cardioprotective actions, and re-cently, it has been proven to be effective for the treatment of Th1-cell mediated chronic inflammatory diseases, but its effect on inflammatory heart disorders has not been addressed yet. In this study, we investigated the effectiveness of OA in prevention/treatment of myocarditis in an experimental autoimmune model that mimics human myocarditis and dilated cardiomyopathy.

Methods and Results: OA was administered at the time (therapeutic, OA21) or 21 days after disease induction in BALB/c mice with a myoc-arditis-inducing peptide. At days 1 and 65 post-immunization animals were sacrificed and both blood samples and hearts were collected. The levels of functional (BNP) and inflammation (Galectin-3, IL-17, IL-6, TNF-α and IL-15) markers, as well as IgG and IgM in sera and V. Wuerzburg were detected by ELISAs. We found that, at both ad-ministration regimens, OA dramatically lessened the disease severity, which was characterized by a reduction in heart weight/body weight ratio and heart weight, suggesting a reduced myocardial edema. A reduced BNP, but also anti-cardiac myosin IgG and IgM titers, compared with the group that received no drug. Histological analysis of the heart showed that OA significantly reduced the infiltration of inflammatory cells, fibrosis and calcium deposits, whereas such effect was not found in placebo-treated EAM mice. Furthermore, levels of the pro-inflammatory and profibrotic cytokines galectin-3, IL-6, IL-17 and TNFα, in serum and heart tissue of the OA-treated EAM animals were significantly lower than of the vehicle-treated EAM mice, while anti-inflammatory IL-10 was markedly up-regulated. Collectively, these results suggest that OA ameliorates experimental autoimmune myocarditis by interfering with both the Th1/Th2/Th17 balance and the generation of cardiac-specific autoimmunity.

Conclusions: OA may be considered a molecular switch for immune responses that improves cardiac function and hence contributes to prevent the development of postmyocarditis dilated cardiomyopathy.

520 Acute myocarditis mimicking ST-segment elevation myocardial infarction: relation between electrocardiographic changes and myocardial damage as assessed by cardiac troponin I
G. Nucciar1, A. Di Chiara2, D. Miani, G. Picozzi, M. Puppazz1, G. Slavich1, D. Gasparini1, A. Proclemer, 1. Cardiovascular Department, University Hospital “Santa Maria della Misericordia”, Udine, Italy; 2. A.S.S.S. n. 3 Alto Friuli, Department of Cardiology, Terni, Italy; 3. "Division of Interventional Radiology, University Hospital “Santa Maria della Misericordia”, Udine, Italy

Purpose: Acute myocarditis (AM) may occasionally mimic ST-segment elevation myocardial infarction.
myocardial infarction (STEMI), since patients may present with chest pain, electrocardiographic (ECG) changes and cardiac troponin elevation. Scarce data are available about the clinical meaning of ECG changes in this group of patients; particularly, few is known about the relation between ECG changes and myocardial damage assessed by cardiac magnetic resonance (CMR) imaging.

Methods: 22 consecutive patients (17 males, mean age 42±10 years) with diagnosis of AM and clinical presentation mimicking STEMI were included. STEMI was ruled out by invasive coronary angiography. AM was diagnosed according to CMR “Lake Louise” criteria, when at least 2 of the following features were present: 1) regional or global myocardial oedema (increased signal intensity in T2W images); 2) hyperaemia (early gadolinium enhancement in post-contrast T1W images) and 3) myocardial necrosis with non-ischemic regional distribution (late gadolinium enhancement (LGE) in inversion recovery-prepared gadolinium-enhanced T1W images). The following ECG changes were recorded: site of ST-segment elevation, sum of ST-segment elevation (sumST), time to normalization of ST-segment elevation, evolution to T-wave inversion. The relation between ECG changes and the presence and extent of LGE, expressed as % of left ventricular (LV) mass (%LV LGE), was evaluated.

Results: ST-segment elevation was observed in inferior or infero-lateral leads in 14 (64%) patients, and in lateral or antero-lateral leads in 8 (36%) patients. SumST was 4.2±2.2 and normalization of ST-segment elevation occurred ≤24 hours from clinical presentation in 14 (64%) patients. Evolution to T-wave inversion was observed within 7 days in 16 (73%) patients. CMR showed LGE in all patients; %LV LGE was 8.7±7.0%. Topographic agreement between site of ST-segment elevation and LGE was 49%; no relation was found between SumST and %LV LGE (p=0.16). Pathology of ST-segment elevation had higher %LV LGE, compared to patients with normalized ECG (10.1±6.2% vs. 4.5±8.1%; p=0.049).

Conclusions: ECG changes poorly predict location and extent of myocardial damage in patients with AM and clinical presentation mimicking STEMI. However, ECG features, such as time to normalization of ST-segment elevation and evolution to T-wave inversion, may help to identify patients with larger area of myocardial injury.

CARDIAC MAGNETIC RESONANCE SPELLS THE FUTURE

Assessment of the warranty time of dobutamine cardiovascular magnetic resonance imaging in 3138 consecutive patients. A bi-center study focusing on wall motion and late gadolinium enhancement

S. Kelle1, E. Nagel2, A. Voss3, G. Gitsioudis4, A. Chiribiri5, C. Klein1, E. Giannitsas6, E. Fleck7, H. Katus8, G. Korosoglou9, 1German Heart Institute Berlin, Department of Cardiology, Berlin, Germany; 2King’s College London, Division of Imaging Sciences, London, United Kingdom; 3University of Heidelberg, Department of Psychology, Heidelberg, Germany; 4University Hospital Heidelberg, Department of Cardiology, Heidelberg, Germany

Purpose: To determine the prognostic value of wall motion assessment during high-dose stress followed by late gadolinium enhancement (LGE) imaging. Outcome data based on hard cardiac events defined as cardiac death and non-fatal myocardial infarction as well as ‘late’ revascularization performed ≥3 months after the scans were prospectively collected at least 6 months after DCMR.

Results: Follow-up data were available in 3138 consecutive patients (mean follow-up 3.3±1.7 years, range 0.5 and 9.7 years). Hard cardiac events occurred in 183 (5.8%) patients during the follow-up period. In 589 (18.6%) patients early revascularization was performed within 90 days after the MR-examination and 257 (8.2%) patients underwent late revascularization. Multivariable analysis showed that inducible wall motion abnormalities (WMA), LGE and resting WMA were independent predictors of hard events (hazard ratio (HR) of 6.5, 95% confidence interval (CI):4.6-9.2; 2.2, 95%CI:1.2-4.1 and 1.6; 95%CI:1.2-2.3, respectively, p<0.001 for all). Within the first 3 years of follow-up excellent outcomes were recorded for patients with normal wall motion during stress (annual hard cardiac event rate of 0.6% and revascularization rate of 1.6%). Over the following 3 years of follow-up however, annual event rates rose for both hard events and revascularization to 1.6% and 3.2%, respectively.

Conclusion: Within the first 3 years after DCMR excellent outcomes (annual hard cardiac event rate <1%) are recorded in patients with normal findings.

Long-term prognosis of adenosine perfusion cardiac magnetic resonance imaging in consecutive patients

P. Dewes, T. Waicher, D. Buckert, P. Bernhardt. University of Ulm, Faculty of Medicine, Department of Internal Medicine II-H Cardiology, Ulm, Germany

Background: Adenosine perfusion cardiac magnetic resonance imaging (CMR) has established for the detection of coronary artery disease (CAD) due to its high diagnostic accuracy. However, little is known about long-term prognosis in large consecutive patient cohorts. Aim of our prospective study was to determine long-term prognosis of adenosine perfusion CMR in consecutive patients presenting with stable angina and intermediate to high CAD risk.

Methods: 1,152 consecutive patients underwent adenosine perfusion CMR in a 1.5T whole-body CMR. After acquisition of cine sequences for the evaluation of left and right ventricular volumes and function first-pass perfusion of a gadolinium-based contrast agent (0.1 mmol/kg) was evaluated after three minutes of adenosine infusion (140 μg/kg/min) using a steady-state free-precession sequence. Ten minutes after contrast administration late gadolinium enhancement images were acquired for visualization of myocardial necrosis. All images were evaluated by two blinded observers in consensus. Patients were followed for 5 years. Primary combined end-point was defined as cardiovascular death, non-fatal myocardial infarction and stroke.

Results: Reversible perfusion deficit was diagnosed in 308 (26.7%) patients. Primary endpoint occurred in 86 patients during observation. Patients with primary endpoint had significantly more often a reversible perfusion deficit (49 [15.9%] vs. 37 [4.4%], p<0.001). Logistic regression revealed reversible perfusion deficit to be an independent predictor for occurrence of a primary endpoint (HR 3.05). In case of no perfusion deficit event-free 5-years survival was 95.6%.

Conclusion: Adenosine perfusion CMR is an independent predictor for long-term event-free survival. Patients without perfusion deficit have a low risk of event occurrence up to 5 years.

Final infarct size by cardiovascular magnetic resonance in patients with st elevation myocardial infarction predicts long-term clinical outcome

J. Loenborg1, N. Veijstrup1, H. Helbaek2, L. Holmvang3, E. Joergensen1, S. Helpesti1, K.A. Ahtarovski1, W.Y. Kim2, P. Clemmensen1, T. Engstoen1, 1Rigshospitalet - Copenhagen University Hospital, Heart Centre, Copenhagen, Copenhagen, Denmark; 2Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark

Purpose: Tailored treatment and risk assessment in patients following ST elevation myocardial infarction (STEMI) is based almost exclusively on left ventricular (LV) ejection fraction (EF). Assessment of final infarct size in addition to LVEF may improve the prognostic evaluation. Thus the purpose of this study is to evaluate the prognostic importance of final infarct size by cardiovascular magnetic resonance (CMR) in patients with STEMI.

Methods: In 309 patients with STEMI final infarct size was measured by late gadolinium enhancement CMR 3 months after initial admission. The clinical endpoint was a composite of all-cause mortality and admission for heart failure.

Results: During the follow-up period of median 807 (IQR 669-1117) days there were 35 events (5 non-cardiac deaths, 3 cardiac deaths, and 27 admissions for heart failure). Patients with final CMR infarct size ≥ median had significantly higher event rates than patients with final infarct size < median (17% versus 6%; Log rank p=0.002). In a multivariable Cox regression analysis, including age, stent implantation, peak troponin T, LVEF, LV volume index, and heart rate, final infarct size remained significantly associated with the occurrence of subsequent events (adjusted hazard ratio 1.13 per 1% increase (1.05-1.21); p=0.001). The overall Wald chi² value of a model including known risk factors was 47.3, which increased to 57.9 when final infarct size was added (p=0.001 for the difference).

Conclusion: Assessment of final infarct size by CMR 3 months after STEMI provides strong independent prognostic information incremental to known risk factors including LVEF.

Grace score and cardiac magnetic resonance for predicting cardiac events after hospital discharge in patients with ST segment elevation acute myocardial infarction


Purpose: Grace Score permits an early stratification of the risk of events in patients with ST segment elevation acute myocardial infarction (STEMI). Cardiac magnetic resonance (CMR) is the reference imaging technique for the complete non invasive characterization of the structural consequences of STEMI. Prognostic implications of a combined analysis of Grace Score and CMR to predict events after hospital discharge in STEMI patients has not been analyzed yet.

Methods: We prospectively included 461 patients admitted with STEMI. Grace Score was determined at the time of admission. CMR was carried out in the first week post-STEMI and a quantitative (% of ventricular mass) and semi-
Cardiovascular risk profile, long term survival and stress cardiac magnetic resonance imaging guided catherization. a post-hoc analysis of a natural experiment

Purpose: Stress cardiac magnetic resonance imaging (CMR) as test for coronary ischemia before catherization was still not recommended 2003. A decision on coronary angiography (CA) was based on clinical judgment (history, risk profile, exercise ECG) and optional CMR. This approach simulated a "quasi-randomization" of two diagnosis pathways (CMR/CA vs. CA).

Methods: A group of patients with CMR guided CA (CMRCA) (N=270) was compared to a matched control group of patients with CA indicated by standard evaluation (SECA) (N=654). The retrospective study included patients with suspected coronary artery disease from 2003-2004. Long term follow-up of selected hard events (death, PCI, CABG, death and number of hospital admissions were significantly different between the TEE and no-TEE cohorts [22 (1.9%) vs. 10 (0.8%)], p=0.001). Risk of events was higher in patients with >5 segments (23/296, 8% vs. 29/92, 31%, p<0.001). The extent of infarction in 0.5 or >5 segments allowed to discriminate the event risk in patients with low 1% vs. 23%, p=0.001), intermediate (10% vs. 23%, p=0.05) and high (11% vs. 46%, p<0.001) risk in Grace Score. Conclusion: Our results illustrate that for predicting events in patients with SECA clinical assessment and the use of sophisticated techniques are both useful. Grace Score permits a simple and early risk stratification that can be optimized by determining the extent of the infarction with CMR.

Cardiovascular risk profile, long term survival and stress cardiac magnetic resonance imaging guided catherization. a post-hoc analysis of a natural experiment

E. Wellhöfer, G. Petrov, S. Kern, E. Fleck, S. Kelle. German Heart Center Berlin, Berlin, Germany

Introduction: Catheter ablation of atrial fibrillation (AF) is associated with a potential peri-procedural risk of thromboembolic complications (TEC) which can occur in up to 2.5 to 5%. Transesophageal echocardiography (TEE) has been demonstrated to be a sensitive tool to detect left atrial thrombi and spontaneous contrast in patients with AF. We sought to determine if the pre-procedural anticoagulation management could reduce the risk for TEC and the need for TEE.

Methods: Data from 6 centers performing catheter ablation of AF with an open ir-reperfusion catheter were collected. In the antibiotic prophylaxis group used at the time of the procedure, patients were divided into two groups: patients undergoing ablation off Coumadin and patients undergoing ablation while on "therapeuti- cally" (INR) TEE examinations and outcome data on TEC during the peri-procedural period were collected and analyzed. Results: A total of 8265 consecutive patients were included in this study. All patients were treated with warfarin for at least 4 weeks prior to the ablation procedure. Warfarin was discontinued 3 days prior to procedure in 1716 patients, and was not discontinued in 6549 cases. TEE was performed in 1048/6549 (16%) patients who were on-warfarin compared to 1132/1716 (66%) of the off-warfarin cases (p<0.001). Overall CHADS2 score of 0, 1, and ≥2 was recorded in 43%, 38%, and 19% patients in the no-TEE group and 38%, 40% and 22% in the TEE group respectively. During the peri-procedural period 32 TEC occurred (all in the off-warfarin population). The incidence of TEC was not significantly different between the TEE and no-TEE cohorts [22 (1.9%) vs. 10 (1.7%) respectively, p=0.74]. A multivariate analysis showed that AF type (odds ratio [OR] 1.8, p=0.03), diabetes (OR 1.3, p=0.02), and pre-procedural warfarin discontinuation (OR 3.8, p=0.01) were associated with an increased risk of TEC. Conclusion: The results of our study demonstrate that performing AF ablation while on "therapeutic" warfarin, eliminate the risk for peri-procedural TEC and the need for TEE. Performing TEE prior to the ablation did not have any impact on the prevention of TEC.

Cardiovascular risk profile, long term survival and stress cardiac magnetic resonance imaging guided catherization. a post-hoc analysis of a natural experiment

533

P550

TEE in patients undergoing AF ablation while on therapeutic coumadin: is it necessary? Result from a prospective multicenter registry

L. Di Biase1, P. Santagiel2, P. Mohanty2, J.D. Burkhart3, S. Themistokleiskilias4, S. Behety5, W. Lewis6, D. Lakkireddy7, A. Dello Russo7, A. Natale7. 1Texas Cardiac Arrhythmia Institute at St David Medical Center, Univ. of Texas and University of Foggia, Austin, United States of America; 2Texas Cardiac Arrhythmia Institute at St David Medical Center, Austin, United States of America; 3Hospital "San Filippo Neri", Rome, Italy; 4Department of Cardiology, Texas A&M University System Health Science Center, Temple, United States of America; 5University of Kansas, Kansas City, United States of America; 6University of Kansas, Kansas City, United States of America; 7Texas A&M University System Health Science Center, Temple, United States of America.

Introduction: In a recent multicenter registry involving 107 centers in 17 countries, no patients underwent TEE during AF ablation while on therapeutic coumadin. In our registry, which included 93 centers, we collected data on the use of TEE during AF ablation while on therapeutic coumadin. We sought to determine if the pre-procedural anticoagulation management could reduce the risk for TEC and the need for TEE.

Methods: Patients were included in the registry if they were undergoing catheter ablation of AF with an open ir-reperfusion catheter and were on therapeutic coumadin. An independent data safety and monitoring board was established to ensure safety and to independently collect and monitor data. Results: A total of 8265 consecutive patients were included in this study. All patients were treated with warfarin for at least 4 weeks prior to the ablation procedure. Warfarin was discontinued 3 days prior to procedure in 1716 patients, and was not discontinued in 6549 cases. TEE was performed in 1048/6549 (16%) patients who were on-warfarin compared to 1132/1716 (66%) of the off-warfarin cases (p<0.001). Overall CHADS2 score of 0, 1, and ≥2 was recorded in 43%, 38%, and 19% patients in the no-TEE group and 38%, 40% and 22% in the TEE group respectively. During the peri-procedural period 32 TEC occurred (all in the off-warfarin population). The incidence of TEC was not significantly different between the TEE and no-TEE cohorts [22 (1.9%) vs. 10 (1.7%) respectively, p=0.74]. A multivariate analysis showed that AF type (odds ratio [OR] 1.8, p=0.03), diabetes (OR 1.3, p=0.02), and pre-procedural warfarin discontinuation (OR 3.8, p=0.01) were associated with an increased risk of TEC. Conclusion: The results of our study demonstrate that performing AF ablation while on "therapeutic" warfarin, eliminate the risk for peri-procedural TEC and the need for TEE. Performing TEE prior to the ablation did not have any impact on the prevention of TEC.
NT-proBNP for risk stratification in atrial fibrillation

L.C. Wallentin1, C. Christersson2, A. Siegbahn3, M. Schollin4, J.H. Alexander5, M. Harno6, E.M. Hylek2, J. Horowitz7, P.R. McMurray3, E.B. Granger4, L. Wallentin5, Uppsala University, Department of Medical Sciences, Clinical Chemistry, Uppsala, Sweden; 5University of Adelaide, Adelaide, Australia; 6Boston University Medical Center, Boston, United States of America; 7Bristol-Myers Squibb, Princeton, NJ, United States of America.

Background: Plasma NT-proBNP concentration is predictive of death and cardiovascular events in healthy elderly subjects and in patients with heart failure. We evaluated the prognostic value of NT-proBNP in patients with atrial fibrillation (AF) and investigated the interaction between NT-proBNP and the effect of treatment with apixaban versus warfarin, taking account of the CHADS2 score and other biomarkers.

Methods: The ARISTOTLE trial randomized 18,201 patients to apixaban 5 mg twice daily or warfarin. NT-proBNP and other biomarkers were measured at randomization in 14,879 patients. Efficacy and safety outcomes were compared across quartiles of NT-proBNP adjusted for the CHADS2 score and other biomarkers. Also the effect of apixaban versus warfarin was compared within NT-proBNP quartiles.

Results: There was a continuous and strong relationship between NT-proBNP concentration and stroke, mortality and major bleeding. The prognostic information provided by NT-proBNP was independent of and additive to the CHADS2 score and other biomarkers. Apixaban consistently reduced stroke, mortality and bleeding, regardless of NT-proBNP level (Table). Conclusions: NT-proBNP is an independent additional risk factor for stroke, death and major bleeding in atrial fibrillation. Apixaban led to better outcomes than warfarin, irrespective of NT-proBNP concentration.

Assessment of stroke risk in the PROTECT AF trial according to CHADS2-VASc scores and final follow-up results

S. Mobius-Winkler1, S. Schuler2, H. Siever3, P. Sick4, V. Reddy4, 1Herzzentrum Leipzig, Leipzig, Germany; 2CardioVascular Care Center Frankfurt, Klinikum Kaiserslautern, Kaiserslautern, Germany; 3CardioVascular Care Center Frankfurt, Klinikum Kaiserslautern, Kaiserslautern, Germany; 4Krankenhaus Barmherzigé Brüder Regensburg, Regensburg, Germany; 5Mount Sinai School of Medicine, New York, New York, United States of America.

Purpose: Thromboembolic stroke originating from the left atrial appendage (LAA) is a major cause of morbidity in patients with atrial fibrillation (AF). The WATCHMAN device uses a self-expanding nitinol frame covered with permeable fabric to close the LAA and prevent embolization of LAA thrombi in patients with nonvalvular AF. In the PROTECT AF trial, the WATCHMAN device was noninferior to warfarin for the prevention of stroke, CV or unexplained death, and systemic embolization at the primary endpoint of 600 patient-year (pt-yr) follow-up. Approximately 32% of patients in this study had a baseline CHADS2 score of 1, indicating intermediate stroke risk according to this score. Recently, the CHADS2-VASc score has been shown to more accurately differentiate stroke risk in AF patients than the CHADS2 score. This post-hoc analysis of the PROTECT AF trial evaluates patients according to CHA2DS2-VASc scores to better determine true stroke risk and presents final follow-up results for the study.

Methods: In PROTECT AF, patients with AF and a CHADS2 score ≥ 1 were randomized to either WATCHMAN plus warfarin or warfarin alone (control group). A total of 24,463 (92.0%) of patients in the WATCHMAN group and 23,244 (94.7%) of patients in the control group had a CHADS2-VASc score ≥ 2. Over all, 1,077/707 (15.1%) patients had a prior MI, 263,707 (37.2%) were aged 65 to 74 years, and 210/707 (29.7%) were female. After 1500 pt-yr of follow-up, the WATCHMAN group had a 29% lower rate of efficacy events compared with control (relative risk: 0.71 [95% credible interval: 0.44, 1.30]; P = 0.39). The relative risk of stroke, cardiac death, or embolization for the WATCHMAN group had a 29% lower rate of efficacy events compared with control (relative risk: 0.71 [95% credible interval: 0.44, 1.30]; P = 0.39). The relative risk of stroke, cardiac death, or embolization for the WATCHMAN group had a 29% lower rate of efficacy events compared with control (relative risk: 0.71 [95% credible interval: 0.44, 1.30]; P = 0.39). There was a strong and positive association between higher D-dimer level and increased bleeding (p < 0.0001) across all HAS-BLED score categories. The significant reduction in bleeding in apixaban as compared with warfarin was consistent regardless of D-dimer level.

Conclusions: In patients with atrial fibrillation, levels of D-dimer are strongly and independently associated with higher risk of major and clinical relevant non-major bleeding events. Compared with warfarin, apixaban caused significantly less bleeding across patients with all levels of D-dimer measured at baseline.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Biomarker level</th>
<th>All patients, N=14,879 (%)</th>
<th>HR (95% CI)</th>
<th>Q1 reference</th>
<th>Apixaban (N=7,432) (%)</th>
<th>Warfarin (N=7,436) (%)</th>
<th>Apixaban vs Warfarin HR (95% CI)</th>
<th>p-value interaction biomarker</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/SEE</td>
<td>&gt;363-713</td>
<td>84 (1.16)</td>
<td>1.14 (0.83-1.57)</td>
<td>40 (1.16)</td>
<td>40 (1.16)</td>
<td>0.90 (0.59-1.39)</td>
<td>0.602</td>
<td></td>
</tr>
<tr>
<td>&gt;363-713</td>
<td>&gt;713-1250</td>
<td>117 (1.28)</td>
<td>1.19 (1.04-1.36)</td>
<td>55 (1.28)</td>
<td>55 (1.28)</td>
<td>0.93 (0.60-1.45)</td>
<td>0.562</td>
<td></td>
</tr>
<tr>
<td>&gt;363-713</td>
<td>&gt;713-1250</td>
<td>147 (2.11)</td>
<td>1.05 (0.82-1.33)</td>
<td>75 (2.11)</td>
<td>75 (2.11)</td>
<td>0.82 (0.59-1.13)</td>
<td>0.668</td>
<td></td>
</tr>
<tr>
<td>&gt;363-713</td>
<td>&gt;713-1250</td>
<td>157 (2.12)</td>
<td>1.05 (0.83-1.32)</td>
<td>82 (2.12)</td>
<td>82 (2.12)</td>
<td>0.86 (0.62-1.20)</td>
<td>0.319</td>
<td></td>
</tr>
<tr>
<td>&gt;363-713</td>
<td>&gt;713-1250</td>
<td>145 (2.03)</td>
<td>0.98 (0.78-1.24)</td>
<td>66 (1.83)</td>
<td>66 (1.83)</td>
<td>0.83 (0.60-1.15)</td>
<td>0.228</td>
<td></td>
</tr>
<tr>
<td>Major bleed</td>
<td>&gt;363-713</td>
<td>363 (5.49)</td>
<td>2.89 (2.40-3.51)</td>
<td>23 (3.63)</td>
<td>23 (3.63)</td>
<td>0.75 (0.44-1.28)</td>
<td>0.9593</td>
<td></td>
</tr>
<tr>
<td>&gt;363-713</td>
<td>&gt;713-1250</td>
<td>335 (4.90)</td>
<td>1.68 (0.95-2.94)</td>
<td>157 (2.12)</td>
<td>157 (2.12)</td>
<td>0.86 (0.59-1.20)</td>
<td>0.5362</td>
<td></td>
</tr>
<tr>
<td>&gt;363-713</td>
<td>&gt;713-1250</td>
<td>1250 (17.98)</td>
<td>1.30 (1.05-1.60)</td>
<td>363 (5.49)</td>
<td>363 (5.49)</td>
<td>0.70 (0.58-0.85)</td>
<td>0.051</td>
<td></td>
</tr>
</tbody>
</table>

p-value adjusted for CHADS2-VASc score.
Effect of apixaban on all-cause mortality in atrial fibrillation: an imputed placebo analysis

J.J.V. McMurray, S.J. Connolly, R. Hart, G. Flaker, R.D. Lopes, J. Wang, M. Hanna, J.H. Alexander, C.B. Granger, L. Wallentin on behalf of ARISTOTLE Investigators. 1University of Glasgow, Glasgow, United Kingdom; 2Population Health Research Institute, McMaster University, Hamilton, Canada; 3University of Texas at San Antonio, San Antonio, United States of America; 4University of Missouri, Columbia, United States of America; 5Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; 6Bristol-Myers Squibb, Princeton, United States of America; 7Uppsala University, UCR-Uppsala Clinical Research Center, Uppsala, Sweden

Purpose: ARISTOTLE demonstrated the superiority of apixaban over warfarin in preventing stroke or systemic embolism (SEE). ARVERDO showed the superiority of apixaban over aspirin in preventing SEE. We used a meta-analysis of earlier warfarin vs. placebo/control (P/C), and aspirin vs. P/C, trials to make an indirect comparison between apixaban and P/C on mortality.

Methods: The meta-analysis of Hart et RG, Pearce LA, Aguilar MI (Ann Intern Med 2007) included 6 warfarin vs. P/C trials (n=2000 patients) and 7 aspirin vs. P/C trials (n=8895). The method of Bucher HC, Guyatt GH, Griffith LE, Walter SD (J Clin Epidemiol 1997) was used to make an indirect comparison of odds ratios (OR).

Results: The meta-analysis reported 143 deaths (in 1450 patients) on P/C and 110 deaths (1450 pts) on warfarin. OR 0.74 (0.57, 0.97). In ARISTOTLE there were 9081 pts in warfarin and 603 deaths (9120 pts) on apixaban, OR 0.89 (0.79, 0.99). An indirect comparison of apixaban with P/C gives an estimated apixaban/placebo OR for death of 0.66 (0.50, 0.88), p<0.004. The meta-analysis reported 204 deaths (1993 pts) on P/C and 184 deaths (1902 patients) on aspirin. OR 0.86 (0.69, 1.07). In ARVERDO, there were 140 deaths (2791 pts) on aspirin and 111 deaths (2807 pts) on apixaban, OR 0.79 (0.62, 1.02). Not a significant difference of apixaban with P/C gives an estimated apixaban/placebo OR for death of 0.66 (0.53, 0.82), p=0.0002 (Figure).

Conclusions: This imputed placebo analysis suggests that apixaban significantly reduces all-cause mortality by about one third in patients with AF.

A comparison of the HAS-BLED and ATRIA bleeding scores for predicting serious bleeding events in a large “real world” anticoagulated atrial fibrillation population

P555

J.P. Bassand1, I.Müller2, L.G. Mantovani3, S. Haas4, S.Z. Goldhaber5, S. Golb6, G.Y.H. Lip7, S.K. Rushton-Smith7, A.K. Kakkad1 on behalf of The GARFIELD Investigators. 1Université de Besancon - Hospital Jean Minjoz, Besancon, France; 2Thrombosis Research Institute, London, United Kingdom; 3University of Naples Federico II, Naples, Italy; 4Technical University of Munich, Munich, Germany; 5Harvard Medical School, Brigham and Women’s Hospital, Department of Medicine, Boston, United States of America; 6Tokai University, Kanagawa, Japan; 7University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

Objective: To describe the use of antithrombotic therapy in relation to the definition of risk for stroke in patients across various age groups in everyday clinical practice.

Methods: The first cohort of the GARFIELD registry enrolled 10,627 patients with AF who were on steady OAC for at least 6 months (INR 2.0-3.0). During a median follow-up of 952 (IQR: 785-1071) days, all bleeding events were recorded. Bleeding events were deemed serious as defined based on the 2005 ISTH criteria. Both HAS-BLED and ATRIA scores were calculated based on medical history; and were compared as quantitative (per point) or as dichotomized (low-moderate vs high risk) variables. Model performance was evaluated by calculating c-statistics, and the improvement in predictive accuracy was evaluated using net reclassification improvement (NRI) and integrated discrimination improvement (IDI).

Results: HAS-BLED and ATRIA scores were 2 (IQR: 2-3) and 3 (IQR: 1-3), respectively. During the follow-up, 77 (8.29%) patients had a serious bleeding event [annual rate 3.2%], including 15 intracranial haemorrhages (annual rate 0.6%), 45 gastrointestinal bleeds (annual rate 1.8%) and 9 bleeding-related deaths (annual rate 0.24%). HAS-BLED score showed a slightly superior model performance to ATRIA bleeding score as dichotomized as quantitative variable. The NRI were 14% (as quantitative) and 19% (as dichotomized), whereas the IDI was 7% for both analyses (all p<0.05). The probability of correctly predicting serious bleeding events using the HAS-BLED was particularly reflected in the percentage of events correctly reclassified.

Conclusions: In anticoagulated AF patients, HAS-BLED shows significantly better prediction ability than the (more complex) ATRIA score. Our findings reinforce the incremental utility of the HAS-BLED score over other bleeding risk scores in patients with AF.

Antithrombotic treatment patterns for stroke prevention in relation to age: insights from the Global Anticoagulant Registry in the FIELD (GARFIELD)

P557

J.P. Bassand1, I. Mueller2, L.G. Mantovani3, S. Haas4, S.Z. Goldhaber5, S. Golb6, G.Y.H. Lip7, S.K. Rushton-Smith7, A.K. Kakkad1 on behalf of The GARFIELD Investigators. 1Université de Besancon - Hospital Jean Minjoz, Besancon, France; 2Thrombosis Research Institute, London, United Kingdom; 3University of Naples Federico II, Naples, Italy; 4Technical University of Munich, Munich, Germany; 5Harvard Medical School, Brigham and Women’s Hospital, Department of Medicine, Boston, United States of America; 6Tokai University, Kanagawa, Japan; 7University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

Background: Atrial fibrillation (AF) management guidelines and risk scores define age ≥75 years as a major risk factor and 65-74 years as a clinically relevant, non-major risk factor. Oral anticoagulation (OAC) is recommended for AF patients at moderate to high risk of stroke and without contraindications.

Aim: To describe the use of antithrombotic therapy in relation to the definition of risk for stroke in patients across various age groups in everyday clinical practice.

Methods: The first cohort of the GARFIELD registry enrolled 10,627 patients at
over 500 sites randomly selected from lists representative of National AF care settings and geographies. Eligible patients are ≥18 years old, newly diagnosed with non-valvular AF, with ≥1 additional investigator-determined stroke risk factor, not limited to risk factors included in existing risk scores. Risk score stratification used the baseline patient characteristics captured to assign a CHADS2 score to each patient enrolled.

Results: Data from 10,504 AF patients from cohort 1 were available; 8.5% had a CHADS2 score of 0, 36.3% a score of 1 and 55.2% a score ≥2. In patients at low risk for stroke, total use of OACs increased in patients aged ≥65 years. In patients at high risk for stroke the use of OACs was highest in the group aged 65-74 years (72.1%) and lowest in the group aged ≥75 years (66.5%).

Table 1. Antithrombotic use according to age group and CHADS2 score: cohort 1 data

<table>
<thead>
<tr>
<th>Age group (years)</th>
<th>CHADS2 score 0 or 1</th>
<th>CHADS2 score ≥2</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;65</td>
<td>66 (74)</td>
<td>83 (79)</td>
</tr>
<tr>
<td>≥65</td>
<td>60 (79)</td>
<td>85 (79)</td>
</tr>
<tr>
<td>CHADS2 score 0 or 1 (n=4700)</td>
<td>CHADS2 score ≥2 (n=892)</td>
<td></td>
</tr>
</tbody>
</table>

OACs only 41.1% 48.6% 48.8% 50.8% 51.9% 51.8% 10.1% 11.7% 10.3% 17.6% 20.2% 14.7%
OACs + antiplatelets (APs) 51.2% 60.3% 59.1% 68.4% 72.1% 66.5% 30.5% 26.0% 25.0% 20.6% 19.9% 23.1%
Neither 18.4% 13.8% 15.9% 11.0% 8.0% 10.4% 18.4% 13.8% 15.9% 11.0% 8.0% 10.4%

Conclusions: These observational data suggest that OAC use is influenced by risk for stroke and by age. Total OAC use is more frequent in high-risk than in low-risk patients in all age groups. In patients at low risk, total OAC use is least frequent in the age group <65 years, whereas in patients at high risk total OAC use is least frequent in the group aged ≥75 years.

High sensitivity troponin-T (hs-TnT) for risk stratification in atrial fibrillation during treatment with apixaban or warfarin

L.C. Wallentin1, C. Christersson2, A. Siegbahn3, M. Schollin4, J.J.V. McMurray9, C.B. Granger5. 1Uppsala Clinical Research Center, Department of Medical Sciences, Uppsala, Sweden; 2Uppsala University, Department of Medical Sciences, Clinical Chemistry, Uppsala, Sweden; 3Uppsala University, UCR-Uppsala Clinical Research Center, Uppsala, Sweden; 4Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; 5Mayo Clinic, Rochester, United States of America; 6Bristol-Myers Squibb, Princeton, NJ, United States of America; 7Bristol-Myers Squibb, Princeton, United States of America; 8McGill University, Montreal, Canada; 9Karolinska Institute, Danderyd Hospital, Department of Cardiology, Stockholm, Sweden

Purpose: Several risk stratification schemas for bleeding have been proposed but some of them are based on complex scoring systems that are difficult to apply in clinical practice. In AF we have few validated risk schemas. The purpose of this study was to evaluate the predictive value of risk stratification schemas in a real life cohort of patients with AF.

Table 1. Outcome in relation to hs-TnT ng/L

<table>
<thead>
<tr>
<th>hs-TnT level</th>
<th>Outcome</th>
<th>N=18,201</th>
<th>N=14,269</th>
<th>N=94,175</th>
<th>N=182,678</th>
<th>N=227,595</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/SEE</td>
<td>≥1.5</td>
<td>70 (0.88)</td>
<td>69 (0.84)</td>
<td>61 (0.67)</td>
<td>56 (0.63)</td>
<td>39 (0.68)</td>
</tr>
<tr>
<td>Death</td>
<td>≥1.5</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
</tr>
<tr>
<td>All patients</td>
<td>≥1.5</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
</tr>
</tbody>
</table>

Conclusions: Hs-TnT is an important additional risk factor for stroke, death and major bleeding in atrial fibrillation. The benefits with apixaban are maintained across different hs-TnT levels.

How well are atrial fibrillation (AF) patients in the real world represented in the Contemporary Novel Oral Anticoagulant (NOAC) AF trials?

T. Simon1, H.-Y. Huang2, R. Kawabata3, A. Azoulay2, L. Friberg2, S. Suissa4, S. Benedict5, M. Schollin6, J.J.V. McMurray9, C.B. Granger5. 1Uppsala Clinical Research Center, Department of Medical Sciences, Uppsala, Sweden; 2City Hospital, Centre for Cardiovascular Medicine, Uppsala, Sweden; 3National Hospital, Department of Cardiology, Tokyo, Japan; 4Département des sciences de l’information, Hôpital de la Salpetrière, Université Paris 7, France; 5Mayo Clinic, Rochester, United States of America; 6McGill University, Montreal, Canada; 7Karolinska Institute, Danderyd Hospital, Department of Cardiology, Stockholm, Sweden

Purpose: Baseline data of AF patients in NOAC trials compared to real world AF patients.

Methods: AF patients identified in 4 RCT data sources were compared to AF patients in 3 contemporary RCT studies (ARISTOTLE, RE-LY and ROCKET-AF) by baseline characteristics including CHADS2 risk score. Data sources: General Practice Research Database (GPRD) in the UK, the Swedish Hospital Discharge Register, claims data from I3 Invision Data Mart and PharmiMetRx in the US.

Results: Descriptive results show that the RW populations have a higher proportion of <75 years and slightly more females compared to the RCTs. Similar CHADS2 scores (except ROCKET-AF) were observed between the RCTs and RW data. 2-fold more AF patients in the RCTs had a history of hypertension, and a higher use of beta blockers and statins. More RCT patients had a prior stroke.

Table 1. Randomized Clinical Trials vs. Real World Observational Cohorts

<table>
<thead>
<tr>
<th>Therapy</th>
<th>ARISTOTLE</th>
<th>RE-LY</th>
<th>ROCKET-AF</th>
<th>GDPRD</th>
<th>General Practice Research Database</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (%)</td>
<td>18,201</td>
<td>18,113</td>
<td>14,269</td>
<td>94,175</td>
<td>182,678</td>
</tr>
<tr>
<td>Mean age (yrs)</td>
<td>70</td>
<td>71.5</td>
<td>73.1</td>
<td>71.1</td>
<td>75.9</td>
</tr>
<tr>
<td>Female (%)</td>
<td>38</td>
<td>40</td>
<td>41.2</td>
<td>41.2</td>
<td>46.5</td>
</tr>
<tr>
<td>Prior stroke (%)</td>
<td>31</td>
<td>44</td>
<td>47</td>
<td>44</td>
<td>66.6</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>87</td>
<td>79</td>
<td>90</td>
<td>80</td>
<td>74.6</td>
</tr>
<tr>
<td>Beta blocker (%)</td>
<td>63</td>
<td>53</td>
<td>65</td>
<td>65</td>
<td>63.2</td>
</tr>
<tr>
<td>Statins (%)</td>
<td>45</td>
<td>44</td>
<td>43</td>
<td>29</td>
<td>26.2</td>
</tr>
</tbody>
</table>

Conclusions: Females and ≥75 yrs are under-represented in the RCTs. I3 and PharmiMetRx under-represent those ≥50 and older so the differences in the RW may be greater than represented here. Beta blockers are used substantially more in the RCTs. The drug use rates are lower in the RW cohorts despite fairly similar conditions, which may be an indicator of less adequate treatment in the RW. Some differences observed between the studies may be due to differences in how conditions were defined. As new therapies come to market, comparative effectiveness studies will be executed. Evaluating baseline data including co-morbid conditions and concomitant medications will be important as we assess the benefits and potential risks of NOACs in the RW.

Predicting bleeding risk in patients with atrial fibrillation: comparison of several risk scores in a real world community based cohort study

I. Lagrenade1, L. Fauchier1, S. Tsaillinder1, A. Bernard1, N. Clementy1, E. Simon1, G.Y.H. Lipt1, D. Babuty1, 2 Tours Regional University Hospital, Hospital Toulouse, Tours, France; 3City Hospital, Centre for Cardiovascular Sciences, Birmingham, United Kingdom

The risk of bleeding in patients with atrial fibrillation (AF) is not homogeneous. Several risk stratification schemas for bleeding have been proposed but some of them are based on complex scoring systems that are difficult to apply in clinical practice. In AF, a few have been validated for risk assessment. The purpose of this study was to evaluate the predictive value of risk stratification schemas in a real life cohort of patients with AF.

Results: Of the 5 tested schemas, the HAS-BLED score performed best in multi-

Abstract P558 – Table 1. Outcome in relation to hs-TnT ng/L

<table>
<thead>
<tr>
<th>hs-TnT level</th>
<th>Outcome</th>
<th>All patients (N=14979)</th>
<th>N=182,678</th>
<th>N=18,113</th>
<th>N=14,269</th>
<th>N=94,175</th>
<th>N=4702</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stroke/SEE</td>
<td>≥1.5</td>
<td>30 (0.74)</td>
<td>40 (1.02)</td>
<td>40 (1.02)</td>
<td>32 (0.97)</td>
<td>37 (1.11)</td>
<td>31 (0.74)</td>
</tr>
<tr>
<td>Death</td>
<td>≥1.5</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
<td>116 (1.1)</td>
</tr>
<tr>
<td>All patients</td>
<td>≥1.5</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
<td>287 (4.3)</td>
</tr>
</tbody>
</table>

Conclusions: Our study findings suggest that hs-TnT is an important additional risk factor for stroke, death and major bleeding in atrial fibrillation. The benefits with apixaban are maintained across different hs-TnT levels.

HR adjusted for CHADS2 score.
High sensitivity cardiac troponin T and interleukin-6 predict adverse cardiovascular events and mortality in anticoagulated patients with chronic atrial fibrillation

V. Roidl1, F. Marini2, J. Diaz3, E. Jover2, S. Manzano-Fernandez4, 5, J. Romera1, T. Casas2, V. Vicente1, G.Y. Lip1  
1University General Hospital Morales Meseguer, Murcia, Spain; 2Hospital Universitario Virgen de la Arrixaca, Murcia, Murcia, Spain; 3City Hospital, Centre for Cardiovascular Sciences, Birmingham, United Kingdom; 4Amsterdam, Netherlands; 5Harvard Medical School, Brigham and Women's Hospital, Boston, United States of America; 6Technical University of Munich, Munich, Germany; 7University Hospital Jean-Minjoz, Besançon, France.

Atrial fibrillation: antithrombotic treatment and beyond

Methods: In this worldwide registry, patients with newly diagnosed AF will be enrolled in 5 sequential prospective cohorts in up to 1000 sites and 50 countries. The first cohort includes a retrospective validation group. Eligibility criteria include age ≥18, HR=2.7, 95%CI 1.96-3.78; p<0.0001) and in those not treated with anticoagulation (intermediate risk, HR=2.52, 95%CI 1.59-3.98; p<0.0001). By multivariate analyses, significant predictors of bleeding were age 65 years or older (hazard ratio [HR]: 1.67, 95%CI 1.40-2.00; p<0.0001); renal impairment (HR: 1.57, 95%CI 1.30-1.92; p=0.003); previous bleeding (HR: 1.46, 95%CI 1.13-1.86; p=0.003); anemia (HR: 2.01, 95%CI 1.26-3.21; p<0.003); concurrent aspirin or NSAID use (HR: 1.28; p=0.003); male sex (HR: 1.26, 95%CI 1.07-1.47; p=0.005) and heart failure (HR: 1.32, 95%CI 1.13-1.54; p<0.0004).

Conclusions: This analysis identifies male sex and heart failure as potential risk factors for bleeding in AF beyond those previously recognized in patients with AF. Of the contemporary bleeding risk stratification schemes, the new HASE-BLED scheme offers useful predictive capacity for bleeding over previously published schemes and may be simpler to apply.

Cost-effectiveness of apixaban versus other novel oral anticoagulants (NOACs) for stroke prevention in atrial fibrillation patients

1University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom; 2St. Michael’s Hospital, Toronto, Canada; 3Bristol Myers Squibb, Princeton, NJ, United States of America; 4Pfizer, Inc., New York City, NY, United States of America; 5Pfizer, Inc., New York City, NY, United States of America; 6Bristol Myers Squibb, Wallingford, CT, United States of America; 7St. Michael’s Hospital, Toronto, Canada.

Purpose: Apixaban (5 mg SID) is a factor Xa inhibitor studied in trials of stroke prevention in atrial fibrillation compared to warfarin and aspirin. Two other novel anticoagulants (NOACs) are dabigatran, a direct thrombin inhibitor (available as 150 mg BD and 110 mg BD in Europe) and rivaroxaban (20mg QD). This study evaluated the cost effectiveness of apixaban against other NOACs from the UK National Health Services (NHS) perspective.

Methods: A Markov model was developed to evaluate the clinical and economic impact of apixaban versus other NOACs over lifetime from a payer perspective.

Conclusions: These observational data from real-world practice suggest low rates of OAC use in patients with paroxysmal AF across all CHADS2 risk groups. A notable proportion of patients at low risk of stroke received OAC therapy. These data highlight discrepancies between clinical practice patterns and guideline recommendations.

Patterns of antithrombotic therapy and type of atrial fibrillation: insights from the Global Anticoagulant Registry in the FIELD (GARFIELD)

1Garon Medical, Toulouse, France; 2University of Tokyo, Japan; 3University of Tokyo, Tokyo, Japan; 4University of Amsterdam, Amsterdam, Netherlands; 5Harvard Medical School, Brigham and Women’s Hospital, Department of Medicine, Boston, United States of America; 6Technical University of Munich, Munich, Germany; 7University Hospital Jean-Minjoz, Besançon, France.

Background: Oral anticoagulation (OAC) is recommended for all patients with atrial fibrillation (AF) at moderate to high risk of stroke and without contraindications, irrespective of type of AF. We sought to compare rates of antithrombotic use according to CHADS2 score and type of AF in an international cohort of patients from the Global Anticoagulant Registry in the FIELD (GARFIELD).

Conclusions: Based on the results of CE model, apixaban will be the cost-effective alternative to dabigatran 150 mg BD, dabigatran 110 mg BD and rivaroxaban 20 mg QD.

Effective alternative to dabigatran 150 mg BD, dabigatran 110 mg BD and rivaroxaban 20 mg QD.
Background: Guidelines for the management of atrial fibrillation (AF) recommend strategies for the treatment of patients with AF and acute coronary syndrome (ACS) that defers who should receive triple therapy (VKA, ASA, and Clopidogrel). Our study aims to show how guidelines are implemented in Berlin, which complications occur, and whether new antithrombotic drugs are being used in everyday practice.

Method: A total of 795 patients with all types of AF (first diagnosed, paroxysmal, persistent, long-standing persistent, permanent) and ACS were included between April 2008 and 30 June 2011. The CHA2DS2-VASc score and data on the HAS-BLED score were collected for each patient.

Results: In 510 (out of 795) patients, a stent was implanted (n=179 DES; n=331 BMS), 62 received a PTCA, and 223 experienced no intervention. Patients treated with a BMS stent were older (79.5 vs. 74.6 years, p < 0.001). Women (48.8% vs. 36.3%, p=0.001), and suffered from previous stroke more often (15.5% vs. 11.9%, p=0.001) than men. There were no statistically significant differences in other risk factors. The prevalence of LA thrombus at TOE was 0.59% (48.7%) at preablation TOE, whereas another 31 patients received conventional therapy with enoxaparin. All subjects were underwent TEE before cardioversion in order to examine LAA contractile function. In enoxaparin group anticoagulation therapy included LA/LAA thrombi. Second TEE was performed 7–10 days after cardioversion.

Conclusions: In fully anticoagulated patients prevalence of LA thrombus at TOE is low but not negligible (2.2%). Current recommendations on preablation TOE do not guarantee patient’s safety. Preablation TOE could be safely avoided only in patients with a CHA2DS2-VASc score of 0. This choice reduces the utilization of TOE in more than 4% of candidates to AF catheter ablation.

### Antithrombotic treatment of patients with atrial fibrillation and acute coronary syndrome: Results from the AfibACS Registry (as part of the Berlin Myocardial Infarction Registry)

S. Behrens, C. Hegerbarth, B. Maier, E. Braun, H. Schulz, R. Schoeller, H. Schuhlen, H. Theres on behalf of BMR, 1 Vivantes Humboldt Hospital, Berlin, Germany; 2 Vivantes Myocardial Infarction Registry at TU Berlin, Berlin, Germany; 3 Humboldt Hospital, Berlin, Germany; 4 Vivantes Auguste-Viktoria Hospital, Berlin, Germany; 5 Charite - University Medicine Berlin, Campus Mitte, Berlin, Germany

Background: Guidelines for the management of atrial fibrillation (AF) recommend antithrombotic treatment at discharge for patients with AF and acute coronary syndrome (ACS) and define who should receive triple therapy (VKA, ASA, and Clopidogrel). Our study aims to show how guidelines are implemented in Berlin, which complications occur, and whether new antithrombotic drugs are being used in everyday practice.

Method: A total of 795 patients with all types of AF (first diagnosed, paroxysmal, persistent, long-standing persistent, permanent) and ACS were included between April 2008 and 30 June 2011. The CHA2DS2-VASc score and data on the HAS-BLED score were collected for each patient.

Results: In 510 (out of 795) patients, a stent was implanted (n=179 DES; n=331 BMS), 62 received a PTCA, and 223 experienced no intervention. Patients treated with a BMS stent were older (79.5 vs. 74.6 years, p < 0.001). Women (48.8% vs. 36.3%, p=0.001), and suffered from previous stroke more often (15.5% vs. 11.9%, p=0.001) than men. There were no statistically significant differences in other risk factors. The prevalence of LA thrombus at TOE was 0.59% (48.7%) at preablation TOE, whereas another 31 patients received conventional therapy with enoxaparin. All subjects were underwent TEE before cardioversion in order to examine LAA contractile function. In enoxaparin group anticoagulation therapy included LA/LAA thrombi. Second TEE was performed 7–10 days after cardioversion.

Conclusions: In fully anticoagulated patients prevalence of LA thrombus at TOE is low but not negligible (2.2%). Current recommendations on preablation TOE do not guarantee patient’s safety. Preablation TOE could be safely avoided only in patients with a CHA2DS2-VASc score of 0. This choice reduces the utilization of TOE in more than 4% of candidates to AF catheter ablation.

### Efficacy and safety of short-term anticoagulation after cardioversion in atrial fibrillation patients with low thromboembolic risk

D.V. Regushhevskaya, M.Y.U. Giljaron, N.A. Novkova, V.P. Sedov, I. M, Sechenov First Moscow State Medical University, Cardiology Clinic, Moscow, Russian Federation

Background: Patients with AF lasting more than 48 h required anticoagulants prior to and after cardioversion. The short-term postcardioversion anticoagulation (STPA) with low molecular weight heparin (LMWH) can decrease the risk of bleeding and does not require regular INR monitoring. Objective: The purpose of our study was to evaluate the efficacy and safety of STPA with second postcardioversion TEE and the evaluation of thrombosis markers such as D-dimers and soluble fibrin monomer complexes (SFMC) in patients with persistent nonvalvular AF.

Methods: 62 patients with AF lasting more than 48 h and low risk (the CHA2DS2-VASc score ≤ 1) were included. The exclusion criteria were acute thrombosis or thromboembolism; intimal hemorrhage; gastrointestinal bleeding or acute peptic ulcer within previous 3 months; urgent cardioversion; contradictions to TEE, to LMWH or oral anticoagulant. 30 patients were treated with enoxaparin 1 mg/kg subcutaneously twice a day 24 h before and 7 days after cardioversion, whereas another 31 patients received conventional therapy with warfarin. All subjects were underwent TEE before cardioversion in order to exclude LA/LAA thrombi. Second TEE was performed 7–10 days after cardioversion to examine LAA contractile function. In enoxaparin group anticoagulation therapy was discontinued if LAA emptying velocity was > 25 sm/s (in absence of ‘atrial stunning’), otherwise patients received warfarin for 3 weeks. In some patients prior to and 7 days and 1 month after cardioversion blood samples was taken for D-dimers and SFMC assays. The follow-up period was 1 month.

Results: Subjects in both groups were similar with respect to demographic, clinical, and echocardiographic characteristics. Efficacy of anticoagulation was similar in both groups during the study period. Conclusions: STPA with LMWH in AF patients with low thromboembolic risk is effective and safe thromboprophylaxis regimen and is not inferior to conventional warfarin therapy. In case of “atrial stunning” with LAA emptying velocity > 25 sm/s and higher risk of thromboembolic events prolonged anticoagulation is essential.
Quality of anticoagulation and bleeding and thrombotic risk in relation to CHADS2 score: analysis of the AF cohort of EPICA study

D. Polo1, E. Anttonen2, C. Cenci3, O. Padletti4, W. Ageno4, S. Apostolakis1, D.A. Lane1, H. Buller2, G.Y.H. Lip1. 1City Hospital, University Department of Medicine, Haemostasis Thrombosis and Vascular Biology Group, Birmingham, United Kingdom; 2Department of Vascular Medicine, Academic Medical Centre, Amsterdam, Netherlands

Purpose: The quality of anticoagulation expressed as time in therapeutic range (TTR) is associated with both bleeding and thrombotic events during vitamin K antagonists treatment. It is unknown if TTR in patients with Atrial Fibrillation (AF) is related to their baseline stroke risk.

Aim of this study is to evaluate TTR in relation to CHADS2 score in the AF cohort of EPICA Study (1).

Methods: We defined patients with TTR>60% as adequately anticoagulated. We calculated the distribution of patients with TTR>60% and the rate of bleeding and thrombotic events in relation to CHADS2 score.

Results: We studied 2015 AF patients (males 45%, median age 63 years, range 80-102 (70-102) years). The total quality of anticoagulation measured as TTR was 31.7% ± 33.4% (median = 55%). In total 251 (11%) safety and 60 (2.6%) efficacy endpoints occurred. The quality of anticoagulation decreased by tertile of serum creatinine (Cr) (Cr >30 ml/min vs. 30-60 ml/min vs. <30 ml/min): HR 95% CI<0.001 (2.35 1.83); 1.54 (1.09-2.19); 0.76 (0.52-1.14) respectively, t=2.9, p=0.004). However, TTR was not independently associated with the highest Cr tertile compared to the middle/lowest tertiles (55% vs. 52% vs. 59%, p=0.2% vs. 58% vs. 58%, respectively) (IQR for TTR= 50-75%). During follow-up 132 major bleeding and 112 thrombotic events were recorded. The distribution of patients with TTR ≥60% and bleeding and thrombotic events in relation to CHADS2 score is reported in table 1.

Conclusions: As expected, the rate of major bleedings and of thrombotic events increased with CHADS2 score. Instead, no difference in the quality of anticoagulation is found in relation to CHADS2 score.

Table 1. Hazard ratios for stroke and SE

<table>
<thead>
<tr>
<th>CHADS2 tertile</th>
<th>TTR&gt;60% (%)</th>
<th>P value</th>
<th>Bleeding events (rate per 100 pt-yrs)</th>
<th>Thrombotic events (rate per 100 pt-yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>41.1</td>
<td>&lt;0.001</td>
<td>21 (1.50)</td>
<td>9 (0.85)</td>
</tr>
<tr>
<td>2</td>
<td>44.9</td>
<td>0.85</td>
<td>38 (1.40)</td>
<td>32 (0.85)</td>
</tr>
<tr>
<td>3</td>
<td>43.8</td>
<td>&lt;0.001</td>
<td>52 (1.70)</td>
<td>26 (1.36)</td>
</tr>
<tr>
<td>4</td>
<td>38.2</td>
<td>0.29</td>
<td>27 (2.40)</td>
<td>20 (2.62)</td>
</tr>
<tr>
<td>5</td>
<td>39.4</td>
<td>0.29</td>
<td>9 (0.30)</td>
<td>13 (3.32)</td>
</tr>
<tr>
<td>6</td>
<td>31.7</td>
<td>0.29</td>
<td>5 (4.80)</td>
<td>3 (2.91)</td>
</tr>
<tr>
<td>total</td>
<td>42.6</td>
<td>0.1</td>
<td>122 (1.73)</td>
<td>112 (1.47)</td>
</tr>
</tbody>
</table>

TTR = time in therapeutic range.

Renal function and outcomes in anticoagulated patients with non-valvular atrial fibrillation: the AMADEUS trial

S. Apostolakis1, D.A. Lane1, H. Buller2, G.Y.H. Lip1. 1City Hospital, University Department of Medicine, Haemostasis Thrombosis and Vascular Biology Group, Birmingham, United Kingdom; 2Department of Vascular Medicine, Academic Medical Centre, Amsterdam, Netherlands

Purpose: The quality of anticoagulation expressed as time within therapeutic range (TTR) is time spent within the target therapeutic INR range (2.0 to 3.0). This randomized controlled trial (ISRCTN8992605) examined the effect of an intensive educational intervention on TTR among AF patients initiating warfarin compared to usual care.

Methods: Warfarin-naive AF patients were randomised (stratified by age, sex and centre (specialist vs. non-specialist)) to receive the intervention, consisting of group sessions (2-8 patients) with therapeutic drug monitoring and integrated information on warfarin, educational booklet, “expert-patient” focused DVD, and worksheets, or usual care (warfarin clinic). Primary endpoint was TTR, assessed by Rosendaal Foundation’s LABO-CHEK device.

Results: 97 patients were recruited: intervention [n=43; mean (SD) age 72.5 (7.4) years, 29 men; median (IQR) CHADS2 score 2 (1-3)] and usual care [n=54; mean (SD) age 74.3 (8.7) years, 34 men; median (IQR) CHADS2 score 2 (1-3)] (see Table). No significant demographic or clinical differences at baseline between the groups were evident. Patients receiving the intensive educational intervention had significantly higher TTR compared to those receiving usual care (78.5% vs. 66.7%, p<0.001). Patients receiving usual care spent significantly more time with sub-therapeutic INRs.

Table 1. Intensive educational intervention improves time in therapeutic range in atrial fibrillation patients initiating warfarin: results from the TREAT study

<table>
<thead>
<tr>
<th>Mean (SD) or (n,%)</th>
<th>Intervention (n=43)</th>
<th>Usual care (n=54)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at baseline, years</td>
<td>72.5 (7.4)</td>
<td>73.2 (8.7)</td>
<td>0.67</td>
</tr>
<tr>
<td>Years in education</td>
<td>11.1 (2.7)</td>
<td>11.2 (2.4)</td>
<td>0.82</td>
</tr>
<tr>
<td>Median (IQR) CHADS2 score</td>
<td>3 (2 to 1)</td>
<td>2 (1 to 3)</td>
<td>0.29</td>
</tr>
<tr>
<td>Overall TTR</td>
<td>78.5 (69.9 to 86.5)</td>
<td>66.7 (68.7 to 74.6)</td>
<td>0.01</td>
</tr>
<tr>
<td>TTR ≥3.0</td>
<td>10.2 (7.8 to 12.6)</td>
<td>13.2 (11.3 to 15.6)</td>
<td>0.42</td>
</tr>
<tr>
<td>TTR ≥2.0</td>
<td>13.3 (7.7 to 16.9)</td>
<td>23.1 (15.8 to 30.4)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

TTR = time within therapeutic range; IQR = inter-quartile range; SD = standard deviation.

Conclusions: Intensive education can improve TTR in AF patients and potentially help improve clinical outcomes. Improving education provision for AF patients is essential to ensure efficacious treatment.

Independent predictors of mortality in patients with non-valvular atrial fibrillation: results from ROCKET AF

J.P. Piccirilli1, S. Stevens1, M.R. Patel1, D.E. Singer2, G. Breithardt3, G.J. Hankey4, J.L. Halperin5, K.W. Mahaffey6, K.A.A. Fox7, R.M. Califf1 on behalf of ROCKET AF Executive Committee. 1Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; 2Harvard Medical School, Massachusetts General Hospital, Boston, United States of America; 3Hospital of the University of Munster, Munster, Germany; 4Royal Perth Hospital, The University of Western Australia, Perth, Australia; 5Mount Sinai Medical Center, New York, United States of America; 6University of Edinburgh and Royal Infirmary of Edinburgh, Edinburgh, United Kingdom; 7Duke Translational Medicine Institute, Duke University Medical Center, Durham, United States of America

Purpose: Identifying risk factors for mortality may help guide interventions in AF.

Methods: Patients with non-valvular AF were randomized to rivaroxaban or dose-adjusted warfarin. Cox proportional hazards regression was used to identify factors associated with all-cause mortality. Adjusted predictors were associated with all-cause mortality (p<0.01) (see Table). Results: See Table 1 (p.57). Median age was 73; mean CHADS2 was 3.5. Over a median follow-up of 1.94 yrs, 1214 (8.6%) pts died. Of these, median age was 76, mean CHADS2 was 3.6, 48% had prior stroke/TIA, 18% were on insulin/other diabetes medications, 16% were on statins, 24% were on beta-blockers. Independent predictors of increased mortality were increasing age, diabetes, hypertension, left ventricular systolic dysfunction and CHADS2. The C-index 0.677 (0.67-0.68) at 12 months was 0.67 (0.66-0.68) at 2 years, and 0.68 (0.67-0.69) at 3 years, and 0.69 (0.68-0.70) at 5 years. Results: The C-index 0.677 (0.67-0.68) at 12 months was 0.67 (0.66-0.68) at 2 years, and 0.68 (0.67-0.69) at 3 years, and 0.69 (0.68-0.70) at 5 years. Results: The C-index 0.677 (0.67-0.68) at 12 months was 0.67 (0.66-0.68) at 2 years, and 0.68 (0.67-0.69) at 3 years, and 0.69 (0.68-0.70) at 5 years.

Table 1. Hazard ratios for stroke and SE

<table>
<thead>
<tr>
<th>HR</th>
<th>95% CI</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Creatinine tertiles</td>
<td>0.008</td>
<td></td>
</tr>
<tr>
<td>Creatinine tertiles (86-102 umol/L)</td>
<td>2.6</td>
<td>1.2-5.7</td>
</tr>
<tr>
<td>Creatinine tertiles (≥102 umol/L)</td>
<td>3.3</td>
<td>1.5-7.3</td>
</tr>
</tbody>
</table>

Model adjusted for age, sex, previous stroke or transient ischaemic attack, hypertension, left ventricular systolic dysfunction and diabetes. SE, systemic embolism; HR, hazard ratio; CI, confidence interval.
Safety and efficacy of switching to antiplatelet agent at 3 months after successful catheter ablation of atrial fibrillation

J.S. Uh1, G.B. Nam2, H.S. Mun1, J. Wi1, J. Shim1, H.J. Hwang1, B. Joung1, M.H. Lee1, H.N. Pac1, Y. Nerses University, Severance Hospital, Seoul, Korea, Republic of;1Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea, Republic of

Introduction: The current guidelines for anti-thrombotic treatment are equal before and after successful radiofrequency catheter ablation (RFCA) of atrial fibrillation (AF). However, warfarin has a significant risk of major bleeding. Therefore, we evaluated safety and the strategy switching from warfarin to anti-platelet agent (APLT) regardless of CHADS2 score after confirming no AF recurrence at 3rd month after procedure.

Methods: Among 706 patients (age, 56.6±11.1; male 77.1%; paroxysmal AF 67.9%; persistent AF 32.1%, CHADS2 score, 0.9±1.0) those did not show clinical recurrence after RFCA, 358 patients were assigned into switching from warfarin to APLT group; CHADS2 score 0.8±1.0 and 350 patients into conventional anti-thrombotic strategy according to CHADS2 score (Conv group; CHADS2 score 0.9±1.0, p=0.708). We compared thromboembolic risk, major hemorrhage risk, and event of overall stroke.

Results: 1. During 12.1±5.8 months follow-up, one patient in APLT group (0.28%) and 4 patients in Conv group (1.14%) developed major thrombotic or hemorrhagic events (p=0.542). 2. In APLT group, a patient with CHADS2 score 4 had transient ischemic attack (TIA) without neurologic sequelae. Eighty-four patients returned to warfarin because of AF recurrence during follow-up period. 3. In Conv group, 2 patients experienced ischemic stroke/TIA (CHADS2 scores 2 and 4) and 2 patients developed intra-cranial hemorrhage (HAS-BLED score 2) and gastrointestinal bleeding (HAS-BLED score 4). There was no major thrombotic or hemorrhagic event in patients with CHADS2 score 0-1 in both groups.

Conclusions: Switching to APLT after successful AF ablation might be a relatively safe and effective anti-thrombotic strategy reducing major hemorrhagic risk in patients with low CHADS2 score and high HAS-BLED score. However, strict rhythm monitoring for AF recurrence is mandatory.

Adding left atrial function to CHADS2. CHADS2-VASc score improve predicting power for thromboembolic risk in atrial fibrillation

M.N. Kim1, D.H. Cho1, S.A. Kim1, Y.H. Kim2, J.I. Choi1, S.M. Park1, S.W. Park1, Y.H. Kim1, W.J. Shim1, Y. Kim1, Y. Kim1, S.K. Korea University, Anam Hospital, Seoul, Korea, Republic of;2Korea University Ansan Hospital, Ansan-Si, Korea, Republic of

Background: CHADS2 and CHADS2-VASc score are used for evaluation of embolic risk in atrial fibrillation(AF) patients. The left atrial(LA) function is an important factor for embolism in AF. The aim of this study was to evaluate the predictive power of CHADS2 and CHADS2-VASc score for presence of SEC and thrombus and by combining LA functional parameters to CHADS2, CHADS2-VASc score can improve predicting power for embolic risk in AF patients.

Methods: 365(M=305, mean age=55±10.4) patients with non-valvular AF who had taken trans-thoracic ecochardography and trans-esophageal ecochardography were included. Seoul, Korea. CHADS2 and CHADS2-VASc scores were calculated. LA volume, LA emptying fraction(EF), LA emptying velocity, LAA EF and the presence of SEC and thrombus were evaluated.

Results: SEC was present in 102 patients and LA thrombus in 2 patients. AUC of CHADS2 and CHADS2-VASc score for the presence of SEC and thrombus were 0.588 and 0.576, respectively(P-value=0.002 and 0.002). Combining the increased LAVI(LAVI=30m/m²) and impaired LAEF(LAEF<25%) with CHADS2 and CHADS2-VASc score showed improved predictive power in detecting SEC and thrombus in LAVI(Table 1). Further, in clinically low risk patients with 0 and 1 CHADS and CHADS2-VASc score, the presence of LA dysfunction and increased LAVI volume was associated with the presence of SEC and thrombus(Odd ratio=9.46 and 5.66, 95%CI=5.26-17.03 and 9.02-9.99, P-value <0.001 and <0.001 respectively).

Conclusion: CHADS2-VASc score may improve the predictive value of presence of SEC and thrombus, especially in clinically low risk group. In clinic, anti-coagulation may be considered to prevent embolism in patients with low risk score when they have LA dysfunction.

Abstract P576 – Table 1

Parameter CHS* square CHADS2 CHADS2-VASc CHADS2-VASc + LAVI CHADS2-VASc + LAEF CHADS2-VASc + LAEF + LAVI

AFP 0.588 0.586 0.639 0.005

LAEF≤30% 0.706 0.670 0.753 -0.001

CHADS2-VASc addition 0.576 0.536 0.630 -0.016

LAEF≤30% 0.674 0.613 0.755 -0.001

P576 Anti-thrombotic therapy and atrial fibrillation in Scotland: results of a national audit

J. Simpson1, I.N. Findlay2, M. Demeni3, D.L. Murdoch1, 1Southern General Hospital, Glasgow, United Kingdom; 2Royal Alexandra Hospital, Paisley, Glasgow, United Kingdom; 3Western General Hospital, Edinburgh, United Kingdom

Introduction and Methods: GP practices across Scotland were invited to participate in an audit of the management of atrial fibrillation (AF) as part of a national audit of Clinical Standards in Heart Disease by Health Improvement Scotland. A primary care database interrogation tool was developed to identify patients with AF, extract relevant data and calculate a CHADS2 score for each patient.

Results: 248 practices with a total practice population of 1,376,834 contributed data. 19,470 patients with AF were identified (prevalence 1.4%) including 18,165 patients with non-valvular AF. The majority of patients with non-Valvular AF (56%) were in a high risk group for stroke (CHADS2>2) and the most prevalent risk factors overall were age≥75 (75%) and hypertension (56%). Formal stroke risk assessment was rarely recorded in primary care (<1%). 79% of patients with AF were prescribed some form of anti-thrombotic therapy, either anti-platelet or warfarin (Table). In patients with non-Valvular AF who had a prior history of ischaemic stroke or TIA, less than half (44%) were on warfarin.

Anti-thrombotic use by CHADS2 score

Stroke risk Number of patients with AF (% of total) Number of patients with AF on anti-platelet (% of group) Number of patients with AF on warfarin (% of group)

CHADS2 0 3158 (18%) 1019 (32%) 791 (25%)

CHADS2 1 5320 (28%) 2039 (38%) 1829 (35%)

CHADS2 2 9016 (50%) 3778 (39%) 3967 (42%)

Conclusion: In Scotland, patients with AF are not receiving anti-thrombotic therapy according to guidelines. Patients at high risk of stroke are undertreated with warfarin and those at low risk of stroke are over prescribed warfarin. Strategies to improve appropriate anti-coagulant use in this group include routine use of simple stroke risk stratification.

Increased prevalence of anxiety and depression in atrial fibrillation patients following oral anti-coagulant treatment initiation

D.E. Smith, H.M. Patterson, G.Y.H. Lip, D.A. Lane on behalf of University Centre for Cardiovascular Science. Center for Cardiovascular Sciences, Birmingham, United Kingdom

Purpose: Evidence suggests atrial fibrillation (AF) confers an increased risk of psychological morbidity, particularly anxiety, which may affect the subsequent management and treatment adherence. Few studies have studied psychological factors over time in AF patients.

Method: Warfarin-naive AF patients were followed up for 6 months after commencing warfarin. Anxiety and depression, and quality of life (QoL) were assessed at baseline, 1, 2 and 6 months using the Hospital Anxiety and Depression Scale (HADS) and AF-QoL, respectively.

Results: 97 patients (mean (SD) age 72.9 (2.2) years, 63 men; median (IQR) CHADS2 score 2 (1-3)) were recruited. Median anxiety and depression scores increased significantly between baseline and 1 month (p<0.001) and remained elevated over the 6-month period. The prevalence of depression presented in Table 1. The prevalence of depression presented in Table 1. The prevalence of anxiety significantly increased between baseline and 1 month (p<0.001) and remained elevated over the 6-month period. The prevalence of depression presented in Table 1. The prevalence of anxiety significantly increased between baseline and 1 month (p<0.001) and remained elevated over the 6-month period. The prevalence of anxiety significantly increased between baseline and 1 month (p<0.001) and remained elevated over the 6-month period. The prevalence of anxiety significantly increased between baseline and 1 month (p<0.001) and remained elevated over the 6-month period.

Conclusion: Anxiety and depression levels increased significantly following commencement of warfarin. Standardised psychological screening at warfarin clinics
**Net clinical benefit of apixaban among patients with atrial fibrillation**

P. Ristler1, R. Nieuwlaat2, D.A. Lane3, H.J.G.M. Crijs3, G.Y.H. Lip3,
1University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom
2Thrombosis Research Institute, London, United Kingdom
3University of Birmingham, Centre for Cardiovascular Sciences, City Hospital, Birmingham, United Kingdom

**Purpose:** Atrial fibrillation (AF) increases stroke risk, warranting oral anticoagulation (OAC) in high-risk patients. Vitamin K antagonists, previously the only OAC, were commonly underutilised, partly due to inconveniences. We therefore evaluated the theoretical impact on clinical outcomes by apixaban, a new OAC, in Europe.

**Methods:** Based on a large European prospective cohort we identified all high-risk (CHA2DS2-VASc score ≥2) patients with non-valvular AF and known one-year follow-up. First, occurrence of stroke/TIA, major bleeding and all-cause mortality were stratified according to antithrombotic regimen. The expected numbers of clinical events on apixaban were modelled using published hazard ratios from ARISTOTLE and AVERROES. Subsequently we calculated the numbers needed to treat (NNT) and harm (NNH).

**Results:** Analyses included 2,485 patients [mean (SD) age 71 (10) years; 1193 (48%) females; mean (SD) CHA2DS2-VASc score 3.6 (1.3)]. During one-year follow-up, 82 (3.3%) patients experienced thromboembolism, 46 (1.9%) major bleeds and 154 (6.2%) died. Table 1 displays event rates, NNT and NNH, by antithrombotic therapy. Overall, use of apixaban would have potentially prevented an additional 15 deaths, 36 strokes and simultaneously lowered the number of major bleeds to 11 within this cohort. Extrapolation to all European AF patients would translate into the annual prevention of 24,378 deaths, 59,762 strokes per year and 5,531 major bleedings.

**Cost-effectiveness of dabigatran etexilate versus warfarin for stroke prevention in patients with non-valvular atrial fibrillation under the public and private healthcare system in Brazil**

V.D. Nasiben1, L. Giangrande1, L. Piega5, M. Figueiredo3, F. Darieux5, S. Martins5, Bethine Gerinheil, Sao Paulo, Brazil
1Institute Dante Pazzanese of Cardiology, Sao Paulo, Brazil
2Unicamp - State University of Campinas, Department of Cardiology, Campinas, Brazil
3Heart Institute (InCor) - University of Sao Paulo Faculty of Medicine Clinics Hospital (HC-FMUSP), Sao Paulo, Brazil
4Federal University of Rio Grande do Sul - Hospital Clinicas of Porto Alegre, Porto Alegre, Brazil

**Objectives:** To compare costs and effectiveness of dabigatran etexilate (DAB) versus warfarin (WAR) in patients with Non-Valvular Atrial Fibrillation (NVAF) from a private and public health care system perspective in Brazil.

**Methods:** A Markov model was built to compare DAB versus WAR to derive the incremental cost effectiveness ratio (ICER) of DAB (150 mg BID or 110 mg BID), based on the international literature and a modified Delphi panel with Brazilian experts (local clinical practice pattern on the management of NVAF patients) assuming in the model a hypothetical population considering similar profile of the RELY trial. The model estimated the number of ischaemic and haemorrhagic strokes, systemic embolisms, intracranial hemorrhages, transient ischaemic attacks, extracranial hemorrhages, minor bleeds and acute myocardial infarctions associated with the respective treatments. To each clinical event costs, disabilities and/or reduction in quality of life, and risk of death were assigned. Only direct medical costs were considered and a discount rate of 5% was assumed, according to Brazilian HTA guidelines. A probabilistic sensitivity analysis was designed to assess uncertainty.

**Results:** Under both, the private and public perspective, DAB was associated with additional 0.30 life years gained (LY) (9.42 life year for DAB versus 9.11 life years for WAR), additional 0.35 OALYs (7.25 QALYs for DAB versus 6.91 QALYs for WAR) and demonstrated a lower incidence of intracranial events versus WAR, resulting in lower event costs ($4,030.31 for DAB versus $4,829.38 for WAR) in the public health care system and $8,767.99 for DAB versus $11,539.30 for WAR in the private healthcare system and follow-up costs ($8,549.87 for DAB versus $9,530.77 for WAR in the public healthcare system and $16,275.83 for DAB versus $19,444.25 for WAR in the private healthcare system). The ICER for DAB versus WAR was $37,740/QALY ($25,252.48/LY and $22,160.20/QALY from the private perspective). Sensitivity analyses confirmed the cost-effectiveness of DAB.

**Conclusion:** Findings suggest DAB can be cost-effective for stroke prevention when used instead of WAR in NVAF patients in Brazil, given that the ICERS were below the threshold of other technologies reimbursed.
pendage (LAA) dysfunction and thrombi in patients with persistent nonvalvar atrial fibrillation (AF).

**Methods:** Transesophageal echocardiography (TEE) were performed in 229 non-valvular patients: mean age 64.1±11 yrs; cohort 1) examined with a second generation dual-source computed tomography (Somatom Definition Flash) prior to AF ablation between August 2010 and July 2011. Amount of contrast media for cardiac CT angiography was individually adapted to the test bolus and a high-pitch scanning protocol was used. A reduced voltage of 100 kV instead of standard 120kV was used for all non-obese patients (weight <90 kg or a body-mass-index <30 kg/m²).

**Results:** The control cohort consisted of 622 patients (mean age 60±10 yrs) who were examined prior to AF ablation between October 2006 and June 2009 with DSCT and TEE (cohort 2). The body-mass-index did not significantly differ between cohorts 1 and 2 (27.5±4.36 vs. 27.4±4.36; p=0.710).

**Results:** The prevalence of LAA-thrombi was 0.3% in cohort 1 and 0.5% in cohort 2.

In cohort 1, 53% of patients were in atrial tachyarrhythmia with a mean heart rate of 74±22 bpm during the CT scan. In cohort 2, 51% of patients were in atrial tachyarrhythmia with a mean heart rate of 66±20 bpm during the CT scan. The percentage of false positive CT scans was significantly lower in cohort 1 compared to cohort 2 (3.7% vs. 10.8%; p=0.001).

Radiation dose was significantly lower in cohort 1 than in cohort 2 (1.57±0.67 vs. 2.79±3.25mSv; p=0.0001).

**Conclusion:** Dual-source computed tomography with an optimized contrast-protocol and high-pitch scanning improves specificity for detection of LAA-thrombi and significantly reduces radiation dose among patients prior to AF ablation.

---

**P581**

**Predictors of left atrium appendage clot detection despite on-target warfarin prevention for atrial fibrillation**

F. Zoppo, G. Brandolino, N. Frigato, M. Micheletto, A. Zanocco, F. Zerbo, E. Bacchiesia, A. Lupo, E. Bertaglia. Dept of Cardiology, Milan, Italy

**Introduction:** The antithrombotic management in atrial fibrillation (AF) is currently based on CHADS2 or CHA2DS2VASC scores. The prevalence of left atrium (LA) thrombus in AF patients has been reported up to 10%. We tried to correlate LAA appendage (LAA) thrombus detection with clinical predictors, in warfarin patients.

**Methods and Results:** A cohort of 430 study patients (mean age 60.3±9.8 years), all on oral anticoagulant (OAC) and undergoing PVI was assessed with transesophageal echo (TEE).

In 10/430 (2.3%) an LA thrombus was found despite therapeutic OAC (mean INR 2.6±1.1, mean CHA2DS2VASC 3.29±1.4). Estimated risk by physicians was divided in low risk 30.1%, moderate 40.3% and high 29.6%. Disturbance for CHADS2 was low 9.9%, moderate 29.6% and high 60.5%. The number of embolic events was 29 (3.8%) with median follow up of 1119 days, anticoagulants were divided in low dose 30%, moderate 40.3% and high 29.6%. Disturbance for CHADS2 was low 9.9%, moderate 29.6% and high 60.5%.

In further 42/430 (9.8%) patients an LA spontaneous echo-contrast (SEC) was detected. Thus, cumulatively 52/430 (12.1%) study patients were found to have both LAA thrombi or SEC. The LA size continued to predict also both the thrombi and SEC presence (OR 1.19 95% CI. 1.07-1.48; p=0.006) predicted LA thrombosis.

**Conclusions:** We found a 2.3% prevalence of LAA thrombi (up to 12.1%) in AF patients suitable for PVI. The thrombus was present despite on-target warfarin prevention. The LA size was the single predictor of the LAA thrombi and 55.6% of SEC 4+ were revealed in the first case of the persistent AF episode.

**Conclusions:** Therefore we concluded that although high CHADS2 or CHA2DS2VASC score may be useful also for prognostics of LAA disturbances in patients with persistent nonvalvar AF, performing of TEE even in cases with low CHADS2 or CHA2DS2VASC score is of importance for more complete stroke risk estimation.

---

**P582**

**Dual-Source cardiac computed tomography for the detection of left atrial appendage thrombus prior to left atrial ablation: Improved specificity and reduced radiation dose by optimized contrast- and scan protocol and high-pitch scanning improves specificity for detection of LAA-thrombus and significantly reduces radiation dose among patients prior to AF ablation.**

C. Jilck, S. Lob, T. Meyer, S. Ammar, T. Reents, S. Fichtner, J. Hausleiter, C. Kolb, G. Hessling, I. Deisenhofer. German Heart Center, Hospital rechts der Isar at the Technical University of Munich, Munich, Germany

**Purpose:** Dual-source computed tomography (DSCT) is used for characterization of pulmonary vein ostia prior atrial fibrillation (AF) ablation. In previous studies, thrombi in the left atrial appendage (LAA) were detected with DSCT with a high negative-predictive value of 99-100 but a low specificity of around 90%.

The objective of the study was to prospectively determine if dual-source technology with high-pitch scanning and a specific contrast-protocol optimized for detection of LAA-thrombi improves specificity and significantly reduce radiation dose.

**Methods:** A total of 353 patients (mean age 64±11 yrs; cohort 1) were examined with a second generation dual-source computed tomography (Somatom Definition Flash) prior to AF ablation between August 2010 and July 2011. Amount of contrast media for cardiac CT angiography was individually adapted to the test bolus and a high-pitch scanning protocol was used. A reduced voltage of 100 kV instead of standard 120kV was used for all non-obese patients (weight <90 kg or a body-mass-index <30 kg/m²).

**Results:** Patients with a LAA that showed complete filling with contrast media were considered as free from thrombus whereas patients LAA filling defects were examined with transesophageal echocardiography the same day to confirm or rule out an LAA thrombus.

**Conclusions:** Physicians showed similar performance in comparison with established risk scores.
Individual approach to antithrombotic management in non-valvular atrial fibrillation patients undergoing electrical cardioversion

G.V. Dyak1, S.A. Pravosudovich2, L.I. Vasileva2, O.S. Kataslykova2, S. Sapoznychenko2, N.F. Anosova2,1
1Dnipropetrovsk State Medical Academy, Hospital Therapy #2, Dnipropetrovsk, Ukraine; 2Regional Clinical Center of Cardiology and Cardiovascular Surgery Dnipropetrovsk, Dnipropetrovsk, Ukraine

Purpose: The goal of the study was to evaluate the prevalence and characteristics of left atrial appendage (LAA) and right atrial appendage (RAA) thrombi in non-valvular atrial fibrillation (NVAF) patients undergoing transesophageal echocardiography (TOE) before electrical cardioversion (ECV); to determine the relation-ship of CHADS2-VASc score with atrial appendages thrombi; to evaluate the importance of TOE-guided strategy of oral anticoagulant (OAC) therapy before ECV.

Methods: A total of 112 patients with NVAF, who underwent TOE before ECV, were included in the study.

Results: The mean age of participants was 60.5±0.9 years. 72% were men. 60.7% of patients had arterial hypertension, 6.2%-coronary artery disease (CAD), 26%-CAD and arterial hypertension, 7%-cardiomyopathy, 60.7%-were obese. The mean term of last AF episode was 5.2±1.3 months. The majority of the patients (67.8%) fell into the high-risk group as CHA2DS2-VASc score ≥2. 27.7% were in the moderate-risk group and 4.5% had CHA2DS2-VASc score of 0. Transesophageal echocardiography (TTE) TOE were done in all patients after at least 3 weeks of effective OAC therapy. Precedence cardioversion TOE depicted LAA/RAA thrombi in non-valvular atrial fibrillation (NVAF) patients undergoing transesophageal echocardiography (TOE) before electrical cardioversion (ECV); to determine the relationship of CHADS2-VASc score with atrial appendages thrombi: to evaluate the importance of TOE-guided strategy of oral anticoagulant (OAC) therapy before ECV.

Conclusions: In patients with Px AF, the source of vWF appears to be limited to the atrial endocardium. In patients with Ps AF, both atrial endocardium and vascular endothelium are the main sources of vWF. These findings suggest specific thrombo-embolic risk patterns in patients with different clinical forms of AF. High LA levels of vWF in both Px and Ps AF patients could explain the similar risk of stroke observed in these patients.

Methods: Our study shows, that prevalence of LAA and RAA thrombi is very low. In the majority of the patients (67.8%) fell into the high-risk group as CHA2DS2-VASc score ≥2 had significantly higher vWF levels compared to patients at low and intermediate risk (CHA2DS2-VASc score = 0) in Px AF group (p = 0.02). In the AF group, subjects at high risk of stroke (CHADS2-VASc score ≥ 2) had significantly higher vWF levels compared to patients at low and intermediate risk (CHADS2-VASc score = 0) (12±5.9 μU/mL vs. 10±3.9 μU/mL, p = 0.04).

Conclusions: In patients with Px AF, the source of vWF appears to be limited to the atrial endocardium. In patients with Ps AF, both atrial endocardium and vascular endothelium are the main sources of vWF. These findings suggest specific thrombo-embolic risk patterns in patients with different clinical forms of AF. High LA levels of vWF in both Px and Ps AF patients could explain the similar risk of stroke observed in these patients.

Methods: Although left atrial (LA) thrombus associated with paroxysmal atrial fibrillation (PAF) is a major risk factor of thromboembolism, the difference of coagulation activity between the LA and systemic circulation is still unclear. The aim of this study was to clarify the relationship between coagulation activity in the LA, systemic coagulation activity, and LA remodeling in patients with PAF.

Results: Ablation procedures were performed in 25% patients with continuous AF, in 25%/25%/50% of patients. There were no differences regard to age, gender, CHADS2 score were associated with AF recurrence (odds ratio [OR] 1.45, 95% confidence interval [CI] 1.16-1.81, P = 0.001), and conversion to permanent AF during AAD (OR 1.64, 95% CI 1.04-2.69, P = 0.03).

Conclusions: CHADS2 score is a useful scheme not only for risk stratification of thromboembolism, but also for outcome of AAD in patients with paroxysmal AF.

Methods: We conducted a case-match analysis considering the variables age, gender, body mass index, creatinine levels, left atrium dimensions, type of arrhythmia. Between May 2010 and January 2012 LAAPs were performed in 27 patients of Dabigatran. Periprocedural anticoagulation therapy (Heiden) heparin doses adjusted for the body weight (and time of procedure) and evaluation for ischemic strokes and bleeding complications were conducted in all participants.

Results: In the Dabigatran group baseline ACT was higher (140.19±41.67 vs 106.79±28.61, P < 0.001). Furthermore less heparin was needed to achieve an ACT between 250 and 300s (796.52±411.94 vs 1067.63±285.01, P = 0.007). One patient under Dabigatran had a perioperative thromboembolic stroke and recovered partially after 13 days follow-up. No major hemorrhagic complications occurred. Minor bleeding complications (gastrointestinal hematomata) occurred in 2 patients on Dabigatran and in 4 patients with continuous warfarinization.
Influence of CYP2C9 gene polymorphism on warfarin efficacy in Uzbek patients with long term atrial fibrillation


Purpose: To study of *2 and *3 polymorphisms of CYP2C9 gene and its carriage association with warfarin induced hypocoagulation in Uzbek patients with atrial fibrillation (AF).

Methods: Study included 92 patients of both sexes (60.5% males) in the age from 38 to 76 years (average age 60.7±9.02 years) with long lasting (5.2±1.6 month inaverage) AF, having not less than 2 risk factors of thromboembolic complications on CHADS2/VASc and have not previously received warfarin. Warfarin was prescribed in addition to basic therapy in initial dose of 2.5-5.0mg/day with control on INR, International Normalized Ratio (INR), Hypocoagulation noted in INR<3. Identification of allelic variants of CYP2C9 variant performed using PCR-RFLP technique.

Results: After genotyping on CYP2C9*2 polymorphism it was revealed that 85 patients (91.4%) have homozgyous CYP2C9*1/*1, genotype, CYP2C9*1/*2 heterozygous genotype 7 patients (7.3%) and 1 (1.08%) patient has CYP2C9*2/*2 homozgyous genotype. Referring to CYP2C9*3 polymorphism it was found that all 92 patients have homozgyous genotype CYP2C9*1/*1.

In 77 patients, who received warfarin less than 3 months, the efficacy and safety of anticoagulation therapy in accordance with carriage of allelic variants of CYP2C9 have been investigated. All patients were divided into two groups: 1st group consisted of 70 patients (65.7% males) having homozgyous genotype by "wild type" allele regarding both CYP2C9*2 and CYP2C9*3 polymorphism. 2nd group included 7 patients (66.6% males) with CYP2C9*1/*2 and CYP2C9*2/*2 genotypes. Both groups did not significantly differ by age, sex and prescribed therapy. The hypocoagulation was noted during 3 months after starting warfarin in 36 (51.42%) patients in the 1st group and in 6 (85.71%) patients in the 2nd one (p=0.057). However patients from 1st group received higher doses of warfarin, required for maintain of proper level of INR in compare with the patients from 2nd group (3.19±0.1 mg/day vs. 2.33±0.63 mg/day, p=0.05).

Conclusions: 1. Genotyped Uzbek patients with AF in most cases have no CYP2C9*3 (95%) neither CYP2C9*2 (100%) polymorphism. 2. The maintenance dose of warfarin was significantly lower in carriers of CYP2C9*2 allele in compare with patients with "wild type" allele carriers. In patients with carriage of CYP2C9*2 allele the hypocoagulation occurred more frequently in compare with patients with "wild type" allele carriers.

Atrial fibrillation: anhytrombothic treatment and beyond / Atrial fibrillation: solving complex problems

A. Sinha, Magadh Hospital and Indira Gandhi Institute of Medical Sciences, Patna, India

Purpose: Proper data is available from Patna, India on AtrialFibril-lation (AF). Most of the informations are from the west, which has diferent predisposing factors and management. Goal of the study is to know lowest details of predisposing conditions and etiological factors and also the difference in treatment status the problem of anti coagulation.

Method: From single centre at Patna, India, patients of AtrialFibrillation were enrol-led from 2008 to 2011. Age varied from 15 to 88 years. The peak incidence was in 70 to 80 years and male female ratio was 55/45%. Patientcharacteristics such as African origin and Atrial Fibrillation, mean age for AF were 40 years, 45% male) in 6 countries, reporting results of a screening program to identify AF. Participants were recruited either from general practitioner (GP) practices, outpatient clinics or community advertisements, and were ≥60 years in 7 trials, ≥60 years in 3, >45 years in 1, and ≥40 years in 3. The age criterion was not reported in 3 trials. Screening methods for AF varied between trials and included 12- or single-lead ECG, and pulse palpation. Prevalence of AF was 3.54% (95% CI, 3.36-3.73%), Overall incidence of previously unknown AF, reported in 12 trials (n=25,466), was 1.43% (CI, 1.21-1.58%). Community advertised programs (4 trials, n=13,379) identified a similar incidence (1.49%, CI 1.29-1.71%) to screening in GP outpatient clinics (8 trials, n=12,087) incidence 1.36% (CI, 1.16-1.58%) (p<0.3). In those with known AF, a significant treatment gap was identified between those eligible for OAC (61%) and those being treated with OAC (31%) (p<0.001), however OAC status was only reported in six trials.

Conclusions: Screening for AF in the community identified 1.4% with previously undiagnosed AF. Many of those identified would be eligible for, and would benefit from OAC to prevent stroke. Given this incidence, community AF screening strategies could potentially reduce the overall health burden associated with AF.
Degree of atrial structural remodeling determines improvement in ejection fraction after catheter ablation for atrial fibrillation in patients with left ventricular systolic dysfunction

M. Aikawa, K. Higuchi, M. Koopman, K. Damal, N. Burgon, C. McGann, N. Marrouche. University of Utah, Comprehensive Arrhythmia Research and Management Center, Salt Lake City, United States of America

Background: Restoration of sinus rhythm by catheter ablation in patients with atrial fibrillation (AF) promises to be an effective therapy to simultaneously improve left ventricular (LV) systolic function, however it is unclear as to which patients may benefit from this therapy. We assessed the improvement in LV ejection fraction (EF) in patients with different stages of atrial structural remodeling.

Methods: One hundred-five patients with impaired LV systolic function (LVEF <50%) who underwent an LGE-MRI prior to ablation for AF were included in this retrospective analysis. We quantified left atrial fibrosis using LGE-MRI and grouped patients into four stages based on the percentage of fibrosis (minimal=<5%, mild=5%–20%, moderate=20%–35 and extensive=>35%). LVEF was determined both prior to and 3 months following pulmonary vein ablation with posterior wall and septal debunking.

Results: The average pre-ablation LVEF in patients with minimal fibrosis (n=3) was 41.7±5.8, 38.3±7.6 in patients with mild fibrosis (n=48), 41.2±9.1% in patients with moderate fibrosis (n=39) and 39.9±8.7% in patients with extensive fibrosis (n=15; P=0.45). While the overall average increase in LVEF following ablation was 11.3±8.4%, greatest increase was seen in patients with less extensive LA fibrosis (minimal=5.3±7.6% and mild=14±8.5%). Patients with moderate and extensive fibrosis had a comparable EF improvement of 9.6±8.0%, and 5.9±6.0%, respectively.

Conclusion: Organized and non-organized fibrillary wave patterns may be recognized on surface ECG in AF patients. Organized pattern predicts a higher probability of conversion to sinus rhythm and is associated with higher voltage and longer duration of the P wave. These findings suggest that organized pattern could be related to atria with better electromechanical properties compared to those with the non-organized pattern.

Characteristics of atrial fibrillation ablation in routine practice: In-hospital results of a French registry of more than 1000 procedures

F. Anselme1, J-P. Cebron2, D. Pavlin3, F. Halimi4, P. Defaye5, K. Gardaye1, S. Boveda1, J-P. Aimari6, 1University Hospital of Rouen, Rouen, France; 2Newoules Cliniques Nantaises (NCN), Nantes, France; 3University Hospital of Rennes - Hospital Pontchaillou, Department of Cardiology and Vascular Disease, Rennes, France; 4Paoli-Calmettes Medical Surgical Center (CMC), Le Chesnay, France; 5University Hospital of Grenoble, Department of Cardiology, Grenoble, France; 6Clinic Pasteur of Toulouse, Toulouse, France

Purpose: This atrial fibrillation (AF) ablation registry was conducted in order to describe the current epidemiology of patients undergoing AF ablation, the techniques used and the results obtained in routine practice in France. We report here the in-hospital data.

Methods: Data were prospectively collected in 6 medium-high volume French centers. All consecutive patients who underwent an atrial fibrillation or a left atrial macro-reentry ablation procedure were included in the registry within a period of 6 to 18 months according to centers.

Results: From January 2010 to December 2011, 1097 consecutive complex left atrial ablation procedures were collected. Patients were predominantly males (75%) with a mean age of 59±10 years old. The targeted arrhythmia was paroxysmal in 57%, persistent AF in 32%, long-standing AF in 4% or left atrial macro-reentry secondary to a previous AF ablation in 7%. Of interest, redo procedures represented 27% of the overall procedures. Pulmonary vein isolation (PVI) was attempted in 96% of the cases, the roof line in 40% and the left isthmus line in 16%. Complex fractionated atrial electrograms were targeted in 20% of the procedures. The procedures were most often performed with an irrigated tip RF ablation catheter (75%) and a 3D navigation system was used in 68% of the procedures. PVI was performed with a cryoballon in 21% or with phased RF technology tools in 3% of the cases. The mean procedure time was 142±56 min, with a mean amount of X-ray exposure of 56±43 Gray.cm². Surprisingly, X-ray exposure was not significantly less when 3D navigation system was used (46±62 vs 49±35 Gray.cm², p=0.31). The overall complication rate was 6.7%. Tamponade occurred in 14 patients (pts, 1.3%, requiring surgical drainage in 2 pts and responsible of death in 1); stroke was documented in 5 pts (0.4%), phrenic nerve palsy was observed in 8 pts during cryoballoon procedures only (8/234, 3.4%). Gastrointestinal bleed occurred in 14 patients (pts, 1.3%, requiring surgical drainage in 2 pts and 1.3%, requiring surgical treatment in 3). Hemoptysis, complete AV block, cardiogenic shock, documented in 1 pt respectively.

Conclusion: This prospective registry allows to get a real vision of how and to whom are performed complex left atrial ablation procedures in routine practice. Detailed data analysis might raise potential issues on which preventive action might further reduce procedures complication rate.

Contribution of left ventricular diastolic function to left atrial mechanical function in patients with paroxysmal atrial fibrillation

J.S. Lee, C.Y. Shim, H.S. Mun, J.W. B. Joung, M.H. Lee, H.N. Pak, Cardiology Division, Yonsei Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of

Purpose: Among diverse mechanisms leading to electroanatomical remodeling of left atrium (LA) in paroxysmal atrial fibrillation (PAF), left ventricular (LV) diastolic dysfunction would be one of the major contributors. The aim of this study was to evaluate the association between LV diastolic function and LA mechanical function.

Methods: We included 286 patients with PAF (male 73%, 57±11 years old) who underwent left atrial radiofrequency catheter ablation (RFCA). The patients had undergone transthoracic echocardiography, transesophageal echocardiography, and cardiac computed tomography before RFCA. LA voltage map was obtained using the NavX contact mapping system.

Results: Patients with impaired LA mechanical function (n=142, LAA-FV<58cm/s) revealed a larger LA diameter (p=0.040), indexed LA volume (p=0.017), lower LA voltage (p=0.047), higher CHADS2 score (p=0.009) and higher rate of cerebrovascular events (p=0.025) than in those with good LA mechanical function (n=144, LAA-FV≥58cm/s). In simple correlation analysis, early mitral filling/diastolic mitral annular velocity ratio (E/E') was significantly correlated with the LA voltage map.
with LAA-FV (r=0.19, p=0.044) and LA voltage (r=0.22, p=0.007). These associations were stronger for subjects ≥55 years of age and LA diameter ≥40mm (LAA-FV, r=0.39, p<0.001; LA voltage, r=0.31, p=0.03). E/E’ was an independent predictor of LAA mechanical function (r=0.19, p=0.021) even after controlling for age, gender, LA diameter and comorbidities.

**Conclusion:** LA mechanical function and its electroanatomical remodeling are closely related to one another, and both of them are under the influence of left ventricular (LV) diastolic function in PAF. The contribution of LV diastolic function to LA mechanical dysfunction was especially important to older patients with large LA diameter.

**High left atrial pressure and its responsiveness to isoproterenol infusion are related to the degree of electroanatomical remodeling of left atrium in patients with atrial fibrillation**

H.N. Pak, J. Shim, J.S. Uhm, J. Wi, H.S. Moon, C.Y. Shim, B. Joung, M.H. Lee. Yongsei Cardiovascular Center, Yongsei University Medical Center, Seoul, Korea, Republic of

**Background:** Although high left atrial pressure (LAP) may affect to atrial remodeling, their direct relationship has not yet been elucidated. The purpose of this study was to compare the clinical, imaging, and electrophysiological data of different area witnessed by isoproterenol infusion in a large group of patients with atrial fibrillation (AF) who underwent radiofrequency catheter ablation (RFCA).

**Materials and methods:** We compared LAP in patients with atrial fibrillation (AF) who underwent radiofrequency catheter ablation (RFCA). Measurements were performed during sinus rhythm and atrial fibrillation. LAPSR was calculated by measuring the difference between the upper limits of the LAA and LAV. LAPAF was defined as the difference between the LAP and mean LA volume.

**Results:** 1. In patients with mean LAPAF ≥3 mmHg, LA size (42.9±6.9 vs. 40.1±5.8 mm, p<0.001), LA volume (141.4±47.9 vs. 122.3±39.2 mL, p<0.006), body weight (71.1±11.0 vs. 68±10.9 kg, p<0.037), and proportion of persistent AF were greater than those with LAPAF <3 mmHg. These findings were consistent when we compared LAPAF>13 mmHg and LAPAF≥13 mmHg. 2. During isoproterenol infusion, LAPSR reduced from 21.6±9.8 vs. 3.1±3.6 mmHg to 18.4±11.0 vs. 4.5±6.9 vs. 1±6.4 mmHg at heart rate 110 bpm (p<0.001). 3. The patients with LAPSR <3 mmHg were older (60.0±11.2 vs. 54.9±11.5 years, p=0.009) and had lower endocardial voltage of LA (1.2±0.9 vs. 1.5±0.9 mV, p=0.038) than those with LAPSR >3 mmHg.

**Conclusion:** LAPAF was closely related to greater LA volume and body weight, and more likely persistent AF. Less significant reduction of LAPAF during isoproterenol infusion was observed in older patients with lower endocardial voltage of LA, suggesting elevated LAP associated with poor functional reserve is reflecting the degree of electroanatomical remodeling of LA in patients with AF.

**Impact of ranolazine in preventing postoperative atrial fibrillation in patients after on-pump coronary artery bypass graft surgery**

G. Tagarakis1, I. Aidonidis2, V. Liouras2, K. Papageorgiou1, C. Panidis1, I. Skoulasingas3, P.A. Plymdyas1, N. Tsilimigras2, 1Univ. of Thessaloniki, 2Thoracic & Cardiovascular Surgery, Univ. Hospital of Larissa, Larissa, Greece; 3Univ. of Thessaly, Dep. of Physiology, School of Medicine, Larissa, Greece; 2University Hospital of Larissa, Department of Cardiology, Larissa, Greece

Postoperative atrial fibrillation (POAF) still remains an unresolved problem after cardiac surgery. Recent experimental research showed that intravenous ranolazine (Ran), a novel late sodium current inhibitor primarily being developed to treat angina, increased atrial refractory period and suppressed inducibility of AF. Therefore, we aimed to investigate the effect of preoperatively administered Ran on POAF in patients (pts) undergoing conventional on-pump coronary artery bypass graft (CABG).

For that purpose, a total of 88 consecutive pts undergoing elective CABG, without history of AF or previous treatment with certain antiarrhythmic drugs, were enrolled and randomly assigned to a Ran group (n=33), 24/48/96, mean age 69.9±12.8 years, and a control group (C group, n=35/57, 58.1±10.9 years). Ran treatment at a dose of 375 x 2 mg/d was started 3 days preoperatively and continued for at least 7 days after the operation. The primary study end point was the occurrence of incessant POAF prior to discharge, documented by continuous ECG monitoring initially in the intensive care unit and then by Holter recordings. Seventeen of 55 pts (31.5%) in the control group developed sustained episodes of POAF a median of 2 postoperative days. Most of these pts (75%) converted to sinus rhythm after amiodarone standard scheme treatment within a mean of 36 hrs continuous infusion. In comparison, repetitive Holter recordings in the Ran group disclosed only 3 of 33 pts (9%), with POAF McMurry’s chi-square test application yielded a significant difference regarding the incidence of POAF between the two treatment groups (placebo vs Ran, chi-square = 28.195, p<0.001).

No statistically significant difference was observed between Ran and control pts regarding left ventricular ejection fraction (52.5±8.6 vs 53.8±8.9%, p=0.021) and mean LA atrial diameter (34.7±3.4 vs 33.7±2.7 mm, p=0.131). Atrial cross-clamp times were longer in the Ran group compared to the control group (62.2±17.1 vs 44.6±5.2 min, p<0.001).

**Conclusion:** Independently on the mechanism involved, Ran significantly reduced the incidence of POAF in pts after on-pump CABG surgery, possibly via a direct electrophysiological action deserving further evaluation.

**Heterogeneous electrical remodeling in atrial fibrillation substrate with heart failure: mechanism of complex fractionated electrograms**

S.L. Chang1, Y.C. Chen1, Y.J. Chen2, S.A. Chen1. 1Taipei Veterans General Hospital, Division of Cardiology, Taipei, Taiwan; 2National Defense Medical Center, Department of Biomedical Engineering, Taipei, Taiwan; 3Taipei Medical University Municipal Wang-Fang Hospital, Department of Medicine, Taipei, Taiwan

**Purpose:** The cellular electrophysiology at complex fractionated electrograms (CFAEs) and high dominant frequency (DF) sites is not fully understood.

**Methods:** Heart failure (HF) rabbits were created 4 weeks after coronary artery ligation. Atrial fibrillation (AF) was induced in 31 HF rabbits by rapid atrial pacing and acetylcholine infusion at open chest in vivo experiments. Real-time 3D substrate mapping (DF and CFAE) by EPLogix™ software (Bard Electrophysiology, MA, USA) were recorded during AF. The LA electrograms were classified as (1) CFAE with high DF, (2) CFAE with low DF, (3) Non CFAE with high DF, (4) Non CFAE with low DF. The electrophysiology of different area was investigated by monophasic action potential recording in whole heart, microelectrode array, and by transmembrane microelectrode recording in isolated tissue.

**Results:** CFAE with high DF site had a longer APD90 and effective refractory period (ERP) compared to the non-CFAE with high DF. It possesses more depolarized resting membrane potential (RMP), highest incidence of early afterdepolarization, as well as steepest maximum slope of APD90 restitution curve (RC) compared to the other 3 groups (Figure). CFAE with high DF exhibited slowest conduction velocity and shortest wavelength at pacing cycle length of 250 ms.

**Digitalis and 12-year Sudden Death after acute coronary syndrome. Results from the ABC Study on ACS**

M. Pellegrini1, G. Bertoni1, F. Caruolo2, R. Cordano3, P. Buttazzi4, N. Sitta5, E. Marras6, L. Coro7, P. Delisle8, Core-line General Hospital, Coregiano, Italy; 2Bassano General Hospital, Bassano, Italy; 3Adria General Hospital, Adria, Italy

**Purpose:** Atrial Fibrillation/Flutter (AF/FL) is a common complication of acute coronary syndrome (ACS) and it increases the mortality risk. The use of digitalis in coronary artery disease is controversial and usually considered unfavorable. Nevertheless little is known on the influence of digitalis in patients with ACS, potentially via trigger activity and breakup of rapid wavefronts. Heterogeneous electrical remodeling of LA may be the underlying mechanism.

**Conclusion:** CFAE with high DF site possesses arrhythmogenesis, which plays an important role in the initiation and maintenance of AF/FL, potentially via trigger activity and breakup of rapid wavefronts. Heterogeneous electrical remodeling of LA may be the underlying mechanism.
justed logistic polynomial regression analysis, AF/FL resulted associated to an excess of mortality due to sudden death (SD) (adjusted HR=2.9; 95%CL=1.2-7.2; p=0.02). Digitalis treatment showed a negative (protective) interaction for all-cause mortality (HR=0.3; 95%CL=0.2-0.7; p=0.002). This protective effect was linked chiefly to SD (adjusted HR=0.1; 95%CL=0.03-0.4; p=0.0003). Even after adjustment for age, gender, heart failure and heart rate the (protective) interaction remained strong (HR=0.3; 95%CL=0.2-0.6; p=0.002 and HR=0.1; 95%CL=0.03-0.4; p=0.0004 respectively). There were significant positive correlations between the disease duration of AF onset (CHADS2) and intraatrial (PA septal – PA tricuspid) electromechanical delay (EMD) vs 45.0±15.1, p=0.021 and 24.6±7.4 vs 20.0±8.1 ms, p=0.004, respectively. There were positive significant correlations between the disease duration and intramyocardial EMD (r=0.565, p=0.001). Positive correlation was also present between the disease duration and PWD (r=0.457, p=0.001).

**Conclusion:** Aftrial EMD is prolonged in patients with SLE. We have also showed that PWD, intramyocardial and interstitial EMD were significantly correlated with disease duration. This study calls attention to measurement of atrial contraction time may be clinically helpful in the definition of cardiac involvement.

**P602 Total atrial conduction time predicts symptoms and quality of life impact in paroxysmal atrial fibrillation patients**

**S. Podd, J.J. Van Zalen, S.S. Furniss, A.N. Sulke, M.R. Young, G.W. Lloyd. Eastbourne District General Hospital, Eastbourne, United Kingdom**

**Background:** Paroxysmal atrial fibrillation (PAF) is a common arrhythmia with multiple presenting symptoms. Total atrial conduction time (TACT [time from the start of the p-wave in lead II to a’ of the left atrial wall – Figure 1]) has been identified as a risk marker of AF occurrence and as a predictor of AF ablation success. It can be hypothesised that patients with shorter TACTs will be more symptomatic from AF episodes due to the loss of atrial function. A’ alone has also been correlated with success rates of PAF ablation. The ratio of A’ to VTI at S VTI has previously been described but may indicate the proportion of atrial input into overall cardiac output.

**Methods:** 18 patients (age 64.3±7.3 yrs, 11 females) undergoing pulmonary vein isolation (TVI for paroxysmal AF) was implanted at monitoring devices (Medtronic, Saint-Antoine, Faculty of Medicine Pierre & Marie Curie Paris 6, Paris, France)

**Spontaneous conversion (SC) occurs in atrial fibrillation patients with a frequency varying from 16% to 72%. Identifying patients prone to have a SC remains challenging in clinical practice. We investigated whether MR-proANP and Copeptine could predict SC in non valvular AF patients.**

**Methods:** Transthoracic echocardiography (TTE) and venous blood test were performed in 46 consecutive patients with an ECG documented AF. MR-proANP and Copeptine were retrospectively measured using immunoenzymatic assays (ThermoFischer). SC was defined as the absence of sinus rhythm between the time of admission and before TEE guided cardioversion.

**Conclusion:** Short TACT correlated well with high symptomatic and reduced quality of life scores suggesting that atrial function impacts on the symptom burden in patients with PAF. This may contribute some explanation to why some patients are highly symptomatic with low burdens of arrhythmia whilst others are symptom free.

**P603 What are the best predictors of spontaneous conversion in non valvular AF patients?**

**N. Haddour, S. Ederhy, S. Lang, S. Adavane, O. Valentín, L. Taibi, H. Raffi, F. Boccara, B. Baudin, A. Cohen. AP-HP - Hospital Saint-Antoine, Faculty of Medicine Pierre & Marie Curie Paris 6, Paris, France**

**Spontaneous conversion (SC) occurs in atrial fibrillation patients with a frequency varying from 16% to 72%. Identifying patients prone to have a SC remains challenging in clinical practice. We investigated whether MR-proANP and Copeptine could predict SC in non valvular AF patients.**

**Methods:** Transthoracic echocardiography (TTE) and venous blood test were performed in 46 consecutive patients with an ECG documented AF. MR-proANP and Copeptine were retrospectively measured using immunoenzymatic assays (ThermoFischer). SC was defined as the absence of sinus rhythm between the time of admission and before TEE guided cardioversion.

**Conclusion:** Short TACT correlated well with high symptomatic and reduced quality of life scores suggesting that atrial function impacts on the symptom burden in patients with PAF. This may contribute some explanation to why some patients are highly symptomatic with low burdens of arrhythmia whilst others are symptom free.

**Baseline characteristics and comparison**

<table>
<thead>
<tr>
<th>SC (n=32)</th>
<th>No SC (n=243)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, years</strong></td>
<td>66.4±15.6</td>
<td>71.0±14.3</td>
</tr>
<tr>
<td><strong>Hypertension</strong></td>
<td>112 (51.6)</td>
<td>150 (61.7)</td>
</tr>
<tr>
<td><strong>Diabetes</strong></td>
<td>34 (15.7)</td>
<td>45 (18.5)</td>
</tr>
<tr>
<td><strong>Copeptine, pmol/L</strong></td>
<td>6.15 ±(2.3-20.8)</td>
<td>9.06 (3.23-29.31)</td>
</tr>
<tr>
<td><strong>Mean CHADS2</strong></td>
<td>1.5 ±(1.0-3.0)</td>
<td>1.0 ±(0.0-2.0)</td>
</tr>
<tr>
<td><strong>Mean MR-proANP, pmol/L</strong></td>
<td>204 (102-378.4)</td>
<td>246 (163-401.4)</td>
</tr>
<tr>
<td><strong>Mean CHA2DS2-VASc</strong></td>
<td>2.5 ±(1.0-4.0)</td>
<td>1.5 ±(0.0-2.0)</td>
</tr>
<tr>
<td><strong>AP ratio</strong></td>
<td>1.42±1.26</td>
<td>1.84±1.28</td>
</tr>
<tr>
<td><strong>Echocardiographic characteristics</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>LV end-diastolic diameter » 40 mm</strong></td>
<td>146 (67.3)</td>
<td>60 (24.7)</td>
</tr>
<tr>
<td><strong>LV end-systolic diameter » 40 mm</strong></td>
<td>47 (21.7)</td>
<td>124 (51.0)</td>
</tr>
<tr>
<td><strong>LV ejection fraction» 40 mm</strong></td>
<td>24 (11.1)</td>
<td>59 (24.3)</td>
</tr>
</tbody>
</table>

**Figure 1**

**Conclusion:** Short TACT correlated well with high symptomatic and reduced quality of life scores suggesting that atrial function impacts on the symptom burden in patients with PAF. This may contribute some explanation to why some patients are highly symptomatic with low burdens of arrhythmia whilst others are symptom free.

**64 Atrial fibrillation: solving complex problems**
Baseline patients' characteristics are depicted in table 1. SC occurred in 217 pa-
tients (47%). MR-proANP and copeptine blood levels were significantly lower in patients with SC compared to those without. LVEF <40%, left atrial diameter >20 cm or left atrial diameter >40 mm were more frequently observed in patients without SC. In the multivariable logistic regression model, only AF onset ≥48h (OR=4.82, 95%CI: 3.00-7.21), and TTE parameters (left ventricular ejection fraction (LVEF) <40% and left atrial area >20 cm² or left atrial diameter ≥40 mm) (OR = 2.34, 95%CI: 1.48-3.70) were independently associated with non SC.

Conclusion: MR-pro ANP and copeptine level were significantly lower in patients with SC compared to those without. In multivariable analysis, LVEF < 40% and/or left atrial area > 20 cm² were independently associated with infrequent SC.

P604 Ventricular repolarization changes following catheter ablation of atrial fibrillation

N. Aloum1, G. Fernandez2, N. Burgon1, A. Amin3, N. Marronche1. 1University of Utah, Comprehensive Arrhythmia Research and Management Center, Salt Lake City, United States of America; 2University of Utah, Salt Lake City, United States of America

Background: Atrial fibrillation (AF) leads to dispersion of ventricular refractori-
ness and QT prolongation has been demonstrated following DC cardioversion. We studied ventricular depolarization changes following catheter ablation of AF.

Methods: 471 patients with AF undergoing ablation at the University of Utah were included. Anti-arrhythmic drugs were discontinued at least 4 half-lives prior to ablation. We measured QT and QTc intervals pre-, immediately post- and 3 months following catheter ablation. Patient demographics, comorbidities including drug treatment were included in the analysis.

Results: 231 patients (49.9%) had paroxysmal and 240 (51.1%) persistent AF. 52.0% patients were prescribed beta-blockers or calcium channel blockers prior toablation. 10.2% were prescribed class I and 7.2% class III AADs. Com-
pared to pre-ablation, immediately post- QT and QTc intervals were significantly longer: 402.6±48.3 vs 410.0±45.8; p<0.01 (QT) and 437.8±33.8 vs 454.7±31.5; p<0.01 (QTc). At 3-months, QT and QTc intervals remained prolonged compared to pre-ablation: 403.4±47.3 vs 412.6±43.0; p<0.01 (QT) and 437.1±33.3 vs 443.6±31.2; p<0.01 (QTc). Comparing immediately pre- to 3-months post-
ablation, the mean QTcshortened from 453.8±30.8 to 443.5±32.5 ms; p<0.01 while the QT interval wasnot significantly different. QT and QTc interval changes remained significant insubgroup analysis by AF type, baseline and recurrent AF after ablation and prior drug treatment.

Conclusions: Catheter ablation of atrial fibrillation is associated with acute pro-
longation of ventricular repolarization. This is independent of AF type, drug treat-
ment occurrence AF.

P605 Renal function, P-glycoprotein-affecting drugs and stroke prevention in atrial fibrillation patients

F. Hoeller1, C. Stoelberger1, C. Dobias1, L. Jungbauer1, C. Wegner1, J. Finsterer1, F. Weidinger1, 1Rudolfstiftung Hospital, Vienna, Austria; 2Rudolfstiftung Hospital, Department of Internal Medicine II, Vienna, Austria; 3Vienna Institute of Demography of the Austrian Academy of Sciences, Vienna, Austria

Introduction: Dabigatran is an oral thrombin-inhibitor which had a similar ef-
fect as warfarin for stroke prevention but a lower complication rate in patients with atrial fibrillation (AF) in the RE-LY study. Renal function as well as the P-
glycoprotein (P-gp) system influence the serum concentration of dabigatran. Aim of this retrospective cross-sectional study was to assess renal function and pre-
scription frequency of P-gp-affecting drugs in hospitalized AF patients.

Methods: P-gp-affecting drugs were searched from the literature. Consecutive patients with AF hospitalized between December 2009 and January 2010 were included. CHADS2 score was calculated, the medication (E-selectin, endothelial damage/ dysfunction) was evaluated using echocardiography and several other pericardial factors were also evaluated.

Results: There were no significant differences between the two groups in baseline patient characteristics or echocardiography findings. Postoperative AF oc-
curred during infusion in 3 patients (4.1%) in Group L and 17 patients (25.0%) in Group C (p = 0.0005). From the time the infusion was stopped until discharge, 17 patients (23.3%) in Group L and 15 patients (22.1%) in Group C developed AF (p = 0.0005). There were no significant differences between the two groups in postoperative left ventricular ejection fraction (Group L: 62.2±13.5, Group C: 64.6±13.1, p = 0.437) or other echocardiographic findings. Multivariate analysis revealed that no receiving postoperative landiolol hydrochloride was a significant risk factor for postoperative AF (odds ratio 0.2, 95% confidence interval 0.05 to 0.82, p = 0.0054).

Conclusions: Landiolol hydrochloride is effective in decreasing the incidence of postoperative AF without disturbing left ventricular function. Landiolol hydrochloride is recommended for all patients undergoing open heart surgery because of its minimally suppressive effect on cardiovascular performance.

P606 Landiolol hydrochloride: prevention of atrial fibrillation after open-heart surgery

H. Osada1, H. Nakajima1, S. Masuyama2, M. Morishima1, T. Su1. 1Mitsubishi Kyoto Hospital, Kyoto, Japan; 2Kosei Kai Takeda Hospital, Kyoto, Japan

Purpose: Postoperative atrial fibrillation (AF) is one of the most common compli-
cations after open-heart surgery and can result in increased mortality and mor-
bidity. Landiolol hydrochloride, an ultrashort-acting beta-blocker, was introduced in 2002. Although its effectiveness for prevention of postoperative AF is becom-
ing clear, few randomized studies which include all types of open-heart surgery have been performed. The aims of this study were to evaluate whether landiolol hydrochloride contributes to the prevention of postoperative AF, and to evaluate the influence of landiolol hydrochloride on periprocedural echocardiography find-
ings.

Methods: From May 2010 to January 2012, a total of 141 patients (97 men, 44 women; mean age: 70±3.8 years) undergoing scheduled open-heart surgery (61 coronary artery bypass grafting, 46 valve surgery, 9 thoracic aorta surgery, 21 bypass grafting and valve surgery, 2 others) were randomly divided into two groups. Group L (n = 73) received landiolol hydrochloride postoperatively and Group C (n = 68) did not. Patients with previous AF and undergoing emergency surgery were excluded. Landiolol hydrochloride 2–3 mcg/kg/min was started soon after arrival in the intensive care unit after surgery and was continued for 48 hours. Blood and urinary sample obtained at coronary artery surgery, postoperative echocardiographic and 48-hour post-
operative cardiac function were evaluated using echocardiography, and several other pericardial factors were also evaluated.

Results: There were no significant differences between the two groups in baseline patient characteristics or echocardiography findings. Postoperative AF oc-
curred during infusion in 3 patients (4.1%) in Group L and 17 patients (25.0%) in Group C (p = 0.0005). From the time the infusion was stopped until discharge, 17 patients (23.3%) in Group L and 15 patients (22.1%) in Group C developed AF (p = 1.0000). There were no significant differences between the two groups in postoperative left ventricular ejection fraction (Group L: 62.2±13.5, Group C: 64.6±13.1, p = 0.437) or other echocardiographic findings. Multivariate analysis revealed that not receiving postoperative landiolol hydrochloride was a significant risk factor for postoperative AF (odds ratio 0.2, 95% confidence interval 0.05 to 0.82, p = 0.0054).

Conclusions: Landiolol hydrochloride is effective in decreasing the incidence of postoperative AF without disturbing left ventricular function. Landiolol hydrocloride is recommended for all patients undergoing open heart surgery because of its minimally suppressive effect on cardiovascular performance.
Sub-optimal heart rate and rhythm control post-hospitalisation in high risk patients with chronic atrial fibrillation: the value of therapeutic ECG Holter monitoring

J. Ball, M.J. Carrington, L. Waite, S. Stewart on behalf of SAFETY Investigators. Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Purpose: Regardless of the therapeutic merits of “rate versus rhythm” control in managing chronic atrial fibrillation (AF), it is imperative to determine if the physician-nominated target is being achieved, particularly in patients at high risk for progressive cardiac dysfunction and future thrombo-embolic events. However, this is rarely assessed.

Methods: As part of a multicentre, randomised controlled trial of a nurse-led, home-based, AF-specific management program vs. usual post-discharge care, we have recruited a large cohort of patients discharged from hospital with chronic forms of AF. We report on the underlying rhythm and heart rate captured on 24 hour ECG Holter monitoring at a home visit (7-14 days post-discharge) of 122 patients discharged from hospital with chronic AF. A trained nurse assessed post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% were diagnosed with persistent or permanent AF. At hospital discharge, 70% and 30% of patients were being managed as “rate” vs. “rhythm” control. During post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% had episodes of AF (33±45% of recording time). Of the 86 patients nominated for rate control, 55% were in AF for 100% of the recording time. Over all, three distinct heart rate phenotypes were evident. Almost half (47%) had a controlled heart rate during monitoring. However, 31% of patients displayed an uncontrolled rate, while the remainder (22%) showed a distinctly labile heart rate. These patients assigned rhythm control were more likely to display a controlled rate compared to rate controlled patients (62% vs. 42%; OR 2.4, 95% CI 1.0 to 5.8, p=0.049). Conversely, those assigned rate control were more likely to display an uncontrolled rate (36% vs. 17%) or labile (22% vs. 21%) heart rate. Clinically significant arrhythmias (other than AF) were identified in 49% of patients overall.

Conclusions: These data confirm the potential value of routinely applying post-discharge, ECG Holter monitoring of heart rate/rhythm to further stratify risk and inform therapeutic choices in recently hospitalised patients with chronic AF. As part of ongoing nomination for rhythm control, 60% of patients with persistent or permanent AF were managed as “rate” control. During post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% had episodes of AF (33±45% of recording time). Of the 86 patients nominated for rate control, 55% were in AF for 100% of the recording time. Over all, three distinct heart rate phenotypes were evident. Almost half (47%) had a controlled heart rate during monitoring. However, 31% of patients displayed an uncontrolled rate, while the remainder (22%) showed a distinctly labile heart rate. These patients assigned rhythm control were more likely to display a controlled rate compared to rate controlled patients (62% vs. 42%; OR 2.4, 95% CI 1.0 to 5.8, p=0.049). Conversely, those assigned rate control were more likely to display an uncontrolled rate (36% vs. 17%) or labile (22% vs. 21%) heart rate. Clinically significant arrhythmias (other than AF) were identified in 49% of patients overall.

Conclusions: These data confirm the potential value of routinely applying post-discharge, ECG Holter monitoring of heart rate/rhythm to further stratify risk and inform therapeutic choices in recently hospitalised patients with chronic AF. As part of ongoing nomination for rhythm control, 60% of patients with persistent or permanent AF were managed as “rate” control. During post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% had episodes of AF (33±45% of recording time). Of the 86 patients nominated for rate control, 55% were in AF for 100% of the recording time. Over all, three distinct heart rate phenotypes were evident. Almost half (47%) had a controlled heart rate during monitoring. However, 31% of patients displayed an uncontrolled rate, while the remainder (22%) showed a distinctly labile heart rate. These patients assigned rhythm control were more likely to display a controlled rate compared to rate controlled patients (62% vs. 42%; OR 2.4, 95% CI 1.0 to 5.8, p=0.049). Conversely, those assigned rate control were more likely to display an uncontrolled rate (36% vs. 17%) or labile (22% vs. 21%) heart rate. Clinically significant arrhythmias (other than AF) were identified in 49% of patients overall.

Conclusions: These data confirm the potential value of routinely applying post-discharge, ECG Holter monitoring of heart rate/rhythm to further stratify risk and inform therapeutic choices in recently hospitalised patients with chronic AF. As part of ongoing nomination for rhythm control, 60% of patients with persistent or permanent AF were managed as “rate” control. During post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% had episodes of AF (33±45% of recording time). Of the 86 patients nominated for rate control, 55% were in AF for 100% of the recording time. Over all, three distinct heart rate phenotypes were evident. Almost half (47%) had a controlled heart rate during monitoring. However, 31% of patients displayed an uncontrolled rate, while the remainder (22%) showed a distinctly labile heart rate. These patients assigned rhythm control were more likely to display a controlled rate compared to rate controlled patients (62% vs. 42%; OR 2.4, 95% CI 1.0 to 5.8, p=0.049). Conversely, those assigned rate control were more likely to display an uncontrolled rate (36% vs. 17%) or labile (22% vs. 21%) heart rate. Clinically significant arrhythmias (other than AF) were identified in 49% of patients overall.

Conclusions: These data confirm the potential value of routinely applying post-discharge, ECG Holter monitoring of heart rate/rhythm to further stratify risk and inform therapeutic choices in recently hospitalised patients with chronic AF. As part of ongoing nomination for rhythm control, 60% of patients with persistent or permanent AF were managed as “rate” control. During post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% had episodes of AF (33±45% of recording time). Of the 86 patients nominated for rate control, 55% were in AF for 100% of the recording time. Over all, three distinct heart rate phenotypes were evident. Almost half (47%) had a controlled heart rate during monitoring. However, 31% of patients displayed an uncontrolled rate, while the remainder (22%) showed a distinctly labile heart rate. These patients assigned rhythm control were more likely to display a controlled rate compared to rate controlled patients (62% vs. 42%; OR 2.4, 95% CI 1.0 to 5.8, p=0.049). Conversely, those assigned rate control were more likely to display an uncontrolled rate (36% vs. 17%) or labile (22% vs. 21%) heart rate. Clinically significant arrhythmias (other than AF) were identified in 49% of patients overall.

Conclusions: These data confirm the potential value of routinely applying post-discharge, ECG Holter monitoring of heart rate/rhythm to further stratify risk and inform therapeutic choices in recently hospitalised patients with chronic AF. As part of ongoing nomination for rhythm control, 60% of patients with persistent or permanent AF were managed as “rate” control. During post-discharge Holter monitoring, of the 36 patients nominated for rhythm control, 59% had episodes of AF (33±45% of recording time). Of the 86 patients nominated for rate control, 55% were in AF for 100% of the recording time. Over all, three distinct heart rate phenotypes were evident. Almost half (47%) had a controlled heart rate during monitoring. However, 31% of patients displayed an uncontrolled rate, while the remainder (22%) showed a distinctly labile heart rate. These patients assigned rhythm control were more likely to display a controlled rate compared to rate controlled patients (62% vs. 42%; OR 2.4, 95% CI 1.0 to 5.8, p=0.049). Conversely, those assigned rate control were more likely to display an uncontrolled rate (36% vs. 17%) or labile (22% vs. 21%) heart rate. Clinically significant arrhythmias (other than AF) were identified in 49% of patients overall.
Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation. Cryoablation has been shown to be a safe and effective technique for pulmonary vein isolation. However, the arrhythmia recurrence rate is high after cryoablation procedures and there are no established strategies for redo procedures in these patients. Therefore, we have summarized our initial experience with two different strategies for redo procedures using radiofrequency catheter ablation.

Methods: Fifty-five patients (paroxysmal AF: 37 patients, persistent AF: 18 patients) had to undergo a redo procedure after initially successful circumferential PV isolation with the cryoballoon technique (Arctic Front Balloon, CryoCath Technologies). The redo ablation procedures were performed using a segmental approach or a circumferential ablation strategy (CAROTO; Biosense Webster) depending on the intra-procedural findings.

Results: During the redo procedure, a mean number of 2.3±0.4 re-conducting PVs were detected (using a circular mapping catheter). In 47 patients, a segmental approach was sufficient to eliminate the residual PV conduction because there were only a few recovered PV foci. In the remaining 8 patients, a circumferential ablation strategy was used because of a complete recovery of the PV-LA conduction. All recovered PVs could be isolated successfully again. At 30-month follow-up, 80% of all patients were free from an arrhythmia recurrence (44/55 patients). There were no major complications.

Conclusion: In patients with an initial circumferential PV isolation using the cryoballoon technique, a repeat ablation procedure can be performed safely and effectively using radiofrequency catheter ablation. In most cases only a few re-conducting PV foci were found and, therefore, a segmental re-ablation approach seems to be sufficient in the majority of patients.

Catheter ablation of atrial fibrillation: radiofrequency catheter ablation for redo procedures after pulmonary vein isolation with the cryoballoon technique - long-term follow-up results

K. Kettering, F. Gramley. University Hospital, Frankfurt, Germany

Atrial fibrillation (AF) is the most commonly diagnosed arrhythmia in clinical practice. Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation. Cryoablation has been shown to be a safe and effective technique for pulmonary vein isolation. However, the arrhythmia recurrence rate is high after cryoablation procedures and there are no established strategies for redo procedures in these patients. Therefore, we have summarized our initial experience with two different strategies for redo procedures using radiofrequency catheter ablation.

Methods: Fifty-five patients (paroxysmal AF: 37 patients, persistent AF: 18 patients) had to undergo a redo procedure after initially successful circumferential PV isolation with the cryoballoon technique (Arctic Front Balloon, CryoCath Technologies). The redo ablation procedures were performed using a segmental approach or a circumferential ablation strategy (CAROTO; Biosense Webster) depending on the intra-procedural findings.

Results: During the redo procedure, a mean number of 2.3±0.4 re-conducting PVs were detected (using a circular mapping catheter). In 47 patients, a segmental approach was sufficient to eliminate the residual PV conduction because there were only a few recovered PV foci. In the remaining 8 patients, a circumferential ablation strategy was used because of a complete recovery of the PV-LA conduction. All recovered PVs could be isolated successfully again. At 30-month follow-up, 80% of all patients were free from an arrhythmia recurrence (44/55 patients). There were no major complications.

Conclusion: In patients with an initial circumferential PV isolation using the cryoballoon technique, a repeat ablation procedure can be performed safely and effectively using radiofrequency catheter ablation. In most cases only a few re-conducting PV foci were found and, therefore, a segmental re-ablation approach seems to be sufficient in the majority of patients.

Cardiac surgery 67

Catheter ablation of atrial fibrillation: radiofrequency catheter ablation for redo procedures after pulmonary vein isolation with the cryoballoon technique - long-term follow-up results

K. Kettering, F. Gramley. University Hospital, Frankfurt, Germany

Atrial fibrillation (AF) is the most commonly diagnosed arrhythmia in clinical practice. Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation. Cryoablation has been shown to be a safe and effective technique for pulmonary vein isolation. However, the arrhythmia recurrence rate is high after cryoablation procedures and there are no established strategies for redo procedures in these patients. Therefore, we have summarized our initial experience with two different strategies for redo procedures using radiofrequency catheter ablation.

Methods: Fifty-five patients (paroxysmal AF: 37 patients, persistent AF: 18 patients) had to undergo a redo procedure after initially successful circumferential PV isolation with the cryoballoon technique (Arctic Front Balloon, CryoCath Technologies). The redo ablation procedures were performed using a segmental approach or a circumferential ablation strategy (CAROTO; Biosense Webster) depending on the intra-procedural findings.

Results: During the redo procedure, a mean number of 2.3±0.4 re-conducting PVs were detected (using a circular mapping catheter). In 47 patients, a segmental approach was sufficient to eliminate the residual PV conduction because there were only a few recovered PV foci. In the remaining 8 patients, a circumferential ablation strategy was used because of a complete recovery of the PV-LA conduction. All recovered PVs could be isolated successfully again. At 30-month follow-up, 80% of all patients were free from an arrhythmia recurrence (44/55 patients). There were no major complications.

Conclusion: In patients with an initial circumferential PV isolation using the cryoballoon technique, a repeat ablation procedure can be performed safely and effectively using radiofrequency catheter ablation. In most cases only a few re-conducting PV foci were found and, therefore, a segmental re-ablation approach seems to be sufficient in the majority of patients.
vs. 109.4±17.3 ms), reduction of tricuspid annular diameter (2.82±0.13 cm vs. 2.4±0.16 cm) and improvement of tricuspid leaflet angulation. RVEF remained unchanged (66.8±6.8% vs. 66.5±6.2%).

Conclusion: Mitral valve repair benefits RV remodeling and improves the geometric and functional features of tricuspid valvular apparatus.

Hybrid thoracoscopic surgery for AF in patients with prior failed catheter ablation or enlarged atria: benefit of electrophysiological measurements

P616

S.P.J. Krul1, A.H.G. Driessen2, A.A.M. Wilde1, J.M.T. De Bakker3, J.R. De Groot1, 1Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; 2Academic Medical Center, University of Amsterdam, Department of Cardiothoracic Surgery, Amsterdam, Netherlands; 3Interuniversity Cardiology Institute of the Netherlands (ICIN), Utrecht, Netherlands

Introduction: Recently, it was reported that non-hybrid thoracoscopic pulmonary vein ablation (TPVI) is effective and safe in patients with a prior failed catheter ablation or large atria and hypertension. We hypothesize that additional periprocedural epicardial electrophysiological confirmation of conduction block across all ablation lines might add to the success of TPVI in these patients. We retrospectively studied the clinical outcome of patients undergoing hybrid-TPVI with previous failed catheter ablation or large atria or hypertension.

Methods: Patients were included for analysis if they had 1) a failed previous catheter ablation, 2) left atrial diameter of ≥ 44 mm or 3) hypertension with a left atrial diameter of 40-44 mm and underwent bilateral TPVI. Ganglionated plexus were ablated and the left atrial appendage was excluded. Patients with non-reactive left atrium AF received additional left atrial lesions (consisting of a superior and a trigone line). Epicardial electrophysiological measurements were performed to assess conduction block across pulmonary vein lines and linear ablation lines. Patients were followed-up with Holter monitoring every three months after the procedure for one year. Primary endpoint was freedom of any left atrial arrhythmia > 30 seconds without the use of anti-arrhythmic drugs at one year follow up.

Results: Out of a total of 58 patients undergoing hybrid-TPVI for AF between 2001 and 2010, 27 (n=11 parasympathetic AF; n=16 non-parasympathetic AF) met the inclusion criteria (n=16 previous catheter ablation, n=11 enlarged atrium ≤ 44 mm), Mean age was 58 (range 43-77 years), 85% (23/27) were male and mean left atrial diameter was 50±5.8 mm (range 40-61 mm). Primary endpoint was reached by 74% (91% parasympathetic, 63% non-parasympathetic). Patients with a prior catheter ablation had a success rate of 75% and 73% in patients with an enlarged left atrium. There were 6 (22%) procedural adverse events; 2 stenotomies, 2 hematomas, 1 pneumothorax and 1 pneumonia.

Conclusion: Hybrid-TPVI is effective and safe in patients with an enlarged left atrium or a failed catheter ablation. Our data show that periprocedural electrophysiological evaluation of conduction block across all ablation lines might increase the success of TPVI in this patient population, without increasing the rate of adverse events.

Frequency and causes of stroke during or after transcatheter aortic valve implantation

P617

R.-J. Nuis1, N.M. Van Mieghem2, C.J. Schultz2, R. Van Der Boon1, A. Van Der Lugt1, P.W. Serruyts2, J. Rodes-Cabau3, R.T. Van Domburg1, P.J. Koudstaal2, P.P. De Jaegere2, 1Erasmus Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, Netherlands; 2Quebec Heart and Lung Institute, Quebec, Canada

Purpose: Transcatheter aortic valve implantation (TAVI) is invariably associated with the risk of clinically manifest transient or irreversible neurologic impairment. We sought to investigate the incidence and causes of clinically manifest stroke during TAVI.

Methods: A total of 214 consecutive patients underwent TAVI with the Medtronic-CoreValve System between November 2005 and September 2011 in our institution. Stroke was defined by the Valve Academic Research Consortium recommendations. Its cause was established by (i) analysing the time of onset of symptoms, (ii) correlating the symptoms with computed tomography (CT) detected defects in the brain and (iii) by analyzing the potential co-existing causes of stroke in addition to a multivariable analysis to determine independent predictors.

Results: Stroke occurred in 19 patients (9%) and was major in 10 (5%), minor in 3 (1%) and transient (TIA) in 6 (3%). The onset of symptoms was early (<24 hours) in 8 patients (42%) and delayed (>24 hours) in 11 (58%). Brain CT scan showed a cortical infarct in 8 patients (42%), a lacunar infarct in 5 (26%), hemorrhage in 1 (5%) but no abnormalities in 5 (26%). Independent determinants of stroke were new-onset atrial fibrillation after TAVI (OR: 4.4; 95% CI: 1.2-15.6) and baseline atrial fibrillation grade II (OR: 3.2; 95% CI: 1.1-9.3).

Conclusion: The incidence of stroke was 9% of which more than half occurred >24 hours after the procedure. New-onset atrial fibrillation was associated with a 4.4-fold increased risk of stroke. These findings indicate that improvements in postoperative care after TAVI are equally if not more important for the reduction of periprocedural stroke than preventive measures during the procedure.
Right ventricular analysis by speckle tracking echocardiography in patients undergoing left ventricular assist device

M. Camelli1, M. Lis1, F.M. Righini2, M. Focardi3, M. Maccherini2, G. Sami1, M. Galderisi3, S. Mondiolo1.

1University of Siena, Department of Cardiovascular Diseases, Siena, Italy; 2Santa Maria alle Scotte Polyclinic, Department of Cardiovascular Surgery, Heart Transplantation Division, Siena, Italy; 3University of Siena, Department of Cardiothoracic Surgery, Siena, Italy.

Background: Right ventricular (RV) systolic function has a critical role in determining the clinical outcome and the success of using left ventricular assist devices (LVADs), in patients with refractory heart failure. RV deformation analysis by speckle tracking echocardiography (STE) has recently allowed a deeper understanding of RV function before LVAD implant, to potentially help in decision-making regarding the clinical outcome and the success of using left ventricular assist devices (LVADs), in patients with refractory heart failure.

Methods: Transhiatal aortic-DeBakey was performed in 9 patients referred for LVAD implant at baseline and with serial echocardiograms after LVAD implant (Jarvik 2000). In a subgroup of patients an additional intermediate echo evaluation, after intra-aortic balloon pump (IABP) implantation, was performed. All echocardiographic images were analyzed off-line to calculate the free wall RV longitudinal strain (RVLS).

Results: All patients, except two, who presented the lowest RVLS values at baseline, showed a progressive increase of RVLS after LVAD implant. Analyzing five patients undergone to IABP as an intermediate step, it was clear that only patients that presented an increase of RVLS after IABP implant, showed progressive increase of RVLS levels after LVAD implant. Three patients, that did not experience an increase of RVLS after IABP implant, presented a RV failure after LVAD implant.

Conclusions: This new parameter of RV myocardial deformation, RVLS, may provide important insights on RV function before LVAD implant, to potentially help in decision-making about the management of this kind of patients, and after LVAD implant, for the follow-up of patients.

Prognostic impact of dramatic alteration of mixed venovenous oxygen saturation from veno-arterial extracorporeal membrane oxygenation


Kitsato University School of Medicine, Department of Cardio-angiology, Sagamihara, Japan; 2odawara municipal hospital, odawara, Japan.

Background: Although low mixed venous oxygen saturation (SvO2) from pulmonary artery blood indicates circulation collapse in general, the clinical significance of SvO2 during veno-arterial extracorporeal membrane oxygenation (VA-ECMO) has not been evaluated.

Methods & Results: We divided 30 patients treated with VA-ECMO for hemodynamic deterioration due to cardiovascular diseases into 2 groups according to having a period of SvO2 >75% during VA-ECMO (Group A: n=19) or not (Group B: n=11). While VA-ECMO was weaned off without severely-deteriorated cardiac output indicated by end-tidal CO2 (ETCO2) >10 mmHg or left ventricular ejection time (LVED) <100 msec in 10 of 11 (88%) of Group B, only 9 of 19 (47%) could show similar results in Group A (P<0.01). A dramatic decrease of SvO2 (85±12–69±7%) was observed together with an increased cardiac index (0.5±0.7–2.3±0.9 L/min/m2), ETCO2 (7.9±9.2–26±6%), and LVED (144±49–227±47 mmH2O) whenever VA-ECMO was subsequently weaned off in survivors of Group A. On the other hand, the rest of Group A patients with sustained high SvO2 (79±12%) during the course never recovered from hemodynamic deterioration requiring VA-ECMO until death (figure).

Conclusion: Extraordinarily high SvO2 of >75% is a useful indicator for severely impaired cardiac output during VA-ECMO and reversed SvO2 to considerable levels can predict the clinical recovery. In addition the decreased SvO2 into considerable levels can predict clinical recovery leading to weaning off VA-ECMO.

Mid-term neurologic complications after off-pump coronary artery bypass grafting with and without aortic manipulation


Funabashi Municipal Medical Center, Funabashi, Japan.

Objective: The aim of this study was to assess the impact of ascending aortic manipulation in off-pump coronary artery bypass grafting (OPCAB) on neurologic complications.

Patients and Method: Of 336 patients who underwent isolated OPCAB between 1998 and 2011, aorta was not touched at all in 264 patients (group A), aorta was manipulated by side-biting clamp or proximal anastomosis in 72 patients (group B). Preoperative characteristics and mid-term survival, cardiac and neurological event were investigated.

Results: Average follow up period was 2.9±2.5 years. Postoperative neurological complications within 1 month occurred in 1 patient in group A (0.4%) and 1
patient in group B (1.4%) (p=0.38). On univariate analysis, age was not different between group A (67.3±8.0) and group B (68.9±9.1) (p=0.15). Preoperative left ventricular ejection fraction was not different between group A (56.4±10.0%) and group B (53.6±16.0%) (p=0.51). The prevalence of triple vessel disease (group A 40.9% vs group B 61.1%; p=0.0003) and left main trunk disease (group A 30.7% vs group B 47.2%; p=0.01) was lower in group A than in group B. The number of diseased vessels (group A 2.18±0.76 vs group B 2.58±0.57; p=0.0013) and the number of bypass graft (group A 2.16±0.97 vs group B 3.00±0.97; p=0.0001) was also lower in group A than in group B. The prevalence of preoperative atrial fibrillation (group A 4.2% vs group B 2.6%; p=0.74) and the incidence of new onset-postoperative atrial fibrillation (group A 34.6% vs B 37.3%; p=0.86) were not different between groups. Survival rate, freedom from major adverse cardiac event were not different between groups (p=0.87, p=0.51, respectively in order by Log rank test). But the rate of freedom from neurological complications was significantly lower in group A (p=0.0006 by Log-rank test). Cox hazard model revealed that atriotic manipulation (p=0.001, OR 14.0, 95%CI 2.7-72.5) were the risk factors for the neurological complications.

Conclusions: Although the incidence of immediate postoperative neurological complications was not different between with or without atriotic manipulations in OPCAB cases, mid-term neurological complications was lower in OPCAB cases without atriotic manipulations.

Methods: We prospectively studied 383 patients undergoing CABG in a single center. Demographic and clinical data were collected preoperatively. The glomerular filtration rate (GFR) was evaluated before surgery and coronary angiography according to the MDRD-equation. We defined CKD when GFR < 60ml/min/1.73m². Patients were categorized into 3 groups (group 1: no CKD prior to surgery; group 2: CKD before coronary angiography and surgery; group 3: no CKD before coronary angiography but CKD before surgery). Multivariate Cox proportional hazard analysis was performed to determine the independent prognostic factors.

The primary outcome was long-term total mortality. The secondary outcome was composite, combining long-term death, acute coronary syndrome, stroke and coronary revascularization.

Results: During a median follow-up of 39.4±14 months, poorer prognosis was observed in groups 2 and 3 vs. group 1 (figure 1). In the multivariate analysis adjusting for confounders, we found an increased risk of mortality (hazard ratio (HR) and 95% confidence interval: 3.9 [1.1-13.5]; p=0.03) and secondary outcome (HR: 3.7 [1.1-12.8]; p=0.04) in group 3 compared to group 1, but no significant risk was found in group 2 (mortality: HR 1.1 [0.5-2.4]; p=0.79).

Conclusions: Recent preoperative renal dysfunction occurring between coronary angiography and surgery is an independent predictor of long-term mortality.
on-pump=86). Primary composite end points were death, myocardial infarction, further revascularization (surgery or angioplasty), or stroke.

Results: The two randomized groups were well-matched for baseline demographic, clinical, and angiographic characteristics. The mean age was 67.2 ± 5.9 years. After 5-year follow-up, there were no significant differences between on-pump and off-pump groups in the composite end points: 27.9% vs 21.1% (hazard ratio 1.17, 95% CI 0.87 to 1.59; p = 0.29) Figure 1. Six patients (7.0%) died in the on-pump group compared with 10 (11.1%) in the off-pump group (hazard ratio 0.78, 95% CI 0.47 to 1.29; p = 0.33). On-pump patients had a higher incidence of post operative stroke or myocardial infarction: 13 (15.1%) vs 5 (6.6%); p = 0.036.

Conclusions: Patients undergoing off-pump surgery had a lower incidence of in-hospital stroke or myocardial infarction. This finding did not add benefit in clinical outcomes at 5-years follow-up.

Evaluation of the EUROSCORE II as predictor of 30 days mortality in very old age patients (>80) submitted to isolated coronary artery bypass grafting


Purpose: The aim of this study is to evaluate the performance of the EuroSCORE and the EuroSCORE II as mortality predictor at 30 days in very old patients (VOP) that underwent isolated coronary artery bypass grafting (CABG).

Methods: Retrospective analysis from a single center of 198 patients with ≥ 80 years of age undergoing CABG between July 2003 and October 2010, mean age 83.2 ± 2 years old, 62% men. The mean of EuroSCORE I was 11.4 ± 8.9 and the mean of EuroSCORE II was 4.2 ± 3.4. The area under the ROC curve (AUC), or statistics-C, was used as a measure of the discriminatory power of both scores for predicting mortality to 30 days and the test used to adjust the model was the Hosmer-Lemeshow. It has been calculated through their ROC curves the best cut-off for each respective score.

Results: Of 198 patients 95% have a full follow-up time of 30 days. During this period there were 8 (4%) deaths, of which 6 (3%) have been in-hospital. The EuroSCORE I is not a good predictor of mortality at 30 days (AUC: 0.65; 0.59-0.72; p = 0.16; Hosmer-Lemeshow: p = 0.787); the EuroSCORE II showed reasonable discriminatory power (AUC: 0.71; 0.63-0.77; p = 0.05; Hosmer-Lemeshow: p = 0.231), although when compared to the EuroSCORE I I haven’t shown superiority (AUC: 0.05; 0.08-0.19; p = 0.423). Both scores had high negative predictive values (97%), with the best cut-off in this population of 16.6% and 9.0% for the EuroSCORE I and II, respectively.

Conclusions: The EuroSCORE I overestimates mortality in octogenarians submitted to isolated CABG. The EuroSCORE II approximates to the actual mortality, but showed no higher discriminatory power for 30 days mortality.

Utility of combined administration of magnesium sulfate and corticosteroids in prevention of postoperative complications and outcomes in patients undergoing coronary surgery

S. Kallel1, Z. Friki2, R. Bouhel1, L. Abidi1, M. Hentati1, I. Friki2, S. Kamoun2, A. Kaciri2, H. Habib bourguia hospital, Department of anesthesiology, Stax, Tunisia; 2Hedi Cheker Hospital, Department of Cardiology, Stax, Tunisia; 2Habib bourguia hospital, Department of cardiac surgery, Stax, Tunisia

Background: Cardiac surgery and cardiopulmonary bypass (CPB) induce an acute inflammatory response contributing to postoperative morbidity and complications including myocardial dysfunction, atrial fibrillation, acute lung injury and postoperative bleeding.

Objectives: The objective of this study is to evaluate the impact of a three-day hydrocortisone hemisuccinate (ICHHS) and magnesium sulfate (MS) administra-

tion on the occurrence of postoperative complications in coronary surgery with CPB.

Materials and Methods: This is a retrospective study that involved 129 patients who underwent coronary surgery with CPB. The patients were divided into 2 groups: Group 1 (G1=64 patients) comprising those who didn’t receive the study protocol and group 2 (G2=65patients) consisted of patients in whom we performed a combined administration of MS and ICHHS. The anesthetist protocol and CPB were the same for all patients in both groups.

Results: There were no differences between the two groups in terms of demographic features and preoperative treatment. The length of mechanical ventilation was higher in G1 (p < 0.02). Both the 2 groups were similar concerning the incidence of postoperative bleeding.

The incidence of postoperative atrial fibrillation (AF) was significantly higher in G1 (23% vs 6%; p = 0.006). SIRS and severe SIRS were significantly more frequent in G1 (respectively 62% vs 35% and 32% vs 16%; CRP levels were also higher in G1 in comparison with G2 (201.3±74.08 vs 142.47±52.57, p = 0.000). Duration of intensive care unit stay (ICU) was significantly longer in G1 (7.57±3.54 vs 5.73±2.8, p = 0.025). Finally, the overall postoperative mortality was higher in G1: (7 cases vs 3, p < 0.05).

Conclusion: Prevention of postoperative complications by combined administration of magnesium sulfate and corticosteroids decreased the incidence of FA, SIRS, the duration of ICU stay and the postoperative mortality.

Long-term outcomes in 714 subjects after endoscopic atraumatic coronary artery bypass grafting (EACAB): single-centre registry data

L. Krzych, M. Cisowski, R. Abu-Samra, A. Bochenek. 1st Department of Cardiac Surgery, Katowice, Poland

Purpose: The assessment of long-term outcomes in consecutive patients who underwent EACAB over a 12-year period.

Methods: The study included 714 patients, 581 males (81.4%), aged 57.9±9.7 years who underwent EACAB from Apr 1998 till Dec 2009. A prospective registry analysis was performed to estimate the incidence of major adverse cerebral and cardiovascular events (MACCE), including all-cause death, myocardial infarction, stroke, or TIA, and the need of repeated coronary revascularization (with assessment whether it was related to a target vessel, LAD, or not). Risk factors for MACCE incidence were estimated on the basis of demographics and clinical data.

Results: The time of observation was 2121±1313 days (median = 1918.5, maximal = 4661 days), the MACCE occurrence was 10.8% (77 patients), with the need of revascularization as the most frequent complication (50 patients, 7%), the second was death (19subjects, 2.7%), then myocardial infarction (17 cases, 2.4%), and the less frequent was stroke/TIA (7 patients, 1%). None of the subjects required CABG. Cardiac death concerned 10/19 persons (52.6%). PCI for myocardial infarction was performed in 10/17 patients (58.8%). Target vessel PCI was done in 19/50 cases (38%), including two patients with myocardial infarction. On the basis of cumulative survival analysis it was revealed that subjects after EACAB had survival ratio of 96.1% in a long-term follow-up. Event-free survival (MACCE-free) was 85.3%. Myocardial infarction-free survival was 96.9%. PCI-free survival was 90.5%. Stroke/TIA-free survival was 98.6%. Older age (≥ 75 y), ejection fraction < 50%, previous PCI and NYHA class II (vs. I) were risk factors for both death and the overall MACCE incidence in a follow-up (p < 0.05).

Conclusions: EACAB ensures good long-term therapeutic results with decreased late survival and MACCE-free survival: older age, lower ejection fraction, previous PCI and moderate heart failure by NYHA class.

Evolution of ventricular function in patients with stable coronary artery disease submitted to on-pump or off-pump coronary artery bypass graft in MASS III trial

K.F. Staszka, W. Hueb, E.G. Lima, B. Biselli, G.L. Garzillo, A.C. Pereira, A.C. Hueb, P.C. Rezende, J.A.F. Ramires, R. Kalil Filho, Heart Institute (InCor) - University of Sao Paulo Clínics Hospital, Sao Paulo, Brazil

Purpose: Ventricular function is a major determinant of prognosis in patients with coronary artery disease (CAD). Few data are available to assess the evolution of ventricular function among patients submitted to off-pump coronary artery bypass graft surgery (OPCAB). To compare the evolution of ventricular function in a long-term follow-up among patients with stable CAD submitted to OPCAB or On-Pump coronary artery bypass graft (ONCAB).

Methods: Patients with stable CAD and preserved systolic left ventricular function were randomized to OPCAB or ONCAB and followed for 5 years. Patients who underwent a new evaluation of ventricular function in this follow-up were studied. Left ventricular ejection fraction (LVEF) was assessed by echocardiogram.

Results: Of 308 patients randomized to OPCAB (n=155) or ONCAB (n=153), 91 had a new assessment of ventricular function by echocardiogram in a 5-year follow-up: 49 in ONCAB group and 42 in OPCAB group. In ONCAB group the initial and final mean of LVEF was respectively 59.5% and 56.1% (p = 0.10). In OPCAB group the initial and final mean of LVEF was respectively 59.18% and 57.8% (p = 0.29).
Conclusions: No difference in the evolution of LVEF among patients with stable CAD randomized to ONCAB or OPCAB in a 5-year follow-up.

Table 1. Identifying the Targets

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>30-Day Readmission</th>
<th>30-Day Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>aOR 95% CI P-Value</td>
<td>aOR 95% CI P-Value</td>
</tr>
<tr>
<td>Male sex</td>
<td>1.01 (0.99-1.02)</td>
<td>1.02 (0.99-1.04) P-Value 0.993</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.36 (1.11-1.71)</td>
<td>1.94 (1.19-3.15) P-Value 0.008</td>
</tr>
<tr>
<td>Chronic Lung Disease</td>
<td>1.99 (1.33-3.48)</td>
<td>0.017</td>
</tr>
<tr>
<td>History of Atrial Fibrillation</td>
<td>1.15 (0.90-1.46)</td>
<td>0.27 (0.76-2.12) P-Value 0.361</td>
</tr>
<tr>
<td>Congenital Heart Failure</td>
<td>1.21 (0.91-1.66)</td>
<td>1.52 (0.87-2.66) P-Value 0.144</td>
</tr>
<tr>
<td>NYHA Class III/IV</td>
<td>0.98 (0.78-1.25)</td>
<td>0.88 (1.79) P-Value 0.34</td>
</tr>
<tr>
<td>Ejection Fraction</td>
<td>0.99 (0.99-1.00)</td>
<td>1.00 (1.00) P-Value 0.976</td>
</tr>
<tr>
<td>Creatinine (mg/dL)</td>
<td>1.08 (0.98-1.19)</td>
<td>1.24 (1.28) P-Value 0.036</td>
</tr>
<tr>
<td>Perfusion Time (min)</td>
<td>1.01 (1.00-1.01)</td>
<td>1.02 (1.00) P-Value 0.001</td>
</tr>
<tr>
<td>Cross Clamp Time (min)</td>
<td>0.99 (0.99-1.00)</td>
<td>0.97 (0.97-0.99) P-Value 0.005</td>
</tr>
<tr>
<td>Value + CABG Procedure</td>
<td>1.11 (0.83-1.47)</td>
<td>0.47 (0.27) P-Value 0.45</td>
</tr>
</tbody>
</table>

Each variable included in the final multivariate model was a significant univariate predictor of the primary outcome (P<0.05).

Conclusions: Thirty-day event rates after cardiac surgery may be influenced by “competing risks” in which lower 30-day mortality rates at individual hospitals may confer higher probability of subsequent readmission. There may be key differences between the prognostic indicators that predict early post-discharge mortality and readmission.

Conclusions: Identifying the targets: are the predictors of 30-day mortality the same as those for 30-day readmission? Eightier cardiac surgery

M. Vaduganathan, A. Adin-Cristian, B. Lapin, N. Homer, S.C. Malaisrie, E.G. Mcege, P.M. McCarthy, R. Lee, Northwestern Univ, Feiberg School of Medicine, Dpt of Medicine/Cardiology & Cardiovascular Surgery, Chicago, United States of America

Purpose: Limited data are available to explore the exact relationship between 30-day mortality and 30-day readmission in individual hospitals after cardiac surgery.

Methods: All consecutive patients (n=4181) who underwent cardiac surgery, excluding LVADs and transplants, from 2004-2011 at a single institution were identified. Primary endpoints of 30-day mortality and readmission were analyzed by multivariate regression models. Expected readmission rates were derived from seven surgery-specific STS national rates and expected mortality scores were based on individual Athers scores.

Results: The observed 30-day mortality rate of 2.6% was substantially lower than the expected rate of 5.9%, while the observed 30-day readmission rate of 12.2% was included in the expected rate of 10.7%. Both increased female sex and longer perfusion times were predictive of both mortality and readmission. Chronic lung disease, NYHA classes III/IV, creatinine levels and cross clamp time were associated with 30-day mortality, but not 30-day readmission.

Conclusions: Each variable included in the final multivariate model was a significant univariate predictor of the primary outcome (P<0.05).

Conclusions: Five years follow-up of on-pump versus off-pump coronary artery bypass surgery in diabetic patients of the MASS III Trial

L.M.A. Costa, C.L. Garzillo, P.C. Rezende, E.G. Lima, D. Favaro, R.M. Vieira De Melo, F.T. Okawa, W. Hueb, J.A.F. Ramires, R. Kalli Filho. Heart Institute (InCor) - University of Sao Paulo Clinics Hospital, Sao Paulo, Brazil

Purpose: Diabetic patients represent one-third of coronary artery disease (CAD) patients, many of whom are treated with revascularization procedures. They are often high risk, including long-term mortality, compared with non-diabetic patients. Few data are available on the effects of off-pump coronary artery bypass graft surgery (OPCAB) on cardiac events and long-term clinical outcomes in this population.

Methods: MASS III is a single-center randomized trial that evaluate 308 patients with stable coronary artery disease and preserved ventricular function assigned for off-pump (n=155) or on-pump (n=153) CABC. The subgroup of 110 diabetic patients were randomly assigned to off-pump CAB (n=56) and on-pump CAB (n=54). Primary composite end points were death, myocardial infarction, further revascularization (surgery or angioplasty), or stroke.

Results: The two randomized groups were well-matched for major baseline demographic, clinical, and angiographic characteristics. After 5-year follow-up, the primary composite end point was not different between groups (event-free survival 83.7% vs 93.7%, P=0.15).

Conclusions: In this analysis, off-pump diabetic patients presented the same incidence of composite end-points compared with on-pump CABG.

Conclusions: Treatment of iatrogenic pseudoaneurysms with cyanoacrylate glue

A. Del Corso,1 G. Vergaro,2 M. Emdin,3 Division of General and Vascular Surgery, Ospedale Cisanello - University of Pisa, Pisa, Italy; 2Gabriele Monasterio Foundation, Pisa, Italy

Purpose: Although the majority of iatrogenic pseudoaneurysm (PSA) are amenable to ultrasound (US)-guided thrombin injection, those causing neuropathy, claudication, significant venous compression or soft tissue necrosis are considered poor candidates for this option and referred to surgery. We thus tested the effectiveness and feasibility of a novel percutaneous cyanoacrylate glue (NBCA)-MS-based technique for treatment of both symptomatic and asymptomatic iatrogenic PSA.

Methods: Over a 2-year period, we prospectively enrolled 68 patients with iatrogenic PSA (total: 71; femoral: 59; brachial 8; radial: 3; axillary: 1). PSA were asymptomatic in 68% of cases, 32% presented with symptoms due to neuropathy, venous compression and/or soft tissue necrosis. All patients signed informed consent and underwent PSA treatment with NBCA-MS injection. We first induced the collapse of the PSA chamber by means of a US-probe, detecting the chamber ostium. Once complete collapse was obtained, a 22-G needle was positioned, under US control, into the thrombus or tissue plugging the PSA chamber ostium and 0.2 ml of NBCA-MS (2 boluses of 0.1 ml, each using 2 different needles and syringes) were injected. Success was assessed immediately, at 1-day and at 3, 12-month ultrasound follow-up.

Results: Mean time of treatment was 17 minutes (range 8-30 minutes). PSA occlusion rate was 99% (70/71). After treatment, mean PSA antero-posterior di- ameter reduction was 64±24%. Neuropathy and vein compression disappeared in 92% (22/24) of cases. Patients with evidence of tissue necrosis (n=6) underwent subsequent outpatient necrosectomy. No bleeding and glue embolization occurred, nor was conversion to surgery necessary.

Conclusions: PSA treatment through NBCA-MS glue injection proved to be safe and effective in asymptomatic patients, as well as in those with neuropathy, venous compression or soft tissue necrosis, currently candidates to surgery. Larger series are needed to further confirm these findings.
Longitudinal compression of third-generation drug-eluting stents: frequency and procedural predictors of the concertina phenomenon


Background: Modern coronary stents include design features that provide greater flexibility to improve deliverability in complex lesions. The platinum-chromium everolimus-eluting stent (Promus Element) has implemented these requirements consistently in a unique scaffold design. Recently, inadvertent longitudinal stent compression during percutaneous coronary intervention (PCI) was noted with this platform. (Figure A: angiography; B: OCT). Aim of this study was to evaluate frequency of longitudinal stent compression during PCI, and define patient and lesion related predictors for this complication.

Methods: All coronary cases treated with an Element stent from January 1, 2010 to October 31, 2011 were analyzed for documented longitudinal stent compres- sion. We compared baseline characteristics and periprocedural data between pa- tients with and without longitudinal stent compression and assessed predictors for this event by multiple logistic regression models.

Results: During 22 months 2,936 Promus Element stents were placed in 1,295 patients and 1,392 PCI cases with 2,839 atherosclerotic lesions. Mean age was 67±11 years, 21.9% were women. Longitudinal compression was reported in 20 patients (1.44%), 20 lesions (0.70%), and 0.68% of all stents. Significant differ- ences were found for number of stents (per case: p<0.001; per lesion:p=0.024), total stent length (p=0.003), ostial segment (p<0.001), and vessel angulation (p=0.002). Ostial segments, number of stents, and the presence of a bifurcation were the only significant predictors (odds ratio [95%-CI]: 8.33 [3.30 to 21.28], 1.57 [1.01 to 2.45], 3.67 [1.36 to 9.35], respectively).

Conclusion: Longitudinal compression of the Element stent is a rare complica- tion and occurs more frequently in ostial or bifurcation lesions and with multiple stents.

Long term prognostic value of high-sensitivity troponin I after elective percutaneous coronary interventions

A. Lapi, A. Rogomi, G.G. Secco, L. Rossi, M. Lazzero, M. Sansa, A.S. Bongo. AOU Maggiore della Carità, Cardiologia Ospedaliera, Novara, Italy

Background: High-sensitivity cardiac troponin (hs-cTn) assays could improve the detection of myocardial damage after percutaneous coronary intervention (PCI) and the prediction of subsequent adverse events. Aim of our study was to evaluate the prognostic value of hs-cTn measured after successful PCI.

Methods: 931 consecutive patients with normal baseline cTnI levels (upper refer- ence limit, URL = 0.04 ng/mL) underwent elective and angiographically success- ful PCI in our Institution. In this population we evaluated the correlation between hs-cTn levels 24 hours after PCI and major adverse coronary events at a median follow up of 3.0 years.

Results: Postprocedural hs-cTnI levels above the URL were common (68.9% of the study population) and met the definition of type 4a myocardial infarction (MI) in 51.9% of patients. Abnormal cTnI levels, even in the range of type 4a MI, were associated with severe coronary atherosclerosis and complex interventions, but failed to predict subsequent cardiac mortality or MI. At univariate analysis only higher levels of hs-cTnI (10 times the URL) were associated with an increased risk of cardiac death (HR 2.16, 95% CI 1.07 to 5.17; p = 0.03) and target vessel failure (HR 1.56, 95% CI 1.02 to 2.42; p = 0.02). After adjustment for concomitant risk factors hs-cTnI levels above 10 times the URL were independent predictors of target vessel failure only.

Conclusions: In a large single-centre population elective PCI patients, hs-cTnI elevation was common and was associated with more complex interventions. However elevated cTnI levels failed to predict long term mortality and MI occur- rence.

Outcomes related to closure methods for cardiac catheterizations

D.R. Doblies, A.L. Cohon, K.R. Barber. Genesys Regional Medical Center, Grand Blanc, United States of America

Purpose: The approach for vessel closure from cardiac catheterization procedures requires closer scrutiny with the advent of 3rd generation devices. Ef- ficacy for the approach of device versus compression has not been examined on a large scale in the clinical setting. The aim of this study was to determine differences in safety and efficacy outcomes between different vessel access pro- cedures.

Methods: This is a real-world, large scale descriptive study utilizing ACC data from multiple clinical sites that were entered prospectively on consecutive patients from over 20 hospitals participating in this cardiovascular registry. All patients un- dergoing a cardiac catheterizations procedure are included in the database of approximately 60,000 patients for the time period between January 1, 2010 and December 31, 2011. Endpoints included complications of bleeding, myocardial infarction, shock, transfusion, and death. Composite scores were calculated for combined bleeding events and for major clinical events. Outcomes were com- pared between site location (fenoral versus radial) and access device (vessel compression versus vessel). Chi square analysis and odds ratio parameters were used to determine statistical superiority at p < 0.01.

Results: A total of 59,530 patients were included (61.5% male, 38.5% female, 91.5% Caucasian, 8.5% minority). PCI was performed on 33,381 (66.0%), Clo- sure methods consisted of compression (manual and mechanical [60.2%] and device [39.5%]). The overall early bleeding (within 72 hr) rate was 1.6%. There was a significant advantage for the device group in all complication outcomes except mortality (1.1% for both groups). Early bleed rate (Device 1.2% Vs Compression 1.8%, p<0.001), composite bleed rate (Device 4.4% Vs Compression 7.2%, p<0.001), and major composite rate (Device 2.9% Vs Compression 4.3%, p<0.001). The effect was as strong among PCI only patients: early bleeding rate (Device 1.8% Vs Compression 2.5%, p<0.001), composite bleed rate (Device 5.7% Vs Compression 8.5%, p<0.001), and major composite rate (Device 4.4% Vs Compression 5.9%, p<0.001). An overall relative risk reduction of 32% was observed favoring device closure.

Conclusions: These findings demonstrate for the first time that device closure is superior to manual compression. The advantage of device closure was demon- strated in terms of bleeding and major complications. It suggests that catastrophic outcomes may be minimized or eliminated with the device approach.

Paraoxonase-1 is not a major determinant of stent thrombosis in the Taiwanese population


Background: Clopidogrel is a prodrug that undergoes in vivo bioactivation to show its antiplatelet effects. Recent studies have shown that cytochrome P450 (CYP), ATP-binding cassette transporters (ABCB1), and paraoxonase-1 (PON1) play crucial roles in clopidogrel bioactivation. Here, we aim to deter- mine the effects of genetic polymorphisms of CYP (CYP 2C19*2, CYP 2C19*3, and CYP 2C19*17), ABCB1 (ABCB1 3435C>T, ABCB1 1298T>C, and ABCB1 2677G>T>A), and PON1 (PON1 Q192R, PON1 L55M, and PON1 108C>T) on the development of stent thrombosis (ST) in patients receiving clopidogrel after percutaneous coronary intervention (PCI).

Methods and Results: We evaluated the incidence of ST (0.64%) in 4964 pa- tients who were recruited in the CAPTURE registry (Chang Gung Atherosclerosis and Percutaneous Transluminal Angioplasty and Interventions). The presence of genetic polymorphisms was assessed in 20 subjects who developed ST after as- pirin and clopidogrel therapy and in 40 age- and sex-matched control subjects who did not develop ST, which was documented after 9 months of angiographic follow-up. ST was acute in 5 subjects, subacute in 7, late in 7, and very late in 1. The presence of CYP 2C19*2 allele was significantly associated with ST (adj- justed odds ratio [ORadj] 4.20, 95% confidence interval [CI]; 1.263–9.544; P = 0.031). However, genetic variations in PON1 and ABCB1 showed no significant association with ST.

Conclusion: We conclude that in a Taiwanese population, PON1 Q192R geno- type is not associated with ST development after PCI. However, the presence of CYP 2C19*2 allele is a risk factor for ST development after PCI.

High Syntax (synergy between percutaneous coronary intervention with taxus and cardiac surgery) score predicts no-reflow in patients with st-elevation myocardial infarction


Purpose: The aim of this study was investigate whether the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score is associated with no-reflow in patients with ST-elevation myocardial infarction (STEMI) undergoing primary percutaneous coronary intervention (PCI).
Methods: Consecutive patients with STEMI undergoing primary PCI in a single tertiary cardiac center were enrolled. No-reflow was defined by means of angiography as the presence of myocardial blush grade 0 or 1 at the end of primary PCI. The SYNTAX score was calculated by 2 independent cardiologists who were blinded to no-reflow assessment. A multiple logistic regression analysis, with the calculation of odds ratios (OR) with 95% confidence intervals (CI), was performed, entering SYNTAX score either as continuous variable or as dichotomous variable (i.e. SYNTAX score >32) in addition to sex, age, main cardiovascular risk factors and known predictors of no-reflow such as anterior myocardial infarction, time from symptom onset, infarct size, admission sestamibi, thombromboly use. A two-tailed p-value < 0.05 was considered statistically significant.

Results: A total of 371 patients, median age 65.3 yrs-old (54.8-73.7, 25th-75th percentile), 268 (72.2%) males, were enrolled. Baseline median value of SYNTAX score was 16 (9.5-23.5, 25th-75th percentile). Patients with no-reflow presented significantly higher values of SYNTAX score as compared to those without no-reflow (18.7 median (10-26.5, 25th-75th percentile) vs. 14 (9-21.5), p=0.017). The incidence of no-reflow was significantly higher in patients with SYNTAX score >32 than in patients with SYNTAX score ≤32 (13.9% vs. 5.1%, p=0.003). At multiple logistic regression analysis, SYNTAX score as continuous variable (OR 1.03, 95% CI 1.001-1.05, p=0.025) or SYNTAX score >32 (OR 2.74, 95% CI 1.23-6.12, p=0.014) was an independent predictor of no-reflow.

Conclusions: In patients with STEMI undergoing primary PCI, high SYNTAX scores are an independent predictor of no-reflow.

Safety and efficacy of modified Mynx TM (vascular closure device) deployment technique in 1,005 consecutive cases

Z. Ijalb, C. Shaw, O. Hasan, L. Wang, R. Tayal, S. Kotev, G. Rana, D. Iyer, M. Cohen, N. Wasty, Newark Beth Israel Medical Center, Newark, United States of America

Purpose: Safety and efficacy of MNYX TM (vascular closure device) has been established in previous studies. To further enhance its safety and efficacy we developed a modified technique of Mynx deployment and studied it in 1,005 consecutive cases.

Methods: In our modified approach; a femoral angiogram is taken to demonstrate the sheath entry point in common femoral artery. The balloon at the tip of Mynx is filled with saline and contrast mixture. After introduction through the sheath, the inflated balloon is pulled back to the arteriotomy site under fluoroscopic visualization, using previously stored image to ensure complete apposition to the arteriotomy site. We prospectively applied this technique to 1005 consecutive cases, who underwent diagnostic angiography and coronary or peripheral interventions. Adverse outcomes consisted of hemotoma >5 cm, retroperitoneal hemorrhage, acute vessel closure, AV fistula, pseudoaneurysm, and blood transfusion. Efficacy was defined as successful device deployment without any need for manual compression. Patients were followed during the same hospital stay.

Results: No complications were noticed regardless of patient characteristics. There were 4 device deployment failures in diagnostic and 5 in intervention subgroup (Table 1).

Use of urinary neutrophil gelatinase-associated lipocalin (NGAL) to assess contrast induced nephropathy in patients with NSTEMI undergoing coronary angioplast (PCI)


1Changi General Hospital, Singapore, Singapore; 2National Heart Centre Singapore (NHCS), Singapore, Singapore; 3National University of Singapore, Biostatistics Unit, Singapore, Singapore

Purpose: We assessed the role of urinary neutrophil gelatinase-associated lipocalin (NGAL) to diagnose contrast induced nephropathy in patients with NSTEMI undergoing coronary angioplast (PCI). This is also the first study evaluating NGAL in a multi-ethnic Asian cohort.

Methods: Patients with NSTEMI and scheduled for PCI were prospectively recruited from 2 tertiary hospitals in Singapore over 1 year. Serum creatinine and estimated glomerular filtration rate (eGFR) were measured at 0, 24 and 48 hours after PCI. Urine NGAL was collected at baseline pre-PCI then 2, 4, 8, 24 and 48 hours after PCI. CIN was defined as a 25% or 0.5 mg/dl rise in serum creatinine within 48 hours after PCI.

Results: 101 patients were recruited, but 2 were excluded due to absence of serum creatinine values at 24h and 48h. 35% of the patients were diabetic. 90% had an eGFR <60 ml/min while the remainder had eGFR 60-90 ml/min. 11 patients developed CIN (11.1%). The mean contrast volume used was 158.9±52.8 ml (95% CI). There was no mortality and none required dialysis. Baseline characteristics of patients who developed CIN and those who did not develop CIN were similar, including age, gender, race, eGFR, smoking, hypertension, diabetes mellitus, volume of contrast used, and renal risk score. However,
ST peak during primary percutaneous coronary intervention predicts final infarct size, left ventricular function and clinical outcome

J. Lønberg1, H. Helbæk1, L. Holmvang1, N. Velstrup1, E. Joergensen1, S. Helqvist1, C.J. Terkelsen1, W.Y. Kim2, P. Clemmensen1, T. Engstroem1, 1Rigshospitalet - Copenhagen University Hospital, Heart Centre, Cardiac Catheterization Laboratory, Copenhagen, Denmark, 2Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark

Purpose: One of third patients treated with primary PCI develop an secondary increase in electrocardiographic ST-segment elevation (ST peak) during reperfusion. The prognostic importance of ST peak remains unknown and the association between ST peak and final infarct size is not fully elucidated. The purpose of the present study is to determine the association between a ST peak, and final infarct size and clinical outcome in patients treated with primary percutaneous coronary intervention (PCI).

Methods: Continuous ST monitoring was performed in 363 STEMI patients from arrival at the PCI centre until 90 minutes after revascularisation. Patients were stratified according to no-ST peak or ST peak. Final infarct size and ejection fraction was assessed by cardiac magnetic vascular resonance. All-cause mortality, cardiac mortality and cardiac event rate (death or admission for heart failure) were recorded after discharge. Results: Patients with ST peak had larger final infarct size (14% vs. 10%; p<0.003) and a lower ejection fraction (53% vs. 57%; p=0.022). At follow-up after median 913 days there were no differences in all-cause mortality (6% vs. 5%, p=0.46), whereas cardiac mortality (8% vs. 3%; p=0.047) and cardiac event rate (19% vs. 10%; p=0.018) were both higher among patients with ST peak. In a multivariable Cox regression analysis, including ST resolution and elevation, ST peak during PCI remained significantly associated with cardiac events (adjusted hazard ratio 2.03 (1.08-3.82)).

Conclusions: ST peak occurring during primary PCI is related to larger final infarct size, a reduced left ventricular ejection fraction, and adverse clinical outcome.

Predictors of persistent renal dysfunction after acute kidney injury in percutaneous coronary intervention

C.J. Kim, I.J. Choi, S.M. Lim, J.J. Kim, M.E. Chang, P.J. Chung, K.Y. Chang, T.H. Kim, Y.S. Koh, K.B. Seung. Seoul St. Mary’s Hospital, Seoul, Korea, Republic of Korea

Backgrounds: Percutaneous coronary intervention (PCI) is often complicated by acute kidney injury (AKI) and resulting in permanent renal dysfunction or restoration of normal renal function. However factors associated with clinical course of AKI during PCI are not well known. The aim of the present study is to investigate factors which predict the clinical course of AKI whether to transient kidney injury or permanent renal dysfunction.

Methods: From January 2004 to December 2009, 7382 patients without history of end stage renal disease or kidney transplantation were selected form COACT (CathOlic medical center percutaneous Coronary Intervention) registry. Mean follow-up period was 26 months. 474 patients diagnosed with acute kidney injury after PCI were selected and stratified into two categories; AKI with transient renal dysfunction and persistent renal dysfunction. Results: At median 913 days no difference in all-cause mortality was observed (6% vs. 5%, p=0.46), whereas cardiac mortality (8% vs. 3%; p=0.047) and cardiac event rate (19% vs. 10%; p=0.018) were both higher among patients with ST peak. In a multivariable Cox regression analysis, including ST resolution and elevation, ST peak during PCI remained significantly associated with cardiac events (adjusted hazard ratio 2.03 (1.08-3.82)).

Conclusions: ST peak occurring during primary PCI is related to larger final infarct size, a reduced left ventricular ejection fraction, and adverse clinical outcome.
such as preexistent antithrombotic/anticoagulation therapy and renal insufficiency may help to further optimize access management.

**Clinical outcomes of unprotected left main PCI and correlation with the type of adjunctive antithrombotic therapy: a pooled analysis from REPLACE-2, ACUTY and HORIZONS-AMI trials**

T. Geisler1, K. Mueller1, A. Karathanos1, E. Deliargyris2, M. Gawaz1, A.M. Lincoln2, G. Dangas1, R. Mehran3, G. Stone6 on behalf ofTuePIC.

**Methods:** This is an analysis of 177 patients with ULMCA from a pooled dataset of 14,326 patients treated with aspirin and clopidogrel who underwent PCI in 3 large randomized trials comparing treatment with heparin plus a glycoprotein IIb/IIIa inhibitor (GP IIb/IIIa) or bivalirudin alone, including the REPLACE-2 (Randomized Evaluation of PCI Linking Angiography to Reduced Clinical Events), ACUTY (Acute Catheterization and Urgent Intervention Triage Strategy) and HORIZONS-AMI (Harmonizing Outcome With Revascularization and Stents in Acute Myocardial Infarction) trials. 30-day clinical outcomes were evaluated.

**Results:** Patients with ULMCA represented a higher risk cohort. Overall net adverse clinical outcomes and non-CABG major bleeding occurred more frequently in patients undergoing PCI of ULMCA compared to the overall study population patients (NACE: 19.8 vs. 10.6; P<0.001; Major Bleeding: 9.6% versus 4.6; P<0.001). In the ULMCA group, bivalirudin was associated with significantly less non-CABG major bleeding compared to heparin plus GP IIb/IIIa (4.5% versus 14.6%, RR 0.31, 95% CI 0.16-0.62; p<0.001). The composite ischemic endpoint of death, AMI, revascularization, and stroke between 30 days was similar in all treatment groups (11.4% vs. 12.4, P=0.513) resulting in a net adverse clinical benefit for bivalirudin over heparin plus GP IIb/IIIa (14.9% vs. 24.7%; RR 0.53; p=0.039).

Conclusions: Among patients undergoing either elective or urgent PCI of ULMCA, bivalirudin was associated with significantly reduced incidence of major bleeding, similar rates of ischemic events and improved net clinical outcome. Bivalirudin may be the preferred anticoagulation strategy in this high risk group of PCI patients exhibiting a high risk for both thrombotic and bleeding events.

**The relationship between hyperuricemia and the risk of contrast-induced acute kidney injury after percutaneous coronary intervention in patients with relatively normal serum creatinine**

J.Y. Chen, Y. Liu, N. Tan, Y.L. Zhou, Guangdong General Hospital, Guangdong Cardiovascular Institute, Department of Cardiology, Guangzhou, China, People’s Republic of China.

**Objectives:** This study evaluated the predictive value of hyperuricemia for risk of CI-AKI in patients with relatively normal serum creatinine (SCr) who were undergoing percutaneous coronary intervention (PCI).

**Methods and Results:** A total of 788 patients with relatively normal baseline SCr (<1.5 mg/dl) undergoing PCI were prospectively enrolled and divided into two groups (hyperuricemic group, n = 211, and normouricemic group, n = 577). CI-AKI occurred in 17 (8.1%) of the hyperuricemic group and 8 (1.4%) of the normouricemic group (P = 0.001). In-hospital mortality (2.4% vs. 0.3%, P = 0.007) and the cumulative 1-year mortality (P = 0.007) were higher in the hyperuricemic group. Multivariate analysis, adjusting for potential confounding factors, resulted in an odds ratio for CI-AKI in the hyperuricemic group, as compared with the normouricemic group, of 9.38 (95% confidence interval, 1.99-45.58; P = 0.001).

**Conclusions:** Hyperuricemia was significantly associated with the risk of CI-AKI in patients with relatively normal SCr after PCI. This needs further prospective trials aimed at examining the effect of uric acid-lowering therapies for prevention of CI-AKI.

**Long term prognosis of contrast induced nephropathy: a prospective study with 3 years follow-up**

M. Pighi, P. Pasoli, G. Pesarini, A. Mugnolo, B. Bolzan, F. Ribichini, C. Vassanelli. University of Verona, Department of Biomedical and Surgical Sciences, Verona, Italy.

**Purpose:** The increased incidence of long-term adverse events (AE) after CI is derived from retrospective analyses of large databases and observational studies of patients. The aim of the present study was to prospectively evaluate, at short and long-term follow-up, the incidence, the predictors of CI and the occurrence of CI-related AE, in a population at risk for acute kidney injury undergoing coronary angiography.

**Methods:** 216 patients at risk for CI, were included in the study and completed all the in-hospital observation mandated by the protocol, including determinations of serum creatinine (SCr) and glomerular filtration rate (GFR), at 12, 24 and 48 hours after exposure to contrast media. CI was defined as an acute impairment of the renal function, expressed as a relative increase in SC concentration at least 25% of baseline values or an absolute increase in SC of at least 0.5 mg/dl (44.2 mmol/l) in the absence of other related causes. The follow-up included telephone contact or office visit, and the collection of clinical data at predefined time-points:30 days, 1-3 years after the index procedure in order to evaluate the occurrence of AE and the renal function in each patient enrolled in the study.

**Results:** Events occurred in 45 patients (20.8%). Minimum relative increase of SC (5-10%) at 12 hours compared to baseline were highly predictive of CI. In late follow-up assessment no significant correlation was found between the occurrence of CI in hospital and major AE, defined as death, myocardial infarction or renal failure at 1 and 3 years follow-up (CE incidence respectively 1.9, 8% (event free survival (EFS):CI=N= 97.2±4.0%, CI=95.1±2.4% vs. p=0.45) and 37±13.9% (EFS CI= 85.2±5.6% CI=84.9±2.9% vs. p=0.06)). However, in-hospital reductions of baseline GFR and increments of SC values after the procedure were strongly correlated with morbidity and mortality at 3 years (GFR<-60/min/EFS77.6±4.2%; GFR>60/min/EFS 92.1±2.7%, p<0.006).

Patients, who developed CI, showed a persistent impairment of renal function proved by significant increment of SC at 1 and 3 years compared to baseline.1.9±0.58 mg/dl; 3y:1.64±1.23 mg/dl; 3y:1.65±1.46 mg/dl (p<0.04). Patients without CI showed instead stable SC values along time (baseline: 1.16±0.39, 1y: 1.22±0.8; 3y: 1.13±1.06, p=n.s).

**Conclusions:** Our findings do no support a direct correlation between in-hospital development of CI and long-term incidence of AE. The study shows a significant relationship between any in-hospital reduction of GFR and the occurrence of AE at long-term, independently of the occurrence of CI as conventionally defined.

**Clinical predictors of contrast-induced nephropathy in the patients undergoing emergent versus elective percutaneous coronary interventions**


1Ikari Research Center, Nihon University; 2Nihon University; 3University of Tsukuba; 4Moriya Daiichi General Hospital; 5Hitachi General Hospital, Department of Internal Cardiology, Hitachi, Japan; 6Hitachi General Hospital, Department of Internal Cardiology, Hitachi, Japan

**Purpose:** The aim of this study was to evaluate an incidence and clinical predictors of contrast-induced nephropathy (CIN) in the patients undergoing emergent versus elective percutaneous coronary intervention (PCI) who had ST-segment elevated myocardial infarction (STEMI) and unstable angina pectoris/non-STEMI (UAP/NSTEMI), and elective PCI who had stable AP.

**Methods:** We enrolled 1309 stable AP (70.3±9.70 year-old, 77%male), 342 UAP/NSTEMI (69.3±11.9 year-old, 76%male), and 718 STEMI (67.9±12.3 year-old, 77%male) in Ikari Research Center Assessment Study (ICAS) registry between April 2007 and August 2011. We also divide into three subgroups on the basis of contrast volume of GFR (GFR<2.0, mid: 2.0-2.9, high: >2.0). CIN was defined as serum creatinine increased 0.5mg/dl or 25% within 1 week from contrast medium injection. Patients receiving dialysis at the time of the procedure were excluded.

**Results:** Incidence of CIN was gradually increased among three groups (stable AP vs. UAP/NSTEMI vs. STEMI, 4.2%, 10.8%, 16.9%, p<0.05) (Figure 1). Among emergent CI/GFR subgroups, incidence of CIN was also gradually increased among three groups (Figure 2). Multivariate logistic regression analysis showed that the significant predictors of CIN were emergent PCI (OR 2.19, 95%CI 1.82-2.62, p<0.001), low ejection fraction (EF<40%, OR 2.29, 95%CI 1.43-3.68, p<0.001), previous infarct (HR=1.10-10.86, OR 2.06, 95%CI 1.02-4.15, p<0.002) after adjusting multiple confounders. The risk of CI was significantly associated with increasing CI/GFR in stable AP group (p<0.05), but not associated in UAP/NSTEMI and STEMI groups.
Conclusions: STEMI patients undergoing PCI regardless of CV/GFR were at high risk for CIN. Minimizing contrast dose on the basis of eGFR might be valuable in reducing the risk of CIN in stable AP group.

P654

Risk factors for the development of coronary stent thrombosis

N. Malik1, A.S. Banning2, A.H. Gerich2. 1University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom; 2University Hospitals of Leicester NHS Trust, Leicester, United Kingdom

Purpose: Despite major advances in coronary stent technology, stent thrombosis (ST) remains the “Achilles heel” of percutaneous coronary intervention, with an incidence of 0.5–4% and a mortality rate of 20–40%. Although there are many patient, procedural and lesion-related predictors for ST, there are no risk-scoring systems to guide the use of newer, more potent antplatelet agents. Therefore, the existing literature was reviewed to develop this.

Methods: Bibliographic databases including MEDLINE, EMBASE, the cochrane databases, database of abstracts of reviews of effects and the health technology assessment database were searched from 1990 to 2010 to identify relevant studies. Studies were included if they had at least 500 participants or at least 50 cases and if they estimated the effects of risk factors using multivariate analyses. A total of 24 studies with risk factors for early ST (<30 days) and 14 studies with risk factors for late ST (30 days to 1 year) were used. Data were pooled according to reporting of similar risk factors between each study.

Results: The risk factors identified to predict early stent thrombosis with pooled OR/HR (95% confidence intervals in brackets) were acute MI at presentation, 13.1 (7.1-23.9), premature antiplatelet discontinuation, 5.3 (3.2-8.8), previous CHF or CHF at presentation, 2.2 (1.4-3.5), renal insufficiency, 5.4 (2.4-12.2), premature antiplatelet discontinuation, 11.3 (8.0-16.0), post-procedure haemorrhage, 4.2 (3.0-6.0), bifurcation lesion, 2.7 (2.0-3.6), thrombus at baseline, 2.5 (1.5-4.1), ACS at presentation, 2.4 (1.9-3.0), previous CHF or CHF at presentation, 2.2 (1.4-3.5), renal insufficiency, 2.1 (1.1-2.2), diabetes mellitus, 2.1 (1.7-2.5) and current smoking, 1.48 (1.18-1.86).

For late stent thrombosis, the risk factors identified with pooled OR/HR were revascularization only did not receive heparin during the procedure, whereas in patients undergoing PCI an additional bolus of 5000 IE of unfractionated heparin was given intravenously. Results: A total of 30 patients underwent diagnostic catheterization and in 3 patients a PCI was performed. 4 patients presented in the setting of acute coronary syndromes. The mean international normalized ratio was 2.3 (±0.5). The incidence of RAO in Duplex sonography was 33.3% (11 patients), all of which received a diagnostic coronary catheterization. Interestingly, RAO was only seen in patients who underwent diagnostic angiography using 5 F sheaths. No patient presented with a critical limb ischemia. There was no evidence of av-fistulas or pseudoaneurysms. We did not see any case of major bleeding requiring transfusion therapy. Procedural success was achieved in 97%, one patients required cross-over to femoral access because of vascular spasm.

Conclusion: The transradial approach for coronary angiography proved to be safe with regard to bleeding complications in patients with ongoing oral anticoagulation. However, the incidence of radial artery occlusion was higher than expected from our prospective radial access registry data in non-coagulated patients. This pilot study therefore raises the question whether an additional heparin bolus needed to be administered in patients undergoing trans-radial coronary angiography on full oral anticoagulation. This question will be addressed in a prospective randomized trial shortly.

AORTA, PERIPHERAL ARTERIAL AND VENOUS SURGERY

P657

Effect of Angiotensin Receptor Blockers on long term aortic events in medically treated patients with type B acute aortic dissection

K. Kato1, N. Inagaki1, H. Horibe2, T. Hibino3, K. Yokoo2, Y. Dohe2, T. Murohara4, G. Kimura2, N. Uslu2, O. Surgit4, F. Uzun4, A. Yildirim2, N. Uslu2, O. Surgit4, F. Uzun4, A. Yildirim2, N. Uslu2, O. Surgit4, F. Uzun4, A. Yildirim2, N. Uslu2. 1Meito Hospital, Department of Internal Medicine, Nagoya, Japan; 2Gifu Prefectural Tajimi Hospital, Department of Cardiovascular Medicine, Tajimi, Japan; 3Nagoya City University, Graduate School of Medical Sciences, Dept. of Cardiology, Nagoya, Japan; 4Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Purpose: Although antihypertensive therapy is the standard of care for type B aortic dissection in both acute and chronic phases, the mortality of patients with type B aortic dissection treated with medication in the chronic phase remains
high. This retrospective case-control study aimed to explore the effect of angiotensin receptor blockers (ARBs) on the outcomes of medically treated patients with type B aortic dissection treated with medication in the chronic phase.

Methods: A total of 87 patients with type B AD were enrolled; mean age was 65.3±12.0 years and the mean follow-up period was 19.5±17.7 months. All patients received anti-hypertensive therapy according to the guideline for standard care of acute aortic dissection, and were followed up by a physician's examination and enhanced computed tomography. Unfavorable outcome in the chronic phase was defined as death, surgical repair, or progression of dissecting aorta.

Results: The group with unfavorable outcomes (unfavorable group) consisted of 31 type B aortic dissection patients in the chronic phase; the remaining 56 patients had favorable outcomes (favorable group). The incidence of true lumen compression, falsed Kany murin, false to true lumen ratio, and maximum dissection diameter were significantly greater (P<0.002, P=0.041, P=0.042, and P<0.011, respectively), and thrombosed false lumen was significantly less frequently present (P<0.001) in the unfavorable group compared with the favorable group. In receiving anti-hypertensive drugs, there were no significant differences between the favorable and unfavorable outcome groups except for the greater percentage of patients receiving ARBs (P<0.002) in the favorable outcome group. Cox regression analysis demonstrated that for type B aortic dissection patients in the chronic phase receiving ARB and thrombosed false lumen were positively associated with favorable outcomes (P=0.002, hazard ratio, 2.15, 95% confidence interval 0.96-5.06; and P=0.009, hazard ratio 0.248, 95% confidence interval 0.087-0.710, respectively). Kaplan-Meier analysis showed that patients receiving ARBs had a significantly lower rate of mortality, aortic surgical repair, and progression of dissecting aorta than those not receiving ARBs (Wilcoxon's test, P=0.048).

Conclusion: This case-control study indicated that administration of ARBS was significantly associated with a decreased risk for death, surgical repair, or progression of dissection in type B aortic dissection patients. The prognosis of type B aortic dissection patients appears to improve by administration of ARB in the long term.

### Predictors of early mortality in patients with critical limb ischemia caused by isolated below-the-knee artery disease

#### Background

Previous study suggests that critical limb ischemia (CLI) patients who are unlikely to live 2 years are probably better served by Endovascular treatment (EVT) first revascularization. In this study, we sought to investigate the predictors of early mortality in patients with CLI caused by isolated below-the-knee (BTK) artery disease.

#### Methods

This study was a multicenter retrospective observational study of type BTK artery disease. From March 2004 to June 2011, total of 684 patients with CLI who underwent angioplasty for de novo isolated BTK artery disease were enrolled. Outcome measure was all-cause mortality within two years and their predictors.

#### Results

Mean follow-up period was 589±527 days. Thirty-eight percent had non-ambulatory status, and 24% had cerebro-vascular disease (CVD). Mean body mass index (BMI) was 21.6±3.3, serum albumin level was 3.5±0.6 g/dl, ejection fraction (EF) was 59±14%. All-cause death within two years was accounted for 25.0%. Cox multivariate analysis was performed to determine predictors in the unfavorable outcome group compared with the favorable outcome group. In receiving anti-hypertensive drugs, there were no significant differences between the favorable and unfavorable outcome groups except for the greater percentage of patients receiving ARBs (P<0.002) in the favorable outcome group. Cox regression analysis demonstrated that for type B aortic dissection patients in the chronic phase receiving ARB and thrombosed false lumen were positively associated with favorable outcomes (P=0.002, hazard ratio, 2.15, 95% confidence interval 0.96-5.06; and P=0.009, hazard ratio 0.248, 95% confidence interval 0.087-0.710, respectively). Kaplan-Meier analysis showed that patients receiving ARBs had a significantly lower rate of mortality, aortic surgical repair, and progression of dissecting aorta than those not receiving ARBs (Wilcoxon's test, P=0.048).

Conclusion: This case-control study indicated that administration of ARBS was significantly associated with a decreased risk for death, surgical repair, or progression of dissection in type B aortic dissection patients. The prognosis of type B aortic dissection patients appears to improve by administration of ARB in the long term.
achieved in 93% and complication rate was 8%. Primary patency at 1- and 3- and 5-year were 97%, 91% and 85%, respectively. Secondary patency was 100% during follow-up period. On multivariate analysis, female gender (P=0.02), and venous to arterial distensibility (P=0.01), were independent predictors of primary patency. Overall survival rates were 90%, 79%, 68% at 1- and 3- and 5-years. On multivariate analysis, age (P=0.02), chronic kidney disease (P=0.003), dialysis (P=0.004), were independent predictors of all cause mortality. Conclusion: Primary stenting for SCD was safe and was effective for the long-term clinical follow-up period.

### Left ventricular contractility impairment in Marfan patients is related to increased aortic stiffness


**Introduction:** Previous studies demonstrated aortic stiffening in Marfan patients by magnetic resonance imaging (MRI). Therefore, left ventricular (LV) contractility could be impaired due to an increased afterload. We aimed to establish the relationship between LV contractility and aorta distensibility in Marfan patients.

**Methods:** MRI and echocardiography were performed in 27 Marfan patients and 15 matched for age, sex, and body surface area controls. Mean time between studies was 4.3±3.6 months. Ascending aorta distensibility and ascending-to-abdominal pulse wave velocity (PWV) were analyzed by MRI. LV volumes, ejection fraction, septobasal tissue Doppler velocity (TDV), global longitudinal strain (GLS) were expressed as percentile of maximal area/10-3 Sec. Aortic size index (maximal aortic diameter/BSA) was calculated for all the patients.

**Results:** LV ejection fraction was similar between Marfan patients and controls. Telediastolic and telesystolic indexed volumes were greater in Marfan compared with controls. Septobasal TDV were similar between Marfan and controls (6.2 cm/s vs 6.5 cm/s, p=0.503). However, GLS and septobasal LS were lower in Marfan compared with controls (-17.1% vs -18.9%, p=0.045 and -19.6% vs -15.6%, p=0.004). Ascending aorta distensibility and ascending-to-abdominal PWV by MRI were impaired in Marfan compared with controls (2.6 vs 4.6 mmHg/10-3 Sec, p<0.001 and 4.0 vs 4.9 m/s, p=0.030). Septobasal TDV was not correlated either with ascending aorta distensibility or PWV. However, GLS and septobasal LS correlated positively with PWV (r=0.392, p=0.035 and r=0.664, p<0.001).

**Conclusions:** Marfan patients have impaired LV contractility and a stiffened aorta. Furthermore, LV contractility is correlated with aortic distensibility. These results provide further insight into the ventriculo-aortic interdependence in Marfan patients.

### MRI evaluation of ascending aorta biophysics: new functional indexes and their relationship with aortic size


1Sant’Anna School of Advanced Studies, Sector of Medicine, Pisa, Italy; 2Fondazione Toscana Gabriele Monasterio, Department of Cardiac Surgery, G. Pasquarini Heart Hospital, Massa, Italy; 3Gabriele Monasterio Foundation-CNR Region Toscana, MRI Laboratory, Pisa, Italy; 4Institute of Clinical Physiology of CNR, Pisa, Italy

**Purpose:** Ascending aorta aneurysm is one of the most common cause of death in cardiovascular patients. Prophylactic surgery to avoid mortality due to dissection is recommended at a aortic diameter of 5.5 cm in otherwise healthy patients. Nevertheless, there are several limitations of this criteria. Aortic size index allows to stratify patients according to the level of risk of dissection/rupture, enabling appropriate surgical decision-making. Recently two new MRI indexes of aortic wall distension and recoil during cardiac cycle were developed. We evaluated two new MRI-derived functional indexes to describe the elastic properties of ascending aorta in patients with different aortic size index.

**Methods:** MRI images were collected in 201 consecutive patients with atherosclerotic thoracic aortic aneurysm undergoing surgery for ascending aortic aneurysm were enrolled in the study. All the patients underwent comprehensive cardiac MRI study. A standard protocol to acquire the MRI images has been followed and MRSD and MRDR were calculated as cross-sectional area of the proximal ascending aorta (5 mm above the sinotubular junction) measured in each cardiac phase was indexed for the maximal end systolic cross-sectional area and plotted against the time. MRSD and MRDR were expressed as percentile of maximal area/10-3 Sec. Aortic size index (maximal aortic diameter/BSA) was calculated for all the patients.

**Results:** We found a significant correlation between MRSD (r=0.28, r²=0.06, p=0.0341) and MRDR (r=0.35, r²=0.12, p=0.0019) and aortic size index (24.98±3.27 mm², range 18.05-30.12 mm²). Aortic index increases, MRSD and MRDR of the aorta decreases. Increased aortic index, which is the predictor for the negative event, correlation with decreased MRSD and MRDR suggest of aortic stiffness in these patients. Furthermore, a significant correlation between the age of the patient and decrease in the MRSD (r²=0.20, p=0.0406) and MRDR (r²=0.26, p=0.0136) of the aorta is observed. As patients get older their aorta becomes stiffer, which is confirmed by significant decrease in these two new indexes.

**Conclusions:** MRSD and MRDR are related to aortic size index and age of the patient. They seem to describe properly the increasing stiffness of enlarged aorta. Further prospective studies are needed to test the prognostic significance of these novel indexes.
Advanced glycation endproducts are elevated and predictive for mortality in patients with peripheral arterial occlusive disease

1 University Medical Center Groningen, dept. of Vascular Medicine, Groningen, Netherlands; 2University Medical Center Groningen, dept. of Vascular Surgery, Groningen, Netherlands

Background/hypotheses: Advanced glycation endproducts (AGEs) are sugar-modified proteins which accumulate during normal aging. AGEs are particularly increased during oxidative and glyceric stress and play an important role in the formation of atherosclerosis. We hypothesized that AGEs are increased in PAOD and predictive for mortality.

Methods: A total of 514 patients with PAOD and 171 age-matched controls were included in this cross-sectional study. Cohort A (n=286) was measured in 2007-2008 and cohort B (n=250) in 2010-2011. AGEs were quantified non-invasively by skin autofluorescence (SAF) measurements. Cardiovascular risk factors were inventoried. The prospective follow-up study on mortality was done in cohort A. Independent p-values obtained via Chi-square tests, Kaplan-Meier and Cox regression analysis were performed. In linear regression analysis, AGE level was the dependent and cardiovascular risk factors were the independent variables. A p-value ≤ 0.05 was considered statistically significant (SPSS 18.0).

Results: The mean age of patients and controls was 65 (SD 11) years. Mean AGEs level was higher in patients compared to controls: 2.77 (95% CI: 2.71-2.83) vs. 2.55 (95% CI: 2.59-2.84), p=0.03. 3D ultrasound data were averaged in patients with AAA compared to healthy volunteers. Based on the spatial raw data by a modified wall motion tracking algorithm with Advanced Cardiac Pack-age (Toshiba, UltraExtend) and circumferential strain (CS) and 3D displacement were calculated. 3D strain were also further analyzed and processed to visualize local strains and displacements on 3D models of the abdominal aorta.

Results: Circumferential strain and 3D aortic displacement were significantly reduced in patients with AAA compared to healthy volunteers. Based on the spatial and temporal data derived from 3D speckle tracking analysis we were able to model the imaged segment of the abdominal aorta and compute the resulting displacements and strains (figure 1).

Figure 1. Models of abdominal aorta in a healthy volunteer (left panel) and a patient with AAA (right panel) with resulting strains.

Discussion: 3D speckle tracking analysis can be successfully used to study the real-time deformation of the abdominal aorta and to estimate local wall strains. Our results show that patients with AAA have reduced wall strain which most likely results from increased aortic stiffness. Aortic wall strain measurement may represent a useful supplement for the in vivo assessment of the biomechanical properties of the aorta.

Nomogram for normal adult aortic root dimensions at cineangiography

1 Institute of Postgraduate Medicine, University of Brighton, Brighton, United Kingdom; 2Department of Public Health, University of Malta, Msida, Malta; 3Mater Dei Hospital, Msida, Malta

Background: Various imaging modalities are available for aortic root assessment. They allow for early detection of pathological dilatation. Ventriculography at the time of coronary angiography may be the first test to raise the suspicion of a dilated root. Therefore, AGES can be used as a risk marker in PAOD patients and could identify patients who may benefit from more aggressive treatment of cardiovascular risk factors.

Methods: The group B, respectively (p=0.045). Freedom from aortic event at 96 months after the operation were 76.0±5.7% and 68.7±6.1%, respectively (p = 0.0079). Freedom from coronary event and freedom from cerebral vascular event were not significant difference between the two groups.

Conclusion: The rate of patients with PAD was 43.8%, preoperatively. Euro score2 and hospital mortality in the patients with PAD were higher than in the patients without PAD, significantly. In the long term outcome, the survival rates and freedom from aortic event in the patients with PAD were significant lower than in the patients without PAD.

Aortic wall strain assessment and in vivo vascular modelling based on 3D-ultrasound speckle tracking analysis

1 University Hospital Giessen and Marburg, Department of Cardiology, Marburg, Germany; 2University Hospital Giessen and Marburg, Department of Heart and Vascular Surgery, Marburg, Germany; 3Institute for Cell Biology and Neuroscience, Goethe-University, Frankfurt, Germany; 4Department of Vascular and Endovascular Surgery, Goethe University, Frankfurt, Germany

Introduction: Ultrasound imaging techniques have been employed to assess arterial wall motion and deformation, providing important insights in arterial mechanics and related pathologies. In the present study, we employed the novel 3-dimensional (3D) ultrasound speckle tracking analysis on the abdominal aorta.

Methods: Abdominal aorta imaging was performed on 10 healthy volunteers and 3 patients with abdominal aortic aneurysm (AAA) with a commercial 3D echocardiography system (Artida, Toshiba Medical Systems, Tokyo, Japan) by means of a 3D transthoracic probe (PST-25SX, 1 to 4 MHz phased array matrix transducer). Aortic wall motion analysis with speckle tracking was performed on the stored raw data by a modified wall motion tracking algorithm with Advance Cardiac Pack-age (Toshiba, UltraExtend) and circumferential strain (CS) and 3D displacement were calculated. 3D data were also further analyzed and processed to visualize local strains and displacements on 3D models of the abdominal aorta.

Results: Circumferential strain and 3D aortic displacement were significantly reduced in patients with AAA compared to healthy volunteers. Based on the spatial and temporal data derived from 3D speckle tracking analysis we were able to model the imaged segment of the abdominal aorta and compute the resulting displacements and strains (figure 1).

Freedom from antihypertensive medication after balloon dilatation with stent implantation in patients with coarctation of the aorta

P. Galvao Santos, M. Matos Silva, P. Amador, C. Figueiredo, S. Condeira, F. Maymonn Martins, A. Francisco, A. Telêira, N. Carvalho, R. Anjos. Hospital West Lisbon, Hospital Santa Cruz, Department of Cardiology, Lisbon, Portugal

We assessed determinants of freedom from medication at long term follow up after stent implantation for coarctation. 65 consecutive patients with native CoAo and ReCoAo underwent stent implantation between January 1998 and November 2011. Six patients with other causes for hypertension, complex heart or arch disease were excluded. Resting blood pressure, medication, imaging, Doppler and invasive data pre and post procedure.
were studied. The remaining 59 patients were included. Mean age (standard deviation) at stent implantation was 28 (10.5) years, 56% male, 63% had native CoAo. 54 patients (92%) were on antihypertensive therapy before stenting, with 33 (61%) on multiple drugs (2-7). Minimal diameter of coarctation was 6 (2.7) mm. Twenty patients (34%) had transverse aorta/aorta diaphragm level (TaAo/AoDiag) <0.8. A total of 64 stents were implanted, of which 39% were covered. A second procedure was performed in 9 patients (15%) because of multistage procedure (n=6), growth (n=2), stent fracture (n=2) and neointima (n=1). Invasive gradient decreased from 46.1 (18.11) mmHg to 5 (5.07) mmHg. There were no major complications nor mortality.

It was possible to discontinue one or more antihypertensive drugs in 39 patients (66%) and 22 patients (37%) became free of medication. Patients who remained medication free were younger 21.6 (7.7) versus 31.4 (15.9) years, p < 0.009; had a lower Doppler gradient [38.9 (19.1) vs 58.3 (19.9) mmHg, p < 0.001] and a lower invasive gradient before intervention [38.9 (14.4) versus 52.8 (23.5) mmHg, p < 0.001]. Patients who had a lower invasive gradient were younger also in this group (2.3 (3.6) versus 6.7 (4.5) mmHg, p = 0.028). In medication free patients, final stent diameter was significantly correlated with BSA (p < 0.005). In patients with TaAo/AoDiag > 0.8, 46% remained medication free, but with TaAo/AoDiag < 0.8 only 23% did not require medication at long term. Results were similar for native CoAo and ReCoAo.

In a mean follow up of 4.8 (2.9) years, one patient died of stroke 4 years after the procedure. Results were similar for native CoAo and ReCoAo.

A total of 64 stents were implanted, of which 39% were covered. A second procedure was performed in 9 patients (15%) because of multistage procedure (n=6), growth (n=2), stent fracture (n=2) and neointima (n=1). Invasive gradient decreased from 46.1 (18.11) mmHg to 5 (5.07) mmHg. There were no major complications nor mortality.

It was possible to discontinue one or more antihypertensive drugs in 39 patients (66%) and 22 patients (37%) became free of medication. Patients who remained medication free were younger 21.6 (7.7) versus 31.4 (15.9) years, p < 0.009; had a lower Doppler gradient [38.9 (19.1) vs 58.3 (19.9) mmHg, p < 0.001] and a lower invasive gradient before intervention [38.9 (14.4) versus 52.8 (23.5) mmHg, p < 0.001]. Patients who had a lower invasive gradient were younger also in this group (2.3 (3.6) versus 6.7 (4.5) mmHg, p = 0.028). In medication free patients, final stent diameter was significantly correlated with BSA (p < 0.005). In patients with TaAo/AoDiag > 0.8, 46% remained medication free, but with TaAo/AoDiag < 0.8 only 23% did not require medication at long term. Results were similar for native CoAo and ReCoAo.

In a mean follow up of 4.8 (2.9) years, one patient died of stroke 4 years after the procedure. Results were similar for native CoAo and ReCoAo.

A total of 64 stents were implanted, of which 39% were covered. A second procedure was performed in 9 patients (15%) because of multistage procedure (n=6), growth (n=2), stent fracture (n=2) and neointima (n=1). Invasive gradient decreased from 46.1 (18.11) mmHg to 5 (5.07) mmHg. There were no major complications nor mortality.

It was possible to discontinue one or more antihypertensive drugs in 39 patients (66%) and 22 patients (37%) became free of medication. Patients who remained medication free were younger 21.6 (7.7) versus 31.4 (15.9) years, p < 0.009; had a lower Doppler gradient [38.9 (19.1) vs 58.3 (19.9) mmHg, p < 0.001] and a lower invasive gradient before intervention [38.9 (14.4) versus 52.8 (23.5) mmHg, p < 0.001]. Patients who had a lower invasive gradient were younger also in this group (2.3 (3.6) versus 6.7 (4.5) mmHg, p = 0.028). In medication free patients, final stent diameter was significantly correlated with BSA (p < 0.005). In patients with TaAo/AoDiag > 0.8, 46% remained medication free, but with TaAo/AoDiag < 0.8 only 23% did not require medication at long term. Results were similar for native CoAo and ReCoAo.

In a mean follow up of 4.8 (2.9) years, one patient died of stroke 4 years after the procedure. Results were similar for native CoAo and ReCoAo.
Independent predictors of operative mortality in acute aortic syndromes

A. Panza1, L. Tedesco1, A. Affanco1, A. Longobardi1, P. Masiello1, E. De Ruberto1, R. Citro2, S. Iesi1, E. Bosso1, G. Di Benedetto1, L. Biassetti1, B. Cesario1, I. Santillo1, F. Carrieri1, F. Tesei1, A. Morigi1, A. Rinero1, G. Dario1, M. Zullo1, C. Ceraso1, M. Ciliberti1, 1Cardiovascular Division, San Giovanni e Riuniti University Hospital, Salerno, Italy; 2Cardiology Division, San Giovanni e Riuniti University Hospital, Salerno, Italy; 3Cava de’ Tirreni-Costa d’Amalfi Hospital, Department of Cardiology, Salerno, Italy

Purpose: Type A Acute Aortic Syndromes (TA-AAS) have still high morbidity and mortality despite advances in management and therapy. Multiple clinical findings upon presentation, various lesion extension and low annual operative center-volume are elements that yield to difficult data evaluation. Few studies have shown that some variables are predictors of operative outcome. We review our experience in the treatment of 200 consecutive surgical cases of TA-AAS and analyzed the preoperative variables associated with operative mortality.

Methods: Several variables (180) have been collected related to demographic, anamnestic, clinical and interventional characteristics at ER presentation, diagnosis establishment and operative table. Those parameters have been correlated to operative mortality. The variables which diverged at initial univariate analysis (p < 0.05) become covariates in Cox regression model.

Results: From March 1993 to December 2011, 200 consecutive patients under- went surgery for TA-AAS (acute aortic dissection= 162, intramural hematoma= 14 and penetrating ulcer= 4). Operative mortality was 28% (57 Pts). Main parameters associated with the operative mortality are listed in the following table. However, at multivariate analysis independent predictors for operative mortality were: 1) Shock or cardiac tamponade at onset [HR= 0.42; IC 0.189-0.949; p=0.03]; 2) Previous cardiac surgery [HR=0.34, IC 0.149-0.775; p=0.01]; 3) New cardiac tamponade at OR [HR=0.45; IC 0.204-1.008; p=0.05]; 4) Age ≥ 85 years old [HR=0.41; IC 0.193-0.870; p=0.02]; 5) Diabetes [HR=0.53; IC 0.282-1.003; p=0.05]; 6) CABG history [HR=0.52; IC 0.285-0.948; p=0.03]; 7) Chronic renal failure [HR=0.53; IC 0.277-1.031; p=0.07].

Conclusions: Our data show that variables which express a severe hemodynamic impairment (shock or cardiac tamponade) or broad lesion extension at the level of the vascular tree (pulse deficit) are independent predictors of operative mortality, rather that surgical strategy adopted.

Elective repair of abluminal aortic aneurysm in patients over 85 years old: results from a 60 patients monocentric cohort

J.M. Alsa1, R. De Blic1, T. Mirault2, E. Messas2, J. Emmrich2, M. Sapoval2, P. Julia1, J.N. Fabiani1, 1AP-H - European Hospital Georges Pompidou, Vascular Surgery Unit, Paris Descartes University, Paris, France; 2AP-H - European Hospital Georges Pompidou, Vascular Medicine Unit, Paris Descartes University, Paris, France

Purpose: Due to aging population, increasing screening of abdominal aortic aneurysms (AAA) and diffusion of minimally invasive surgical techniques, proportion rise of older patients are eligible for AAA elective repair. Few data exist in the literature on the expected benefits and risks ratio of such prophylactic intervention in this old population. The purpose of this single-center study was to evaluate the short- and medium-term results of AAA repair in patients older than 85 years.

Methods: Between 2004 and 2011, data of all patients over 85 years-old and treated for an elective AAA in our university center were collected prospectively. In line with current recommendations, patients were treated by endovascular repair (EVAR) in case of suitable anatomy. Open repair (OR) was performed in patients with peripheral occlusion or bicuspid aortic valve. The type of repair (EVAR or OR), and the short- and mid-term postoperative results were analyzed. Primary endpoints were 30-day mortality rate and actuarial survival rate.

Results: Of the 1016 patients operated electively for an AAA during the 8-year period studied, 60 patients (5.9%) were aged ≥ 85 years (54 men; mean age = 87.2 ± years), with a mean AAA diameter of 63.1±10.2 mm. Twenty nine (48%) were treated by EVAR and 31 by OR. The global 30-day mortality rate was 3.3% (EVAR=3.4%, OR=3.2%, p=N.S). The median of follow-up was 30 months (range 3-15). Actuarial survival rates after 1, 3 and 5 years were 90%, 79% and 64%. No patient died of AAA related cause during the follow-up.

Conclusions: Elective repair of AAA in patients over 85 years old is associated with acceptable perioperative mortality and life expectancy. The survival rates return to the ones of population with same age without AAA. Although EVAR does not present a significant benefit on postoperative mortality compared to OR in our series, it seems reasonable to propose this less invasive treatment as first-line when the anatomical conditions are suitable.

Mortality for peripheral artery disease and coronary artery disease in the Korean population: 5-15 years follow-up

S.Y. Jang1, E.Y. Ju2, S.I. Cho3, S.W. Lee2, S.W. Park1, D.K. Kie1, 1Samsung Medical Center, Cardiovascular Imaging Center, Cardiovascular and Vascular Center, Seoul, Korea, Republic of; 2Seoul National University, Graduate School of Public Health, Seoul, Korea, Republic of

The objective of this study is to analyze long-term survival of the subjects with peripheral artery disease (PAD), and coronary artery disease (CAD). The sample included 4,526 Korean patients aged ≥45 years who were hospitalized from 1994 through 2004. 405 subjects had PAD confirmed by computed tomography angiography, while 3,475 subjects had CAD confirmed by cardiac catheterization among PAD or CAD patients. Mortality data were obtained from all participants between 1994 and 2009 from the Statistics Korea. All-cause mortality was measured at 5 and 10 years.

The mean ages (years) of PAD subjects was 65.1 ±8.4 and that of CAD subjects was 62.4 ±8.7 (p<0.001). For age group, 45 to 64 year-old group was 45.2% in PAD and 59.6% in CAD. During the 5 to 10 years follow-up, all-cause cumulative mortality rate were 31.8% in PAD and 28.2% in CAD. The mean survival time was 8.77 ±(±0.24) years in PAD and 11.4 ±(±0.08) years in CAD. Ten years survival rate was 59% in PAD and 71% in CAD. The independent predictors of mortality were included but not limited to, age, diabetes, and chronic kidney disease (CKD) in PAD and age, male gender, diabetes, dyslipidemia, smoking, CKD and anemia in CAD. Interestingly, overweight and obesity showed lower hazard ratio in PAD or CAD group.

In this study, we found that cardiovascular risk factors contributed to mortality. However, it seems that there is no similarity between PAD and CAD for their mortality rate.

Racial differences in acute aortic dissection: insights from the International Registry of Acute Aortic Dissection


1University Hospital San Giovanni di Dio e Ruggi d’Aragona, Salerno, Italy; 2Hadassah-Hebrew University Medical Center, Jerusalem, Israel; 3Sant’Orsola-Malpighi Polyclinic, Bologna, Italy; 4Duke University Medical Center, Durham, United States of America; 5University of Colorado Denver, Aurora, United States of America; 6University of Michigan, Ann Arbor, United States of America; 7University Hospital Rostock, Rostock, Germany; 8Massachusetts General Hospital, Boston, United States of America; 9University of Tokyo, Tokyo, Japan

The sample included 1,354 patients (mean age 62.8±15.3 years; 36.4% women) enrolled in 13 United States centers participating to International Registry of Acute Aortic Dissection (IRAD). Race was recorded as black in 14% of these patients.

Results: Type B AAD was more frequent in the black patient cohort (52.4% vs 39.3% in whites; p<0.001). Black patients were younger accounting for 20% AAD patients under 40, but only 5% of those age ≥70 years. Furthermore they were more likely to have a history of cocaine abuse (12% vs 1.6%, p<0.001), hypertension (89.7% vs 73.9%, p<0.001) and diabetes (13.2% vs 6.4%, p<0.001). In contrast, they were less likely to have a history of bicuspid aortic valve (1.8% vs 5.8%, p=0.029), Marfan Syndrome (1.6% vs 4.2%, p=.099), iatrogenic AAD (0.5% vs 4.5%, p<0.010) and prior AAD repair (7.7% vs 12.8%, p=.047). Pre-sentation features were similar with the exception of more frequent abdominal pain (44.6% vs 30.6%, p<0.001) and electrocardiographic evidence of left ventricular hypertrophy (44.2% vs 20.1%, p<0.001). Use of various imaging modalities and management of AAD (medical vs invasive) were similar in the 2 groups. Complications of hypertension/shock/cardiac tamponade was less common (7.6% vs 20.1%, p<0.001) whereas acute kidney failure more common (41.0% vs 21.7%, p<0.001) in blacks with AAD. In- hospital mortality was similar in the 2 groups (14.3% in black patients vs 19.1% in white patients, p= .110).

Peripheral arterial and venous surgery

82
Conclusions: Our study provides important insights into the clinical characteristics and outcomes of patients with AAD. Despite younger age, similar management and a lower incidence of hypotension/shock/cardiopulmonary tamponade, blacks have similar mortality compared with whites with AAD. These findings may have implications in terms of optimizing societal efforts to prevent, diagnose earlier, and more effectively treat AAD in black patients.

Intraoperative flowmetry for assessment the success of vertebral artery reconstruction

V.A. Yanushka, D.V. Turluk, V.F. Kardash, L.C. Filonova, O.V. Krasko, Republican Scientific and Practice Centre Cardiology, Minsk, Belarus

Objective: Intraoperative ultrasound has become an integral part of surgical procedures and influences on both the intermediate intraoperative course and long-term outcome. Unlike coronary and carotid surgery vascular arteries (VA) reconstruction is not provided by flowmetry. This study reviewed our experience with intraoperative ultrasound evaluation of graft performance in third vertebral artery segment.

Material and Methods: We prospectively evaluated 30 patients (pts) (mean age 53 years) with vertebral insufficiency who had underwent VA reconstruction due to lesion of its 2-3 segments. In all cases flow and pulsatile index (PI) of VA in situ, first and second cervical vertebral, internal carotid artery (ICA) and external carotid artery (ECA) prior to intervention and all anastomosis components following the reconstruction were measured by intraoperative flowmeter.

Results: Successful rate of VA revascularization was achieved in 86.6%. Recurrence of vertebral insufficiency was revealed in 4 pts (13.4%). No death or acute cerebrovascular events were observed. PI of ECA and volume flow gain from VA after operation were significant predictors of bypass patency (p<0.05). Mean flow volume in VA increased on 22.0 ml/min (95% CI 17.2-26.7), PI of ECA decreased by 23.3% (95% CI 10.9-35.8) intraoperatively. Pts with sub-acute thrombosis had significantly lower VFVG (p=0.03) compared to pts without uneventful period as well as higher pulsatile ECA index (p=0.02).

Conclusions: The intraoperative flowmetry is rapid noninvasive and sensitive technique. This procedure allows to assess accurately the third segment of vertebral artery anastomosis. A poor VFVG and high ECA PI after VA reconstruction can alert surgeons to potential difficulties with donor vessel, anastomosis or recipient brachial artery anastomosis. A poor VFVG and high ECA PI after VA reconstruction can alert surgeons to potential difficulties with donor vessel, anastomosis or recipient vessel during surgery.

Aortic diameter predicts acute type a aortic dissection in marfan patients but not in non-marfan patients

E.K. Kim, C.H. Kim, S.H. Choi, Y.H. Cho, D.K. Kim, Samsung Medical Center, Sungkyunkwan University, Seoul, Korea, Republic of

Purpose: Among the parameters considered during watchful follow-up for the genesis of acute type A aortic dissection, aortic size has been considered a cardinal factor. Preventive surgery of the aorta in asymptomatic patients on the basis of size alone is still controversial in patient populations lacking risk factors for aortic dissection. The aim of this study was to assess the feasibility of aortic diameter as a current criterion for elective aortic surgery to prevent the development of aortic dissection in non-Marfan and Marfan (MFS) patients.

Method: We reviewed the data for patients diagnosed with acute type A aortic dissection from December 1994 to March 2009 at our institute. Results: Among 237 patients who presented with acute type A aortic dissection were enrolled, of which 31 were diagnosed with MFS. The maximal ascending aortic size was 46.7 mm (42.9-51.6) in non-MFS patients and 58.5 mm (43.8-64.9) in MFS patients (p < 0.001). Two thirds (74.1%) of MFS patients had a maximal aortic root size ≥ 45 mm. However, 86.9% of the 206 non-MFS patients had aortic diameters ≤ 55 mm. Non-MFS patients presenting with an acute size ≤ 55 mm developed aortic dissection at a younger age and had a higher body mass index than those with aortic sizes ≥ 55 mm.

Conclusion: Aortic diameter is of limited value and is not a critical parameter for aortic dissection in non-MFS patients.

MULTIDETECTOR COMPUTED TOMOGRAPHY IN DIAGNOSIS AND CHARACTERIZATION OF CORONARY ARTERY DISEASE

Relationship of dyspnea and typical angina to coronary artery plaque severity, distribution, and composition risk

R. Nakashiki, J.S. Rana, V.Y. Cheng, H. Granser, S.W. Hayes, L. Thomson, J.D. Friedman, D.S. Berman, J.K. Min. Cedars-Sinai Medical Center, Los Angeles, United States of America

Objective: Dyspnea and typical angina are associated with poor prognosis, although their relative risk to mortality in relation to coronary artery disease (CAD) characteristics has not been examined. The aim of this study was to evaluate coronary plaque distribution, severity, composition and risk among individuals undergoing coronary CT angiography (CCTA) presenting with versus without dyspnea or typical angina as a chief complaint.

Methods: We studied 1443 consecutive individuals (mean age 61 years, 61.6% men) undergoing CCTA, comprised of 170 individuals with dyspnea, 249 individuals with typical angina (TyAng), and 1024 individuals without dyspnea or TyAng (Reference group). Multivariable logistic regression was performed to evaluate the association of Dyspnea or TyAng to the presence of obstructive CAD (≥70% diameter stenosis); plaque distribution determined by a segment involvement score (SIS) [defined as the total number of segments with plaque]; and plaque composition (categorized as noncalcified, mixed, calcified). Risk of mortality in relation to Dyspnea or TyAng was evaluated with multivariable Cox proportional hazards models.

Results: During a follow-up of 2.9±1.0 years, 63 individuals died (4.4% of total population): 17 (10.0%) with Dyspnea; 13 (5.2%) with TyAng; and 33 (3.2%) in the Reference group. By multivariable logistic regression, both Dyspnea (OR 2.1, 95%CI 1.3-3.5, p=0.001) and TyAng (OR 1.8, 95%CI 1.1-2.9, p=0.03) were associated with the presence of obstructive CAD when compared to Reference individuals, but neither symptom type was associated with greater plaque distribution or any plaque composition type. Despite similarities in rates of obstructive CAD, those with Dyspnea experienced a 3-fold higher mortality (3.3%/year vs. 1.1%/year, p<0.001) compared to Reference individuals, while those with TyAng did not (1.0%/year vs. 1.1%/year, p=0.03). By multivariable Cox models, individuals with Dyspnea experienced higher mortality risk (HR 2.3, 95% CI 1.2-4.3, p=0.008) yet those with TyAng did not (HR 1.1, 95% CI 0.5-2.1, p=0.7).

Conclusion: Both Dyspnea and TyAng are associated with increased prevalence of obstructive CAD, which is associated with heightened risk of mortality in individuals with Dyspnea but not TyAng if operation or a worsened prognosis for individuals with Dyspnea warrants further investigation.

Prospectively-triggered, 320-row cardiac CT angiography increases aspirin but not statin prescriptions compared to myocardial perfusion imaging in low-risk, symptomatic patients in the emergency room

W.M. Odeh, K.N. Bhatt, P.H. Joshi, S. Rinehart, B. Kirkland, Z. Glian, A. Sharma, J.G.V. Figueroa, S. Voros. Piedmont Heart Institute, Atlanta, United States of America

Purpose: Compared to myocardial perfusion imaging (MPI), prospectively-triggered, 320-row volumetric cardiac computed tomography (CTA) reduces the length of stay (LOS), hospital cost, and radiation exposure in low risk, symptomatic patients presenting to the ER. However, influence on discharge prescription rates of lipid-lowering and anti-platelet therapies is unclear.

Methods: Between January 2010 to June 2011, 212 patients presenting to the ER with chest pain, a non-ischemic ECG, and negative initial cardiac markers, were evaluated by either CTA or MPI based on the discretion of the treating physician. LOS, cost, total radiation dose, prescription rates of statins and aspirin, and lipids were compared between those undergoing CTA vs. MPI. Prospectively triggered, contrast-enhanced CTA was performed on a 320 detector row platform (Aquilion ONE; Toshiba, Tustin, CA; Tube Voltage 120-35kV, Tube current 300-550 mA). Mann-Whitney test was utilized to compare non-normally distributed variables and square root was used to compare categorical variables; p<0.05 was considered test. Results: There were 107 patients (52±12.4 years, 42% M, BMI 31.17) evaluated by CTA and 105 patients by MPI (59±13.2, 38% M, BMI 29.3). As seen in Table, the costs in prescriptions upon discharge were similar in both groups, while aspirin prescriptions were significantly higher in those undergoing CTA. LOS, radiation dose, and total hospital cost were significantly lower in the CTA group.

Cardiac CTA vs. MPI in ER patients

Cost (US$) MDCT 1321 (830-2219) 1536 (1207-2287) p=0.0078
Radiation Dose (mSV) 5.2 (0.4-10.2) 13.0 (12.1-13.7) p<0.0001
Statin Rx at Discharge 40% 46% p=0.40
Aspirin Rx at Discharge 58% 40% p=0.02

Conclusions: In a “real-world” population of low risk patients presenting to the ER with chest pain, prospectively-triggered volumetric CTA as a first line test may be the dominant strategy by reducing LOS, hospital cost and radiation dose. Compared to MPI, CTA did not influence rates of statin prescription at discharge, but was associated with an increase in aspirin prescriptions.

Coronary artery ectasia and coronary calcification: pathologial relation or just an association?

A.A.M. Farrag, A. El Faramawy, M.A. Saleem, R. Abdel Wahab, S. Ghareeb. Cairo University, Kasr-Aly Medical and Allied Hospitals of Medicine, Department of Cardiology, Cairo, Egypt. Cairo, Egypt, Cairo, Egypt, Cairo, Egypt, Cairo, Egypt, Cairo, Egypt, Cairo, Egypt, Cairo, Egypt, Cairo, Egypt

Introduction: Coronary artery ectasia (CAE) is considered a variant of coronary artery atherosclerosis, however, a definite link is not yet confirmed. The aim of this study was to evaluate the prevalence of CAE, angiographic characteristics, its
Coronary atherosclerosis and circulating biomarkers in patients with opposite for risk factor profiles and no clinical ischemic heart disease. CAPSIRE study: preliminary findings

M. Magnoni1, G. Pontone2, S. Masson3, M. Gorinii4, M.G. Rossii5, F. Angelozzi6, P. Marraccini7, A.P. Maggioni8, R. Latin9, A. Maseni10 on behalf of CAPSIRE investigators.1 Heart Care Foundation, Florence, Italy; 2Cardio Center Monzino, Department of Radiology, Milan, Italy; 3The Mario Negri Institute for Pharmacological Research, Department of Cardiovascular Research, Milan, Italy; 4ANMCO Research Center, Florence, Italy; 5Cardiocentro Tino, S.R.C., Lugano, Switzerland; 6A. Muni Hospital, Department of Cardiology, Ferrara, Italy; 7IFC CNR – Fondazione Toscana G. Monasterio, S.A. Emodinazione, Pisa, Italy

Purpose: To identify distinctive anatomical and biological features in patients who develop coronary artery disease (CAD) despite a low risk factor (RF) profile (“outlier”).

Methods: Coronary multidetector computed tomography (MDCT) and circulating biomarkers were centrally analyzed in 110 patients with LVEF ≥50% subdivided into three groups based on CAD extent and RF (family history, hypertension, dyslipidemia, smoking, diabetes). Group 1: 56 without CAD and ≤1 RF excluded diabetes (No-CAD/low-RF); group 2: 28 “outliers” with diffuse CAD (≥5/16 coronary segments) and ≤1 RF excluded diabetes (CAD/low-RF), and group 3: 26 with diffuse CAD and ≥3 RF (CAD/high-RF).

Results: CAD/low-RF showed angiographic findings similar to CAD/high-RF. In absence, stenosis severity and plaque composition. Circulating hs-cTnT, C-reactive protein and creatinine were not different between the two CAD groups but were significantly higher in CAD/low-RF than in no-CAD/low-RF.

Conclusions: Outlier patients with diffuse CAD in spite of low risk factors have similar plaque morphology and composition to patients with multiple RF but have significantly higher values of hs-cTnT, CRP and creatinine, thus may be possible markers of atherosclerotic risk independent of traditional RF.

Impact of serum uric acid levels on the characteristics of coronary plaques using computed tomography angiography

T. Kimura, A. Sato, T. Adachi, Y. Kakufuda, E. Ojima, H. Watabe, Y. K. Aonuma, University of Tsukuba, Tsukuba, Japan

Background: Uric acid may have effects on vascular remodeling and atherosclerosis. The purpose of this study was to evaluate the relationship between serum uric acid (SUA) levels and presence of coronary vulnerable plaque assessed by computed tomography angiography (CTA).

Methods: Five hundred twenty-nine patients with suspected coronary artery disease (CAD) underwent 64-slice CTA to evaluate the prevalence of CAD and plaque morphology. Coronary vulnerable plaque was defined as positive vessel remodeling (PR) (Ri<1.1) and low-attenuation plaques (LAP) (<50 Hounsfield Units). SUA level was divided into 4 groups: ≤5, 5 to ≤6, 6 to ≤8, ≥8 mg/dl.

Results: The number of vulnerable plaques per patient was significantly higher in patients with SUA >6 mg/dl. Only 8.6% of ectatic coronary segments showed various degrees of intimal calcification. Pearson’s correlation coefficients showed negative correlation with SUA levels. SUA >5 mg/dl to 6 mg/dl had CACS >0. Only 8.6% of ectatic coronary segments showed various degrees of intimal calcification. Pearson’s correlation coefficients showed negative correlation with SUA levels.

Conclusions: SUA level was associated with the presence of coronary vulnerable plaques. Assessment of SUA level may be useful to identify the high-risk patients with suspected CAD, and SUA may have a pathophysiologic effect on atherosclerosis.
P684 The effect of LDLR-negative genotype on CT-coronary atherosclerosis in asymptomatic, statin treated patients with heterozygous familial hypercholesterolemia

G.J.R. Ten Kate1, L.A. Neeffjes1, A. Dedci1, J.E. Roeters Van Lennep2, A. Moelker1, K. Niemann3, G.P. Krestin1, E.J. Sijbrands2, P.J. De Feyter1
1Erasmus Medical Center, Department of Radiology, Rotterdam, Netherlands; 2Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands; 3Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands

Background: In asymptomatic patients with heterozygous familial hypercholesterolemia (FH), the influence of LDL receptor (R) mutational status on coronary atherosclerosis is largely unknown. We measured plaque burden by means of CT-coronary angiography in patients with FH.

Methods and Results: One hundred and forty four clinically diagnosed FH patients (92 men; mean age 52±8) underwent LDLR mutational screening. We distinguished two groups: A) 54 patients (38%) with LDLR-negative mutations and B) 90 patients (62%) with either LDLR-defective (d) or LDLR-unidentified (u) mutations.

The plaque burden score was the primary endpoint defined as the integrated sum of the stenosis severity and number of diseased coronary artery segments (score=1 for <50% stenosis, score=2 for >50-70% stenosis and score=3 for >70% stenosis) (median, IQR).

The primary analysis was the comparison of plaque burden between groups A and B and additionally between LDLR-d and LDLR-u mutational FH. The median plaque burden score in group A was significantly higher as compared to group B (4 (3-5) and 2 (0-6); P=0.031). There was no significant difference in plaque burden scores between LDLR-d and LDLR-u mutational FH.

Conclusion: LDLR-negative mutational status in asymptomatic statin treated FH patients is associated with the highest extent of subclinical CT-coronary atherosclerosis.

P685 Cardiac CT for clinical decision making results of a 8-years follow-up

T. Drosch1, A. Bentzen1, M. Heuschmid2, C. Burgstahler3, S. Schroeder1. 1Klinik am Eichert, Cardiology, Geopingen, Germany; 2Department of Radiology, Tubingen, Germany; 3Department of Sports Medicine, Immanuel Clinic V Tübingen, Germany

Aim: The diagnostic accuracy of cardiac multi-detector row computed tomography angiography (MDCTA) is well studied, but the prognostic value of MDCTA described in the most studies on short-term follow-up. Therefore, the aim of this study was to determine the long-term prognostic value of MDCTA.

Methods and Results: Our study included 210 patients (138 men, age 67±11 years) referred to our outpatient clinic because of unclear chest pain. 8 years after MDCTA, a clinical follow-up was performed by telephone reporting, re-activation of invasive coronary angiography (ICA), need for revascularization, cardiac death and myocardial infarction.

Follow-up information on 180 patients (85%) could be obtained. During a mean follow-up of 8±6.9 months we observed 54 index events in 50 patients (5%). These pts were significantly older (72±9 years vs. 66±11 years, p < 0.0001), had more then 2 cardiovascular risk factors (48% vs. 21.5%, p < 0.05), and the Agatston-Score was significantly higher (1205 vs. 190, p<0.001). Ten index events were deaths, four were of cardiac origin. Two myocardial infarctions occurred. 100% event free survival in the group of exclusion of CAD was documented. In contrast, the event free survival rate dropped to 45% (n = 27/60) in pts with significant CAD.

Conclusions: Even after 8 years of follow-up MDCTA was found to be of prognostic importance in pts with unclear chest pain. Especially, the absence of any CAD provided an excellent prognosis. In contrast, the cardiac event rate increased in pts with proven CAD and in pts with non-diagnostic image quality.

P686 Can computed tomography coronary angiography (CTCA) be used as a non-invasive estimate of the extent of coronary artery atherosclerosis?

J. Lessick1, S. Abad2, E. Abergel1, A. Solomonica1, A. Kenner1
1Rambam Health Care Campus, the Technion, Israel Institute of Technology, Dept of Cardiology, Haifa; 2Israel Ramathan Health Care Campus, Dept of imaging, Haifa, Israel

Purpose: The SYNTAX score is used for evaluation of patients with complex coronary artery disease undergoing revascularisation. It is usually calculated off-line, meaning that in suitable patients, percutaneous intervention is performed at a later date. The ability to non-invasively estimate SYNTAX score would allow the heart team to recommend optimal treatment prior to invasive coronary angiography (ICA), thus enabling the diagnostic and therapeutic procedure to be performed at the same session. We aimed to test the agreement between CTCA and ICA in patients who had undergone both procedures within a 2 month period and had at least one significant stenosis by ICA.

Methods: CTCA scans were performed on a 64 slice scanner following injection of 80ml IV contrast medium. SYNTAX score was independently and blindly calculated by 2 experienced readers of CCTA and 2 invasive cardiologists in 104 patients, age 57±10, with significant (>50%) stenoses in 1.7±0.7 vessels. Calcium score averaged 597±727 Agatson units.

Results: Agreement between ICA and CTCA for conventional vessel based analysis (presence of >50% stenosis per vessel) was good with kappa 0.66 and sensitivity, specificity and accuracy of 70%, 93% and 83%, respectively. The mean SYNTAX score was 14.5±10.0 by ICA and 10.2±6.8 by CTCA, with a significant underestimation of 4.0±8.2 by CTCA (p<0.001). Weighted kappa was 0.33, indicating only fair agreement. If only good quality CCTA’s were used, kappa improved to 0.56. Analysis of the cause of the bias showed ICA to identify more lesions per patient (2.2±1.3 vs. 1.7±1.0; p<0.001), while the mean score per lesion was not different (6.4 vs. 5.9, p=0.5). SYNTAX score per lesion showed good agreement (Kappa=0.69).Regarding various components of the SYNTAX score, CCTA identified 12/24 occlusions (kappa 0.6); agreement for calcified lesions was fair (kappa 0.36), while agreement regarding bifurcation lesions and long lesions was poor. Interater agreement was good for ICA (kappa 0.84) and moderate for CCTA (kappa 0.51).

Conclusion: CCTA, despite having a good agreement by conventional vessel based analysis, showed only a fair agreement for the calculation of SYNTAX score, and cannot be currently used as a substitute for diagnostic ICA for this purpose.

P687 Impact of visceral abdominal adipose tissue on unstable coronary plaque formation detected by multidetector computed tomography in non-diabetic patients

K. Osawa, T. Mihoshi, S. Sato, H. Morita, K. Hashimoto, S. Nagase, K. Kohno, K. Nakamura, K. Kusano, H. Ito. Okayama University, Okayama, Japan

Background: Visceral abdominal adipose tissue (VAT) may play an active role in the coronary plaque, since visceral adipose tissue secretes many inflammatory cytokines. This study investigated the relation between VAT and unstable coronary plaques detected by multidetector computed tomography (MDCT).

Methods: We measured VAT and determined presence and characteristics of coronary plaques using MDCT in consecutive 161 patients suspected of coronary artery disease (88 men; age, 64±13 years). Unstable plaque was defined as the plaque with an attenuation less than 50 HU.

Results: The unstable plaque was detected in 19% subjects. The VAT in patients with unstable plaque was significantly greater than that in patients without unstable plaque (120±60 cm² vs. 89±70 cm², median±IQR, p<0.02). Patients with unstable plaque had higher age (p=0.03), greater percentage of male (p=0.01), higher prevalence of diabetes (p<0.01), lower HDL-cholesterol (p<0.02), and higher HemoglobinA1c (p<0.01). When all subjects were categorized on the basis into three groups, low VAT group (<62cm², n=32), moderate VAT (62cm², <116cm², n=34), high VAT (≥116cm², n=34), the presences of patients with unstable plaque were 8%, 19%, 29%, respectively, p=0.02. In all subjects, multi-variate logistic regression analysis revealed that high VAT tended to be associate with the presence of unstable plaques (odds ratio: 2.69, p<0.11). However, sub-analysis according to diabetes demonstrated that those associations remained significant only in non-diabetic patients (odds ratio: 4.92, 95%CI: 1.27 to 110.1, p=0.03), but not in diabetic patients.

ORs for unstable plaque in non-DM

<table>
<thead>
<tr>
<th>Factor</th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td>OR (95% CI)</td>
<td>P value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Age</td>
<td>1.05 (0.996-1.11)</td>
<td>0.06</td>
</tr>
<tr>
<td>Hypertension</td>
<td>5.39 (1.23-22.65)</td>
<td>0.02</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.03 (0.97-1.09)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.23 (0.37-4.16)</td>
<td>0.74</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>1.89 (0.56-6.39)</td>
<td>0.31</td>
</tr>
<tr>
<td>Visceral adipose fat</td>
<td>4.92 (1.52-15.93)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Conclusion: The VAT is an independent determinant of unstable coronary plaques detected by MDCT in non-diabetic patients.

P688 The impact of chronic kidney disease in the development of coronary atherosclerosis: 128 Multi-slice CT study

Y. Suzuki, M. Ehara, S. Murase, O. Matsuda, A. Murata, T. Matsubara. Nagoya Heart Center, Nagoya, Japan

Aim: The several reports have mentioned that chronic kidney disease (CKD) is associated with the occurrence of cardiovascular event. The aim of this study is to investigate the correlation between CKD stage and the prevalence of coronary atherosclerosis using Multi-slice computed tomography (MSCT).

Methods: We investigated consecutive 865 cases underwent 128-MSCT for evaluation of suspected coronary artery disease. We investigated the correlation between CKD stage (stage 1=GRF<90, 2= eGFR=60-90, 3a; eGFR=50-60, 3b; eGFR<30), various measurements, and severity of coronary artery stenosis by MSCT.

Results: The results are shown in the table. The severity of coronary artery atherosclerosis such as Agatston score, the prevalence of coronary artery plaque, and significant stenosis was significantly higher in the advanced CKD patients.
Coronary computed tomography angiography predicting major adverse cardiac events

J.J. Gai, L. Gal, B. Heil, H.Y. Qiao, S.Y. Zhang, Z.W. Guan, J. Yang, Y.D. Chen; on behalf of NA. Department of Cardiology, Chinese PLA General Hospital, Beijing, China, People’s Republic of; 2Department of Nuclear Medicine, Chinese PLA General Hospital, Beijing, China, People’s Republic of

Objective: Framingham study discovers the coronary risk factor by long term follow-up. However, the prediction of events is only moderate accurate. The plaque characteristics by Coronary Computed Tomography Angiography (CCTA) may be more accurate in predicting the events.

Methods: The patients who underwent CCTA from Jan 2008 to Feb 2010 were included in the study. Any patients who later developed acute ST elevated myocardial infarction (STEMI), non ST elevated acute myocardial infarction (NSTEMI) or cardiac death after CCTA was considered a MACE. Bothe grayscale and color coding analysis of the plaque were performed. The plaque score system was established to quantify the lesions. The plaques were classified into the complex lesion, severe localized stenosis, positive remodeling, mild to moderate lesions, drug eluting stent, complete occlusion, defused moderate lesions and calcification. The plaque score times the number of segments was the total plaque score. Event risk was calculated as follows: death 3 points, heart failure 2 points, STEMI 0.5, NSTEMI 0.5, multiplied by the number of abnormal segments. Clinical Plaque score plaque score > [modified ACIF score]. Two-way analysis of variance and linear regression were performed between clinical plaque score and event risk score.

Results: A total of 8557 consecutive cases of CCTA were performed in the institution. Among them 25 patients developed MACE after CCTA, including 6 cases of deaths, 2 cases of heart failure, 11 cases of STEMI and 6 cases of NSTEMI. Of the 6 deaths 4 revealed complex lesions which included erosive lesions, chronic occlusion, calcified plaque, soft plaque, fibrous plaque and ulcers on the color coded CCTA. One patient died of DES thrombosis without significant stenosis on CCTA. One patient had only moderate lesion on CCTA before the death. Two patients suffered from heart failure. They all belonged to the complex lesions. Of the 2 heart failure, 1 patients who suffered from STEMI and 1 had DES on CCTA before the MACE. Of the 6 patients who suffered from NSTEMI, 2 had severe localized stenosis, 2 and moderate lesions on CCTA before the MACE. The complex lesions and severe localized stenosis were the powerful predictors of MACE, P<0.001. Clinical Plaque score was correlated closely with clinical Syntax score, R=0.54, P<0.001.

Conclusion: The plaque characteristics of CCTA are predictive of MACE. The complex plaques and severe localized stenosis were powerful predictors of MACE. Incorporation with clinical indices significantly improves the prediction of MACE.

Methods: Between March 2008 and March 2010 a total of 181 consecutive patients scheduled for aortic valve replacement were included. All patients underwent pre-surgical CTCA (64-110) or 64-slice (n=60) CT scanner) as well as an invasive coronary angiography. CTCA and invasive coronary angiography analyses were performed blinded to each other. Significant coronary artery disease was defined as a stenosis > 70%.

Results: The mean (SD) age was 71 (9) years and 59% were male. The prevalence of significant coronary artery stenosis by invasive coronary angiography was 36%. Average heart rate during CTCA was 65 (16) beats per minute and median (range) coronary artery calcium score was 529 (0-8596) by Agatston score. On coronary vessel level 97% of vessels (705/724) were considered evaluable. The vessel-by-vessel sensitivity was 61% and specificity 94%. On a patient-by-patient level 94% of patients (171/181) were considered fully evaluable and CTCA had a sensitivity of 68%, specificity of 91%, a positive predictive value of 81% and a negative predictive value of 83%. Multivariate logistic regression analysis identified advanced age, coronary artery calcium score > 400 and heart rate > 62 beats per minute as independent predictors of invasive coronary angiography/CTCA disagreement. Excluding all patients > 70 years old resulted in: sensitivity 82%, specificity 98%, positive predictive value 95% and negative predictive value 92% (n=71).

Conclusion: In patients referred for surgical aortic valve replacement the diagnostic accuracy of CTCA to identify significant coronary artery disease was found to be moderate. Results may be improved by selecting patients with age < 70 years, coronary artery calcium score < 400 and by lowering the heart rate to ≤ 62 beats per minute.

Detection of significant coronary artery disease using computed tomography coronary angiography in patients with aortic stenosis referred for surgical aortic valve replacement

L.H. Larsen, K.F. Kolodziej, M. Dalsgaard, T. Kristensen, H. Elming, D.A. Steinbruch, L. Kroeber, H. Kelbaek, C. Hassager. rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark; Rigshospitalet - Copenhagen University Hospital, Department of Radiology, Copenhagen, Denmark; Roskilde Hospital, Roskilde, Denmark; Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiothoracic Surgery Copenhagen, Denmark.

Purpose: The diagnostic accuracy of computed tomography coronary angiography (CTCA) to identify significant coronary artery disease was evaluated in patients referred for surgical aortic valve replacement. In patients referred for aortic valve replacement a pre-surgical assessment of coronary artery disease is mandatory to determine the possible need for additional coronary artery bypass grafting. CTCA has been useful for detection of significant coronary disease in other populations, but coronary calcification due to advanced age and predominately male gender, may limit the use of CTCA in patients with aortic stenosis.

Methods: Six hundred and one patients (613±10 years, 461 men) with chest pain and no history of CAD performed ex-ECG and MDCT and were followed-up for 44±12 months. The endpoints were “all cardiac events”, defined as unstable angina, myocardial infarction, cardiac death and revascularization, and “hard cardiac events”, defined as all cardiac events excluding revascularization.

Results: Ex-ECG and MDCT were positive in 419 (61%) and 274 (40%) out of 681 patients, respectively. Myocardial infarction, unstable angina, revascularization and cardiac death occurred in 31 (4%), 31 (4%), 178 (26%), 11 (2%) and annual rate of all and hard cardiac events were 10% and 3%, respectively. In univariate analysis, both ex-ECG and MDCT were predictors of all cardiac events (HR=1.29 [1.5-2.8], p<0.001) and hard cardiac events (HR=1.8 [1.1-3.2], p=0.02 and HR=6.8 [3.9-12.0], p<0.001), respectively) and hard cardiac events (HR=1.8 [1.1-3.2], p=0.02 and HR=6.8 [3.9-12.0], p<0.001), respectively) and hard cardiac events (HR=1.8 [1.1-3.2], p=0.02 and HR=6.8 [3.9-12.0], p<0.001), respectively), while in a multivariate analysis CAD with 50% stenoses detected by MDCT was the only independent predictor of hard cardiac events (HR=2.1 [1.2-6.0], p<0.01). Kaplan-Meier curves (Figure 1) for hard cardiac events in patients with a negative both ex-ECG and MDCT (A), positive both ex-ECG and negative MDCT (B), negative ex-ECG and positive MDCT (C) and positive both ex-ECG and MDCT (D) showed that ex-ECG provides a further and better risk stratification only in patients with low to intermediate pre-test likelihood of CAD and positive MDCT.

Conclusions: A higher prognostic value of MDCT as compared to ex-ECG was found in patients with suspected CAD, mainly in those with a low-to-intermediate pre-test likelihood of CAD.
**Prognostic value of coronary computed tomography angiography during 5 years of follow up in patients with suspected coronary artery disease**

M. Hadamitzky, S. Tannebert, S. Desvee, S. Martinoff, A. Schoemig, J. Hausleiter. German Heart Center Munich, Germany

**Background:** The capability of coronary CT angiography (CCTA) to predict subsequent cardiac events is well known. However, the follow-up period is limited to approximately 2 years in most studies; data on prognosis over five years of follow up are very limited.

**Methods:** We analyzed 1453 patients with suspected coronary artery disease (CAD) undergoing CCTA between December 2003 and November 2006. Amongst other known CCTA parameters, the number of abnormal segments (having either a nonstenotic plaque or a stenosis) and presence of nonobstructive and obstructive CAD were recorded. Endpoint was the occurrence of hard cardiac events defined as all cause death or nonfatal myocardial infarction.

**Results:** During a median follow-up of 5.6 years (IQR 5.1 to 6.2 years), there were 58 hard cardiac events. The annual event rate ranged from 0.2% for patients normal coronary arteries to 0.7% and 1.2% for patients with nonobstructive and obstructive CAD respectively. See Figure below. Both the presence of (non)obstructive CAD and the number of abnormal segments significantly improved the predictive value of the Morise score as best clinical risk predictor (p=0.003 and p=0.001 respectively).

**Conclusion:** The 5 year follow-up results after CCTA extent the available follow up data, confirming that the exclusion of atherosclerotic changes in CCTA is associated with an excellent prognosis during 5 years. Both the presence of obstructive CAD and the number of abnormal segments in CCTA improve the predictive value of clinical risk assessment.

**A comparative cost impact study of diamond forrester and coronary calcium score criteria given by NICE at rapid access chest pain clinics**

P. Mckavanagh1, L. Luska2, R. Ball3, T. Timnick4, E. Duly4, C. McQuillan5, S. Shehin6, G. Walls7, M. Hartkinson2, P. Donnelly1. On behalf of Cardiac: 1Ulster Hospital, Belfast, United Kingdom; 2Queen’s University, Centre for Vision and Vascular Science, Belfast, United Kingdom

**Purpose:** NICE clinical guideline 95 (CG95) proposed the use of a Diamond Forrester (DF) calculator to determine cardiac investigations for patients with stable chest pain in the UK. Patients with DF scores ≤10% do not require further investigation; 10-29% calcium score CT (CS); 30-60% stress imaging; and >60% invasive angiography (IA). For those patients receiving a CS, a score of 0 requires no further investigation; 1-400 CT angiogram (CTCA); and >400 IA.

**Method:** This study was part of an ongoing RCT evaluating the cost effectiveness of cardiac CT as a primary investigation for stable patients. The sub-study evaluated the cost of DF and CS as risk stratification tools for guide the diagnostic tests. DFs were calculated in 250 patients who proceeded to CS and CTCA performed on a 64 detector platform. CTCA was taken as the reference point for coronary artery disease (CAD) severity, with disease classified via the most significant lesion from none to severe. The theoretical cost and number of investigations was determined using the two models: the DF and the CS criteria.

**Results:** Of 250 patients, 4 withdrew. 57% (140) were male with a mean age of 57.7±10.3 years. The mean DF was 47.84±31.68. The average CS was 172.50±487.60. CTCA demonstrated 47 patients with severe disease, 29 moderate, 58 mild, 106 no disease, and 6 inconclusive. Of the 91 that had a DF ≤60%, 38 had severe disease but 17 had no CAD. All patients with a CS >400 had moderate or severe CAD, except 1 inconclusive. The cost analysis is seen in table 1.

**Conclusion:** The use of CS to triage all patients with stable chest pain appears to be more cost effective and prevents downstream testing.

**Detection of left atrial appendage thrombi using multidetector CT-angiography compared with transoesophageal echocardiography**

J. Knot1, R. Pits1, H. Linkova1, J. Daniel2, M. Labos2, P. Widimsky1, *1Charles University Prague, 3rd Faculty of Medicine, 3rd Clinical Dept of Internal Med.-Cardiology, Prague, Czech Republic; 2Charles University Prague, 3rd Faculty of Medicine, Department of Radiology, Prague, Czech Republic

**Introduction:** The presence of left atrial appendage (LAA) thrombi is the important risk factor for cardioembolic stroke. Transoesophageal echocardiography (TEE) is recognized as a gold standard for detecting intracardiac thrombi. TEE has limitations, which are exacerbated by motion. The cardiac phases with the least motion may yield the best image quality but these phases have been found to change with heart rate. We sought to evaluate 1) the relation of three-dimensional cardiac motion to image quality of PHV during the various phases of the cardiac cycle and 2) whether this relation changed at higher heart rates.

**Methods:** We analyzed 1453 patients with suspected coronary artery disease (PHV). MDCT may complement echo-Doppler findings by uncovering obstructive masses and false aneurysms that cannot be found with echocardiography due to acoustic shadowing. However, PHV commonly consist of metal components that emanate artifacts which are exacerbated by motion. The cardiac phases with the least motion may yield the best quality image but these phases have been found to change with heart rate. We sought to evaluate 1) the relation of three-dimensional cardiac motion to image quality of PHV during the various phases of the cardiac cycle and 2) whether this relation changed at higher heart rates.

**Results:** From January to December 2011 a total number of 107 patients underwent contrast MDCT for different indications. All patients were simultaneously examined within 7 days by TEE. The presence of LAA thromb/lling defects were assessed and statistically analyzed.

**Conclusion:** Of a total number of 107 patients examined by MDCT the filling defect was found in 11 (10.3%) patients. Using the TEE, LAA thromb were detected in 6 (5.6%) patients. With TEE as a reference method the sensitivity of MDCT in LAA thrombi detection was 100% (95% confidence interval [CI]: 56-100%), specificity 95% (95% CI: 92-95%) and diagnostic accuracy 95% (95% CI: 90-95%). The agreement of both methods for the detection of LAA thrombi was high: 96 in 96 patients there were no thrombi detected using MDCT and TEE, in 6 patients were thrombi found using MDCT and TEE, in 5 patients were thrombi detected using MDCT but not proven by TEE (kappa = 0.683 [95% CI: 0.544-0.863]).

**Conclusion:** 256 MDCT is a noninvasive imaging method with high sensitivity, specificity and diagnostic accuracy for LAA thromb detection. When compared to TEE, this method is burdened with radiation exposure.
quantified by blinded and randomized pair-wise comparisons of ECG intervals using a two-alternative forced-choice test. PHV velocity and image quality were compared for heart rates <60/min (n=11), 60-90/min (n=25) and >90/min (n=7) as defined by medians and interquartiles range (IQR). Results: PHV velocity varied considerably during the cardiac cycle. Median PHV velocity for all patients was least during 30 to 40% (15.0mm/sec, IQR 10.8-24.5) and during 70 to 90% (16.8 mm/sec, IQR 6.9-26.2) Maximal systolic and diastolic image quality scores were 47 and 71 at 30% and 75%, and coincided with end-systolic and mid-diastolic velocity tsorts. Systolic velocity was increased at 90/min (28.7 mm/sec, IQR 24.3-43.4) when compared with 60-90/min (13.8 mm/sec, IQR 11.2-20.6, p=0.015) and >90/min (50.1 mm/sec, IQR 12.2-64.0, p=0.003). Image quality score for <60, 60-90 and 90/min was 49, 46 and 48 at 30%, and 79, 70 and 59 at 75% respectivley. Conclusions: CT image quality of PHV in mid-diastole is superior to systolic phases and remains superior at higher heart rates. The use of beta-blockers is warranted for optimized MDCT image quality of PHVs.

**Results:** PHV and TFV were significantly higher in patients with significant coronary artery stenosis (p<.0001). Logistic regression was done p value was 0.54 for PHV, and 0.003 for TFV. Partial correlation was done controlling for age and BMI, R = 0.59 for TFV, and -0.56 for PHV, p < 0.0001 for both.

**Conclusions:** PFV and TFV are significantly higher in patients with significant coronary artery stenosis. TFV is more indicative for significant coronary artery disease. TFV and PFV are predictive of significant coronary artery stenosis beyond and independent from body mass index and age.

**Results:** TFV and PFV were significantly higher in patients with significant coronary artery stenosis. TFV is more indicative for significant coronary artery disease. TFV and PFV are predictive of significant coronary artery stenosis beyond and independent from body mass index and age.

**Conclusions:** PFV and TFV are significantly higher in patients with significant coronary artery stenosis. TFV is more indicative for significant coronary artery disease. TFV and PFV are predictive of significant coronary artery stenosis beyond and independent from body mass index and age.

**Results:** TFV and PFV were significantly higher in patients with significant coronary artery stenosis (p<.0001). Logistic regression was done p value was 0.54 for PHV, and 0.003 for TFV. Partial correlation was done controlling for age and BMI, R = 0.59 for TFV, and -0.56 for PHV, p < 0.0001 for both.

**Conclusions:** PFV and TFV are significantly higher in patients with significant coronary artery stenosis. TFV is more indicative for significant coronary artery disease. TFV and PFV are predictive of significant coronary artery stenosis beyond and independent from body mass index and age.

**Association between atrial fibrillation recurrence and pulmonary vein contraction after radiofrequency catheter ablation: assessment by 320-slice computed tomography**

M. Motooka, Y. Hayama, S. Nakajima, M. Miyake, T. Tamura, H. Kondo, H. Nakayama, JNA Cardiovascular Biomedical Research Unit, Tenri, Tottori University, Tenri, Tottori, Japan

**Background:** Left atrial (LA) remodeling has been reported to be an important factor in atrial fibrillation (AF) recurrence after pulmonary vein (PV) radiofrequency catheter ablation (RFCA). We hypothesized that multi-slice computed tomography (MSCT) would be useful for the evaluation of patients post PV isolation by delineating LA and PV remodeling.

**Materials and methods:** Fifty-four patients (62.8±9.3 years, 48 males) with non-paroxysmal AF were enrolled. MSCT was performed before and after RFCA. Images were reconstructed at 15 phases of one cardiac cycle (from 5% to 95% of the R-R interval). Using multi-planar reconstruction, the location of the PV ostium was defined, and the ejection fraction (EF) of each PV was calculated as the volume change at the first 10mm from the ostium using Simpson’s disc methods. The maximal LA volume and the EF of LA and each PV (right superior PV; RIPV, left superior PV; LSPV, left inferior PV; RIPV) were calculated before and after RFCA. Patients were divided into two groups according to AF recurrence. The maximal LA volume and the EF of LA and each PV were calculated and compared before and after RFCA in the two groups.

**Results:** The maximal LA volume significantly decreased after RFCA in both groups. In patients with AF recurrence (n=22), the EF of LA and each PV did not change significantly. However, in patients without AF recurrence (n=32), the EF of LA significantly improved and the EF of PV significantly decreased in RSPV, RIPV and LSPV (see Table).

**Conclusion:** It is suggested that PV contraction is retained in patients with AF recurrence. MSCT may have clinical implications for the non-invasive evaluation of pulmonary vein isolation procedural success and follow-up.

**Association between thoracic and pericardial fat quantified by 64-multidetector computed tomography and the presence of obstructing coronary atherosclerotic plaque**

L. Sallam, F. Aboelemen, M.A. Abdelhay, M. Marwan, M. Nawar, D. Dey, D. Popescu, S. Achenbach, 1. Alexandria Police Hospital, Alexandria, Egypt; 2. Alexandria Faculty of Medicine, Alexandria, Egypt; 3. University of Erlangen-Nuremberg, Department of Cardiology, Erlangen, Germany; 4. Cedars-Sinai Medical Center, Los Angeles, United States of America

**Introduction:** Pericardial fat is emerging as an important parameter for cardiovascular risk stratification. We tried to extend that concept to investigate the relation between thoracic fat volume (TFV) and pericardial fat volume (PFV) and the presence of significant coronary artery stenosis.

**Materials and Methods:** TFV and PFV were quantified using the Qfat software from noncontrast CT scan in 178 consecutive patient.(figure 1) Patients were divided according to presence of significant coronary artery stenosis. TFV and PFV were examined in relation to Body Mass Index (BMI), age, and standard coronary risk factors.

**Results:** TFV and PFV were significantly higher in patients with significant coronary artery stenosis (p<.0001). Logistic regression was done p value was 0.54 for PHV, and 0.003 for TFV. Partial correlation was done controlling for age and BMI, R = 0.59 for TFV, and -0.56 for PHV, p < 0.0001 for both.

**Conclusions:** PFV and TFV are significantly higher in patients with significant coronary artery stenosis. TFV is more indicative for significant coronary artery disease. TFV and PFV are predictive of significant coronary artery stenosis beyond and independent from body mass index and age.

**Comparison of size of ilio-femoral system in different populatations: implication on transcatheter aortic valve implantation access route**

P.H. Chan, 1. H.L. Shek, 2. S.C.W. Cheung, 3. M. Rubens, 1. C. D. Maria, 1. Royal Brompton Hospital, NHF Cardiovascular Biomedical Research Unit, London, United Kingdom; 2. Queen Mary Hospital, Department of Radiology, Hong Kong, Hong Kong SAR, People’s Republic of China

**Aim:** To demonstrate the variation in size of ilio-femoral arteries among different ethnic origins which affects the feasibility of utilizing the femoral access (requiring 18-Fr sheath) as an outer diameter of 7.2mm for TAVI and potential vascular access complication rate.

**Method:** From Jan 2011, to two institutions (Hospital in London, United Kingdom and Hospital in Hong Kong, China), first 100 patients aged 70 or above undergoing contrast-enhanced computed tomography (CT) scan with femoral artery visualization were recruited. Indications for CT, background demographics, iliac and femoral artery size and degree of calcifications were analyzed. Minimal luminal diameters on each side of ilio-femoral artery were identified and compared. Degree of calcifications was evaluated and graded: no calcification (0), mild calcification (1), moderate calcification (2) and heavy/circumferential calcification (3).

**Results:** 100 patients in each institution (with similar age, sex and incidences of DM, HT and PVD) who underwent contrast-enhanced CT were recruited. In Chinese population, the average minimal diameters of ilio-femoral arteries were 6.4±1.7mm (R-side) and 6.2±2.0mm (L-side) while those in Caucasian population were 8.2±1.5mm (R-side) and 7.5±1.5mm (L-side). Degrees of vessel calcifications were 1.1±0.9 (R-side) vs 3.3±1.0 (L-side) in the former and 1.3±1.0 (R-side) vs 1.4±1.1 (L-side) in the latter. Comparing the larger side of ilio-femoral arteries in the two populations, Chinese population has a significantly smaller caliber of ilio-femoral arteries (8.5±1.5mm vs 8.4±1.4mm, p<.0001) but with similar degree of calcification (p=0.19 for R; 0.49 for L).

**Conclusion:** In selected Chinese population, the possibility of safely utilizing femoral access for TAVI requiring 18-Fr sheath might be lower when compared with Caucasian who generally has larger caliber ilio-femoral arteries. Careful case selection or consideration for alternative access route might be needed in TAVI candidates to prevent vascular complications.

**Comparison of Ultra low dose MDCT protocol for thoracic aorta using low tube voltage and low concentration contrast media versus standard protocol with high iodine concentration contrast media**

A. Annoni, 1. A. Formenti, 1. G. Pontone, 1. D. Andreini, 1. G. Ballerini, 1. A. Baggiano, 2. E. Nobili, 2. P. Montorsi, 2. M. Pepi, 1. Cardiology Center Monzino (IRCCS), Department of Cardiovascular Sciences, University of Milan, Milan, Italy; 2. Cardiology Center Monzino (IRCCS), Service Hemodynamics, Milan, Italy

**Aim:** Aim of the study is to compare feasibility and effective radiation dose (ED) of ultra low dose MDCT angiography of thoracic aorta using a combined ED-saving strategy including prospective electrocardiogram (ECG) triggering, adaptive statistical iterative reconstruction protocol, 80 kVp tube voltage and low concentration contrast media (Group 1) versus standard protocol with 100 kVp tube voltage and high iodine concentration contrast media (Group 2).

**Materials and Methods:** We enrolled 62 patients (67±9.7 years, male 48) referred to our hospital for thoracic aorta evaluation by multidetector computed tomography (MDCT). Each patient was randomized to Group 1 (MDCT angiography with prospective ECG triggering, adaptive statistical iterative reconstruction algorithm, 80 kVp tube voltage and low concentration contrast media Visipaque 320) or Group 2 (MDCT angiography with prospective ECG triggering, adaptive statistical iterative reconstruction algorithm, 100 kVp tube voltage and high con-
320-Slice CT characteristics of coronary arteries in 4 types of aortic aneurysms evaluated for surgery.

A. Schuhbaeck1 , J. Leipsic2, J.K. Min3, S. Achenbach1 . 1Justus-Liebig University Giessen, Medical Clinic I, Cardiology, Giessen, Germany; 2St. Paul's Hospital, Vancouver, Canada; 3Cedars-Sinai Medical Center, Los Angeles, United States of America

Purpose: The exact evaluation of the aortic aneurysm dimensions in patients with high-grade aortic stenosis, scheduled for TAVI, is essential. It is unknown whether these parameters should be measured in systole or diastole and to what extent they differ between the phases.

Methods: Contrast-enhanced ECG-triggered CT angiography data sets of 75 patients, scheduled for TAVI, were analysed. The diameters in short- and long-axis view, the area and circumference of the aortic aneurysms were analysed by two independent observers in systolic (35%) and diastolic reconstructions (75% of the RR cycle). Intra- and interobserver variability were analysed. Systolic and diastolic parameters were compared to each other.

Results: There was no statistical significant difference between systolic and diastolic diameters of short- (2.13±0.21 cm vs. 2.07±0.22 cm) and long-axis view diameters (2.64±0.29 cm vs. 2.62±0.33 cm), the area (4.82±0.86 cm² vs. 4.69±1.01 cm²) and circumference (7.94±0.72 cm vs. 7.84±0.87 cm) of the aortic annulus. Interobserver variability results are shown in the table. Intra-observer results showed significant differences of short- and long-axis view diameters in systolic reconstructions (2.07±0.23 cm vs. 2.12±0.23 cm, P = 0.004 and 2.60±0.23 cm vs. 2.64±0.31 cm, P > 0.003), whereas in diastolic reconstructions, there was no significant difference of all aortic annulus parameters.

Conclusions: Dimensions of the aortic annulus in CT imaging do not differ significantly between systolic and diastolic data sets. Interobserver variability is independent of the reconstructed phase.

P702 Increased epicardial adipose tissue volume predicts presence of insulin resistance and coronary artery disease in non-obese subjects without metabolic syndrome.

T. Narumi, T. Watanabe, S. Kadowaki, Y. Otaki, H. Takahashi, T. Arimoto, T. Shishido, T. Miyashita, T. Miyamoto, I. Kubota. Yamagata University School of Medicine, Yamagata, Japan

Backgrounds: It is well known that obesity and overabundance of visceral fat are important risk factors of coronary artery disease (CAD). Visceral fat produces various adipokines which are associated with development of CAD. Recently, epicardial adipose tissue (EAT) was also reported to secrete various adipokines such as tumor necrosis factor-alpha, resistin and monocyte chemoattractant protein-1. It is reported that EAT volume is significantly associated with insulin resistance (IR) and CAD in patients with obesity or metabolic syndrome. However, it remains uncertain whether CAD is associated with IR even in lean subjects. The purpose of this study was to investigate the impact of EAT on IR and CAD in non-obese subjects without metabolic syndrome.

Methods and Results: We prospectively studied 624 consecutive patients who underwent multi detector computed tomography (MDCT) at the Yamagata University Hospital between January 2009 and June 2011. Obesity was defined as body mass index (BMI) ≥ 25 kg/m² and metabolic syndrome was defined according to the criteria from the National Cholesterol Education Program Adult Treatment Panel III. After we excluded 385 patients with obesity or metabolic syndrome, 239 patients were enrolled in the present study. EAT volume was measured by using 64-slice MDCT. There were 102 (42.7%) subjects with IR (homeostasis model assessment-IR > 2.5) and 86 (36.8%) subjects with CAD. Subjects with IR had higher EAT volume, higher BMI, higher serum low-density lipoprotein cholesterol level and higher prevalence of CAD compared with those without IR. Subjects with CAD (AAA) were younger and showed higher EAT volume, lower serum high-density lipoprotein cholesterol level and higher prevalence of IR compared with those without CAD. After adjustment of age, gender and BMI, increased EAT volume (35 ml of mean EAT volume) was independently associated with IR (hazard ratio 2.6, 95% confidence interval 1.5-4.8). Increased EAT volume was also associated with CAD (hazard ratio 1.9, 95% confidence interval 1.0-3.6) after adjustment of age, gender, BMI and presence of IR.

Conclusion: Increased EAT volume may play a key role in development of IR and CAD even in non-obese subjects without metabolic syndrome.

P703 Conformational pulsatile changes of the aortic annulus: impact on prosthesis sizing by computed tomography for transcatheter aortic valve implantation (TAVI) proper techniques

P. Blanken1, M. Russe2, J. Leipsic2, U. Ebersberger1, M. Siepe1, J. Reinohri1, P. Suranyi1, M. Langer2, U.J. Schoepf1 . 1Medical University of South Carolina, Charleston, United States of America; 2University Medical Center Freiburg, Freiburg, Germany; 3St. Paul’s Hospital, Vancouver, Canada

Objectives: To investigate pulsatile changes of the aortic annulus and their impact on prosthesis selection by computed tomography (CT).

Background: Precise non-invasive prosthesis sizing is a prerequisite for transcatheter aortic valve replacement (TAVR).

Conformal pulsatile changes of the aortic annulus were measured by CT imaging with an additional 2D projection for the aortic annulus and the prosthesis. EAT volume was measured as described above. The CT images were reconstructed in a sagittal plane (maximal EAT volume) and in a coronal plane (maximal EAT volume) for each cardiac phase and each cardiac cycle. The results were compared with the results of the standard CT approach and with the results of the standard CT approach and with the results of the standard CT approach and with the results of the standard CT approach.

Results: There was no statistical significant difference between systolic and diastolic diameters of short- (2.13±0.21 cm vs. 2.07±0.22 cm) and long-axis view diameters (2.64±0.29 cm vs. 2.62±0.33 cm), the area (4.82±0.86 cm² vs. 4.69±1.01 cm²) and circumference (7.94±0.72 cm vs. 7.84±0.87 cm) of the aortic annulus. Interobserver variability results are shown in the table. Intra-observer results showed significant differences of short- and long-axis view diameters in systolic reconstructions (2.07±0.23 cm vs. 2.12±0.23 cm, P = 0.004 and 2.60±0.23 cm vs. 2.64±0.31 cm, P > 0.003), whereas in diastolic reconstructions, there was no significant difference of all aortic annulus parameters.

Conclusions: Dimensions of the aortic annulus in CT imaging do not differ significantly between systolic and diastolic data sets. Interobserver variability is independent of the reconstructed phase.
Peri-atrial epicardial adipose tissue is associated with changes affect prosthesis selection. Prosthesis selection by diastolic perimeter-sizing by DA-75% or DP-75% nominal prosthesis diameter was smaller than DA and peri-ventricular EAT volumes (p=0.01, p<0.001, respectively) were independent predictors for future AF. The sensitivity and specificity for the prediction of AF using peri-atrial EAT volume index of 13 paroxysmal AF and 4 persistent AF. Patients with AF were more likely to be calculated as the sum of EAT area and subsequently divided into peri-atrial and with no history of AF who underwent MDCT examination. EAT volume was calculated as the sum of EAT area and subsequently divided into peri-atrial and peri-ventricular EAT. The classical contributors to future AF, LA volume and, the length product. Coronary artery disease underwent coronary Dual-Source CT (DSCT) angiography (prospectively ECG-triggered at 70% of RR-interval, 100kV, 165 mAs, 2x128x0.6mm collimation, 60mL contrast at 6mL/sec) prior to invasive catheterization (FBP) and using a raw-data based IR algorithm. Subsequently, the accuracy to detect significant coronary artery stenosis (≥50%) was assessed for FBP and IR by two independent observers blinded to the results of invasive catheterization. Additionally, differences in subjective image quality (0 to 3 points), image noise, signal- and contrast-to-noise-ratios (SNR, CNR) were determined in the aortic root and left ventricle. In comparison with FBP, use of 20%, 40%, 60%, 80%, and 100% ASIR resulted in reduced image noise between groups (7.7%, 18.8%, 27.9%, 39.9%, and 48.6%, respectively; p < 0.001) without our difference in signal (p = 0.60). With ASIR algorithms image noise and Agatston coronary calcium scoring significantly decreased compared with FBP algorithms (837.3±130.3; 802.2±124.9; 771.5±120.7; 744.7±116.8; 724.5±114.2, and 709.2±112.3 for 0%, 20%, 40%, 60%, 80%, and 100% ASIR, respectively, p < 0.001). Volumetric score decreased in a similar manner (p < 0.001) while calcium mass remained unchanged. Mean effective radiation dose was 0.81 mSv±0.09 mSv.

Conclusion: ASIR results in image noise reduction. However, ASIR image reconstruction techniques for MDCT scans decrease Agatston coronary calcium scores. Thus, one needs to be aware of significant changes of the scoring results caused by different reconstruction methods.

MULTIDETECTOR COMPUTED TOMOGRAPHY: TECHNICAL ISSUES

Coronary artery calcium scoring: influence of adaptive statistical iterative reconstruction using 64-MDCT

C. Gebhard1, M. Fiechter2, T.A. Fuchs2, J.R. Ghardi2, B.A. Herzog2, F. Kuhn2, J. Stehli3, E. Mueller3, O. Gaemperli1, P.A. Kaufmann1

1University of Zurich, Department of Cardiology, Zurich, Switzerland; 2University Hospital Zurich, Zurich, Switzerland

Background: Assessment of coronary artery calcification is increasingly used for cardiovascular risk stratification. We evaluated the reliability of calcium-scoring results using a novel iterative reconstruction algorithm (ASIR) on a high-definition 64-slice CT scanner, as such data is lacking.

Methods and Results: In 50 consecutive patients Agatston scores, calcium mass and volume score were assessed. Comparisons were performed between groups using filtered back projection (FBP) and 20%-100% ASIR algorithms were measured in the coronary arteries, signal and noise were assessed.

Conclusions: This MDCT study demonstrated that peri-atrial EAT volume predicted new-onset AF in patients with CAD, independent of LA enlargement.

Should computed tomography coronary angiography be used when the coronary artery stenosis exceeds a certain threshold in patients with chest pain?


Hospital Clinic San Carlos, Madrid, Spain

Introduction: There is ongoing debate about whether a computed tomography coronary angiography (CTCA) should be used when the calcium score (CS) exceeds a certain threshold in patients with chest pain. The aim of this study was to determine whether specific "cutpoints" regarding coronary artery CS could be determined to predict severe coronary stenoses assessed by CTCA.

Results: 294 consecutive patients evaluated for chest pain, without known coronary artery disease and submitted for 64-CT between January 2007 and December 2010 were enrolled. Subjects underwent Agatston CS and CTCA using current 64-slice technology.

Conclusions: Raw-data based iterative reconstruction along with prospective ECG-triggering improves diagnostic accuracy for detection of coronary artery stenosis when compared to standard filtered back projection and allows substantial reduction of radiation exposure in coronary CT angiography.
Low radiation dose with high-pitch dual-source CT. Accidental noncardiac findings in 16cm range through plane cardiac area in conventional scan acquired by 320 slice computed tomography.

Chiba University Graduate School of Medicine, Chiba, Japan

**Purpose:** In 320 slice CT, although organs other than heart, such as lung are also irradiated, fields of view (FOV) are usually focused only on heart, and non-cardiac findings are usually not assessed. To investigate frequency of non-cardiac findings in cardiac imaging with routine 320 slice CT, we made full FOV axial images and had them diagnosed by radiologists.

**Methods:** A total of 1291 subjects (830 male mean 62 yrs) underwent enhanced conventional ECG gated 320 slice CT (Aquilion one) (0.5mm slice thickness with 320 slices = 16cm) to evaluate coronary arteries (617 subjects), myocardium (216 subjects). Early phase and non-contrast or late phase images were reconstructed with full FOV axial images. Cardiologists assessed the heart, while radiologists reviewed the other organs.

**Results:** 18 patients (1.4%) had already known malignant tumor by the CT scan. A total of de novo 1050 non-cardiac findings were identified in 813 patients (63.0%). Among them, 730 findings (69.5%) were observed in lung, 88 (8.4%) in pleura, 122 (11.6%) in liver, 24 (2.3%) in mammary gland, 69 (6.6%) in mediastinum, and 12 (11.4%) in bone. In 7 subjects (0.7%), malignancy was confirmed (two lung cancer, two malignant lymphoma, one esophageal cancer, one breast cancer. Malignancy was strongly suspected in 30 subjects (2.3%), non-calcified nodule and suspected lung cancer.

**Conclusions:** There were a significant number of non-cardiac findings in the cardiac area in conventional scans by 320 slice CT, possibly because subjects who undergo CT tend to be older. To avoid missing clinically important findings, radiologists and cardiologists who analyze cardiac MSCT scans should reconstruct full FOV axial images at any cardiac phase and should carefully evaluate all organs irradiated in the scan.

Low radiation dose with high-pitch dual-source computed tomography angiography before Transcatheter Aortic Valve Implantation

A. Alsaleek, M. Al-Mallah, M. Alharriri, A. Omran. King Abdulaziz Medical City, King Abdulaziz Cardiac Center, Riyadh, Saudi Arabia

**Purpose:** To determine the impact of an ECG-triggered computed tomography angiography (CTA) utilizing high-pitch spiral dual source CT on radiation dose and image quality with full FOV axial images and had them diagnosed by radiologists.

**Methods:** This was a retrospective analysis of consecutive patients evaluated for TAVI. It is associated with a significantly lower radiation dose while maintaining sufficient image quality.

**Results:** A total of 43 patients (age 75+8 years, males were 72%) were included. The body mass index was 31.1+9.4. The total amount of contrast per exam was 95±11 mL (no significant difference between the groups). The effective radiation dose was significantly lower in patients who underwent gated flash compared to the gated spiral and non-gated CT, the median was 5.6 vs. 29.9 and 16.6 mSiV, respectively, p<0.0001 (figure 1). The image quality was well maintained across all the groups; the root CNR was 21.8±10.4, 14.0±6.5 and 15.7±9.1; the femoral artery CNR was 17.1±7.4, 10.2±4.5 and 15.0±7.6 in non-gated, gated spiral and gated flash CT respectively.

**Conclusion:** High-pitch prospectively triggered CTA is an attractive protocol to assess the entire aorta and iliofemoral arteries in evaluating patients prior to TAVI. It is associated with a significantly lower radiation dose while maintaining sufficient image quality.

Noninvasive assessment of in-stent restenosis by high definition computed tomography coronary angiography with new gemstone detector

T. Tsuda, H. Mihrara. Yokkaichi Municipal Hospital, Yokkaichi, Japan

**Purpose:** Noninvasive assessment of in-stent restenosis (ISR) by computed tomography coronary angiography has been challenging. Recently, high definition computed tomography coronary angiography (HDCTCA) with new gemstone detector has been developed, which has high spatial resolution, so it may lead to significant improvement of accuracy to diagnose ISR. The purpose of this study is to assess ISR using HDCTCA and to exam the diagnostic accuracy of HDCTCA by comparing with invasive coronary angiography (ICA).

**Method:** We enrolled consecutive 154 patients with previous coronary stents implantation who were received HDCTCA (GE Discovery CT750 HD) for clinical indications. Image quality for the evaluation of ISR was assessed using 5 point grading scale: IQ score (1=excellent, 5=non-assessable). Significant ISR was defined as ≥50% luminal narrowing in the stent lumen or the presence of significant stent edge stenosis.

**Result:** 119 male and 36 female (age 68±8.0 years) with 305 stents (2.0 stents/patient, average stent diameter 3.0±0.5mm,average IQ score 2.2±1.0) were evaluated. 38 stents (12%) were not assessable for the poor image quality (IQ score 4 or 5) (feasibility 88%). In assessable 267 stents, 18 stents (6.7%) were diagnosed as ISR and 249 stents were diagnosed as no-ISR by HDCTCA. In the 18 stents which were all received ICA, 17 stents were diagnosed as ISR by ICA. In the 249 stents, 60 stents were received ICA, all of which were diagnosed as no-ISR by ICA. In this study, the sensitivity was 100%, specificity was 96%, positive predictive value was 94%, and negative predictive value was 100%, respectively.

**Conclusion:** In the assessable stents, HDCTCA has high accuracy with ICA about detecting ISR, which is useful to rule out ISR.
P711 Premedication with beta blocking agents for coronary CT angiography: analysis of efficacy and safety in the German cardiac CT registry

J. Rixe1, S. Achenbach1, M. Hadamitzky2, T. Limburg3, O. Bruder1, G. Kordes1, W. Moshage1, A. Schmerrnud1, J. Haasler1, J. Senges1
1University Hospital Giessen and Marburg, Medical Clinic I, Cardiology and Angiology, Giessen, Germany; 2German Heart Center, Clinic for Heart Disease, Munich, Germany; 3Research Institute for Heart Attack Ludwigshafen (HfH), Ludwigshafen, Germany; 4University Hospital of Essen, Department of Cardiology, Essen, Germany; 5University Hospital of Heidelberg, Department of Cardiology, Heidelberg, Germany; 6Hospital Traunstein, Department of Cardiology, Traunstein, Germany; 7Cardiology Centre Bethanien (CCB), Frankfurt, Germany

Objectives: Premedication with beta blocking agents is recommended for heart rate control prior to coronary CT angiography. However, there is insufficient data about the use in daily practice, effectiveness and safety issues of beta blockers for this purpose.

Methods: Patient characteristics and peri-procedural parameters of patients undergoing coronary CT angiography were submitted by ten experienced centers to the German Cardiac CT Registry. A total of 3203 patients were analyzed with regards to the use of beta blockers, procedural data such as heart rate and peri-procedural complications.

Results: Of 3203 patients included into the registry (mean age 60.1 ± 12.38% female), 2414 received beta blockers (75.4% of all patients). 1443 received oral, 628 patients only oral beta blockers (63.9% and 26% of all patients on beta blocking agents). Both i.v. and oral beta blocking agents were administered in 243 patients (10.1%, respectively). Mean heart rate during CT was 77.3 ± 8.5bpm. It was significantly higher for patients on beta blockers (mean/max heart rate 59.8 ± 6.4bpm/67.9 ± 27.3bpm) than for patients without (mean/max heart rate 51.1 ± 10.2bpm/67.9 ± 22.2bpm, p < 0.001/p=0.05). Oral was more effective than i.v. and combined beta blockade (mean/max heart rate 57.6 ± 8.7bpm/69.0 ± 31.8bpm and 62.2 ± 6.7bpm/69.0 ± 15.1bpm, p < 0.001 for both). The rate of patients with all vessels evaluable for stenoses was insignificantly higher in patients on beta blockers (96.3% vs. 94.9%, p = 0.19). Peri-procedural complications were rare (33% of 3203 patients, only 7 patients with adverse events attributable to pre-procedural medical treatment) and did not show any significant differences for patients with and without beta blockers.

Conclusions: Beta blockers are consistently used for heart rate control prior to coronary CT angiography, with oral being more effective than i.v. - beta blockade. In general, the administration of beta blocker is not associated with an increased incidence of peri-procedural complications.

P712 The usefulness of landiolol, an ultra-short-acting beta1-adrenergic blocker, for 256-slice cardiac computed tomography with iterative reconstruction

Y. Kuga, H. Ueda, A. Kido, S. Matsuhashi, K. Asawa, N. Yoshida, Y. Ioku, M. Yasumaki, K. Ueda, Y. Nishida, Kouenoseki Takai Hospital, Cardiovascular Center, Tepn, Japan

Background: The hybrid iterative reconstruction (IR) technique for 256-slice coronary computed tomography (CT) with improved temporal resolution can reduce radiation exposure and provide sufficient image quality. Furthermore, the administration of a short-term beta-blocker is the first-line option for effective heart rate (HR) reduction and reducing motion artifacts during coronary CT angiography.

Purpose: The aim of this study was to evaluate the efficacy of the administration of intravenous landiolol, an ultra-short-acting cardioselective beta-blocker, for both reduction of the radiation dose and improving the image quality using CT imaging with high temporal resolution and an IR algorithm (IDose). We compared the non-IR images with those obtained by IR with the same effective dose of radiation and qualitatively analyzed the image quality. The primary study endpoint was to show the diagnostic non-inferiority of the high-pitch CT angiography protocol compared to the conventional-first CT angiography protocol in patients scanned with IR.

Methods: A total of 400 patients with HRs ≥65 beats/min before 256-slice coronary CT angiography were prospectively randomized to a beta-blocker (n=200) or a control group (n=200). Landiolol (0.25 mg/kg) was administrated intravenously before CT scanning in the beta-blocker group. IR was provided with moderate level (iDose level 4) and a helical scan with tube current modulation was performed in all patients. The radiation dose and image quality were systematically analyzed. The image quality of all coronary segments was graded on a 4-point scale (1=best to 4=worst) by two experienced observers. In general, the administration of beta blocker is not associated with an increased incidence of peri-procedural complications.

Results: Intravenous landiolol was administered in 200 patients without adverse events. The mean HRs were significantly reduced (76.8 ± 10.0 to 63.0 ± 10.3, p < 0.01) 4 minutes after administration of landiolol, and 68% of patients showed an HR < 65 beats/min. The mean effective radiation dose in the beta-blocker group was lower than that in the control group (4.20 ± 1.46 vs. 5.05 ± 2.03 mSv, p < 0.01). The image quality was grater in the beta-blocker than that in the control group (1.08 ± 0.11 vs. 1.21 ± 0.20, p < 0.01).

Conclusion: Intravenous landiolol administration is useful to both reduce radiation exposure and improve image quality of IR CT.

P713 How the use of iterative reconstruction affects assessment of patients with stable chest pain

P. Mokanavangi1, L. Lusik1, P. Ball1, T. Trinick1, E. Duly1, G. Walls1, M. Alkhatil1, S. Mccusker1, M. Harbison2, P. Donnelly1,1Glister Hospital, Belfast, United Kingdom; 2Queen's University, Centre for Vision and Vascular Science, Belfast, United Kingdom

Purpose: This study was designed to evaluate the impact of a novel iterative reconstruction (IR) algorithm on cardiac computed tomography (CT) image quality and effective radiation dose (ED).

Methods: As a sub-study of the larger CAPP (CT for Assessment of Pain and Plaque) trial, this study enrolled 250 consecutive patients with stable chest pain. The CAPP study was designed to evaluate the implementation of NICE guideline 95 on patients with stable chest pain. CT examinations were performed on a high 64 multi-detector scanner. Scan protocols were patient specific and at the discretion of imaging clinician. Images were reconstructed with either a standard filtered-back projection (FBP) or IR. Image noise was measured within regions of interest (ROI), and image quality was qualitatively assessed by two clinicians blinded to the reconstruction method. Images were also assessed for the presence of noise artefacts.

Results: 4 patients withdrew. 246 patients (140 males) underwent cardiac CT. 124 consecutive patients underwent image reconstruction with FBP (72 with retrospective, 52 with prospective). 122 patients underwent scanning with IR (112 with retrospective and 10 with prospective). Demographics are in Table 1. The mean estimated EDs were 8.3 mSv (FBP) and 4.4 mSv (IR) (dose savings of 47% using IR for retrospective cohorts and 6.5 mSv (FBP) and 4.3 mSv (IR) (dose savings of 34%) overall (p = 0.0001). There was no statistical difference in noise or mean attenuation in the ROIs. The mean IR image quality score was 3.7 ± 1.0 compared to 3.3 ± 1.2 for FBP images (p = 0.001). 27 of the 52 IR prospective studies had at least one noise artefact, with 2 of the 10 IR demonstrating the same.

Conclusion: IR in cardiac CT offers substantial ED reduction without compromise in image quality. This work suggests IR influenced clinical practice, as its availability promoted the use of retrospective protocol with practitioners opting for its diagnostic reassurance.

P714 Prospective randomized trial on radiation dose estimates of CT angiography in patients scanned with a high-pitch-first scan strategy - the protection IV trial

J. Hausleiter1, S. Desiere1, F. Pugliese2, E. Alexanderson3, A. Meave4, M. Hadamitzky1, T. Meyer1, A. Wil1, E. Hendrich1, S. Martinoff1 on behalf of PROTECTION IV investigators.
1German Heart Center, Hospital recht des Isar at the Technical University of Munich, Munich, Germany; 2Barts and The London NHS Trust, London, United Kingdom; 3National Institute of Cardiology “Ignacio Chavez”, Mexico City, Mexico

Background: Concerns have been raised about the radiation exposure during coronary CT angiographies (CCTAs). For a prospectively ECG-triggered high-pitch CT protocol and even sub-millisievert radiation doses have been reported for CCTA, but it is unclear, whether image quality is maintained when compared to conventional CCTA. The multi-center, prospective, randomized PROTECTION IV study investigates the impact of the high-pitch CT protocol on image quality and radiation dose.

Methods: 303 patients with suspected coronary artery disease and low and stable heart rate were randomized to either a high-pitch-first or a conventional-first CCTA strategy. In the conventional-first CCTA arm, ECG-triggered axial or ECG-gated low-pitch helical CT data acquisitions were used. If image quality was defined insufficient with the first CCTA scan, a second scan was performed. The primary study endpoint was to show the diagnostic non-inferiority of the high-pitch scan protocol, which was assessed by a 4-point image quality grading score (1: nondiagnostic to 4: excellent image quality; predefined non-inferiority margin of 25 score points). Total radiation dose, the need for a second CCTA scan as well as the rate of downstream testing during 30-day follow-up were assessed as secondary endpoints.

Results: 150 and 153 patients were randomized to high-pitch-first and conventional-first CCTA groups, respectively. The mean heart rate and BMI were 57.6 ± 4.0 bpm and 26.5 ± 3.7 kg/m², respectively. A second CCTA scan was performed in 14.0% and 9.2% of patients in the high-pitch-first and conventional-first groups, respectively (P = 0.18). The resulting total CCTA dose was 2.0 ± 2.4 mSv
A total of 16 patients have been studied up to date, including 10 men and 6 women with a mean age of 65.10 years. NICa showed significant stenotic lesions in 11 patients (68.8%) involving 3 vessels in 2 (12.5%), 2 vessels in 5 (31.2%), and 1 vessel in 4 (25%). Although not required for the present study, an invasive coronary angiography had been performed in these 11 patients, showing no discrepancies with NICa. MDCTperf showed adenosine-induced myocardial perfusion defects in 54% of coronary territories (26/48) and fixed defects (present at rest study) in 6% (3/48). Concordance between perfusion defects from MDCT-perf and CCM-perf was 70.8% (34/48) globally. In discordant instances, CMR-perf showed defects in 6 coronary territories (12.5%) which were not present from MDCT-perf, and the opposite was true in 8 coronary territories (16.7%). In all discordant cases MDCT-perf had correlated with coronary anatomy. Sensitivity of MDCTperf for detecting significant coronary artery disease at NICa was 86% and specificity was 79%. Positive and negative predictive values were 86% and 79%, respectively.

Conclusions: NICa and MDCTperf with a 320-row system is a feasible technique with a high diagnostic value for the presence, severity, and functional significance of coronary artery atherosclerotic lesions.

MULTIDETECTOR COMPUTED TOMOGRAPHY IN THE ASSESSMENT OF MYOCARDIAL PERFUSION

Diagnostic value of 320-row MDCT stress perfusion study in comparison with CMR

Methods: This prospective study includes patients referred with a clinical indication for a stress/rest adenosine myocardial perfusion study by Cardiovascular Magnetic Resonance (CMR perf). In addition to the CMR study patients were asked, and expressed their consent, to be submitted to a Multidetector Computed Tomography (MDCT perf) study. The combination of CTCA and CTP can identify ischemic defects due to coronary artery stenosis. TPRs demonstrate good correlation with perfusion defects.

DISCORDANCE OF ANATOMICAL AND FUNCTIONAL CORONARY STENOSIS ASSESSED BY 320-ROW COMPUTED TOMOGRAPHY

Methods and Results: We investigated 26 vessels of 25 patients who underwent both 320-row CTCA before invasive coronary angiography and FFR measurement. Quantitative coronary angiography (QCA), CXT (cross-sectional area stenosis), and CT-density derived stenosis assessment (CTDA) were performed to determine the severity of a stenosis that was compared with FFR measurement. A significant anatomical or functional stenosis was defined as > 50% diameter or 75% area stenosis, lumen CT density at most stenotic site < 200HU, or an FFR < 0.80. A total of 26 stenoses were evaluated of which 69.2% (18 of 26) had an FFR > 0.80. The diagnostic accuracy of QCT, CTDA, and CXT to detect a hemodynamically significant coronary artery lesion was 42.3%, 42.3%, and 80.8%, respectively. Correlation between QCT and CTDA with FFR measurement was not significant or weak.

Conclusions: The anatomical assessment of the hemodynamic significance of coronary artery stenoses assessed by 320-row computed tomography is not a reliable method for the reliable determination of coronary artery stenosis.

REFERENCES: We sought to determine the diagnostic performance of 320-row CTCA and quantitative computed tomography coronary angiography (QCT) to predict the hemodynamic significance of de novo discrete coronary stenoses, using fractional flow reserve (FFR) as a reference standard.

Methods and Results: We investigated 26 vessels of 25 patients who underwent both 320-row CTCA before invasive coronary angiography and FFR measurement. Quantitative coronary angiography (QCA), CXT (cross-sectional area stenosis), and CT-density derived stenosis assessment (CTDA) were performed to determine the severity of a stenosis that was compared with FFR measurement. A significant anatomical or functional stenosis was defined as > 50% diameter or 75% area stenosis, lumen CT density at most stenotic site < 200HU, or an FFR < 0.80. A total of 26 stenoses were evaluated of which 69.2% (18 of 26) had an FFR > 0.80. The diagnostic accuracy of QCT, CTDA, and CXT to detect a hemodynamically significant coronary artery lesion was 42.3%, 42.3%, and 80.8%, respectively. Correlation between QCT and CTDA with FFR measurement was not significant or weak.

Conclusions: The anatomical assessment of the hemodynamic significance of coronary artery stenoses assessed by 320-row computed tomography is not a reliable method for the reliable determination of coronary artery stenosis.

REFERENCES: We sought to determine the diagnostic performance of 320-row CTCA and quantitative computed tomography coronary angiography (QCT) to predict the hemodynamic significance of de novo discrete coronary stenoses, using fractional flow reserve (FFR) as a reference standard.

Multidetector CT: technological issues / Multidetector CT in the assessment of myocardial perfusion

P715 Influence of heart rate on the accuracy of dual source CT for coronary stenosis detection in patients with intermediate likelihood of disease: results of the international multidetector MEDIC trial

S. Achenbach1, A. Schubbaek2, U. Hoffman3, S. Abbbara3, P. Aubach4, D. Beerman5, M. Leil6, W.G. Daniel2, C. Hamm7, J. Hausleitner8, University of Erlangen-Nuremberg (Friedrich-Alexander-University), Erlangen, Germany. 2Justus-Liebig University Giessen, Medical Clinic I, Cardiology, Giessen, Germany; 3Harvard Medical School, Massachusetts General Hospital, Cardiac MRI PET CT Prog. Dept of Radiology, Boston, United States of America; 4Siemens Healthcare, Forchheim, Germany; 5 Cedars-Sinai Medical Center, Los Angeles, United States of America; 6German Heart Center, Clinic for Heart and Circulatory Diseases, Munich, Germany.

The accuracy of dual source CT (DSCT) for the detection of coronary artery stenosis was significantly lower (60%) in patients with stenosis detection has an impact on the patients' final results. The 45 patients had undergone a dual source CT coronary angiography (CTCA) with a 320-row system. The final results including the image quality score will be presented.

Conclusions: The final results including the image quality score will be presented. The initial patient group, sensitivity of DSCT for the detection of individuals with at least one coronary artery stenosis was 95% (104/120, 95%CI: 88%-98%). Specificity was 95% (289/305, 95%CI: 92%-97%), which was independent of heart rate. The presence of at least one coronary artery stenosis > 50% on a per-patient basis. The mean heart rate during DSCT was 67±20 beats/min. Mean DLP was 424±237 mGy*cm (5.9 mSv). In the entire patient group, sensitivity of DSCT for the detection of individuals with at least one coronary artery stenosis was 95% (104/110, 95%CI: 88%-97%), the positive predictive value was 84% (104/120) and the negative predictive value was 98% (289/295). Heart rate did not significantly influence accuracy (heart rate ≤ 60/minute: sensitivity 98%, specificity 94%, n = 145; heart rate > 60/minute: sensitivity 92%, specificity 95%, n = 270; p = n.s.).

Conclusions: In the largest multidetector trial to date concerning the detection of coronary artery stenoses by CT angiography, dual source CT demonstrated a high accuracy for the identification of patients with significant coronary lesions, which was independent of heart rate.

ASSESSMENT OF MYOCARDIAL PERFUSION

ADENOSINE-STRESS CT MYOCARDIAL PERFUSION AND CT ANGIOGRAPHY FOR ASSESSMENT OF CORONARY ARTERY DISEASE: INITIAL RESULTS

G. Koulouzidis1, T.M. McArthur2, M.T. Tighe2, S.M. Mallift2, P.J.J. Jenkins2, C.D. Davies3. 1Heart Centre and Department of Public Health & Clinical Medicine, Umea University, Umea, Sweden; 2European Scanning Centre, London, United Kingdom.

Introduction: Computed tomography coronary angiography (CTCA) has been widely accepted as a reliable, non-invasive modality, when studying the coronary arteries. However, it cannot assess the functional implications of any detected stenosis. It can be demonstrated if combined with myocardial stress CT perfusion scan (CTP). This is the first report of our experience, with the use of CTP in evaluating the severity of coronary artery disease (CAD).

Methods: Fourteen patients with angioma symptoms, underwent a standardized cardiac CT (Aquilion ONE, Toshiba) protocol, consisted of prospectively ECG-triggered CTCA, which, in cases of >50% obstruction in any of the coronary arteries, was combined with rest/stress myocardial perfusion imaging (3 min iv adenosine infusion at 0.14 mg/kg/min and 5-20 mg iv metoprolol for baseline heart rate above 70 beats/min). An experienced cardiologist visually assessed myocardial perfusion defects, and CTP analysis was based on transmural perfusion rate-. TPR (subendocardial attenuation density/ subepicardial attenuation density).

Conclusions: The combination of CTA and CTP can identify ischemic defects due to coronary artery stenosis. TPRs demonstrate good correlation with perfusion defects.
coronary stenoses determined by QCT, CTDA, or QCA does not correlate well with the functional assessment of FFR. Determining the hemodynamic significance of an angiographically intermediate stenosis remains mandatory for patient management.

**P719**

**Ct myocardial perfusion - correct scan timing for ischemia detection from time attenuation curves**

K.T. Ho1, Q.W. Yang2, 1Mount Alvernia Hospital, Singapore, Singapore; 2Tan Tock Seng Hospital, Singapore, Singapore

**Purpose:** CT Myocardial Perfusion Imaging (CTMPI) has been reported with various types of scanners. The 2nd generation dual-source scanners generate complete time-attenuation curves (TACs) for the heart & allow differentiation between normal & ischemic myocardium. For non dual-source scanners relying on imaging at a single time point, the accurate identification of appropriate time to scan in detecting ischemia is less precise. We utilized the 128-slice DSCT to study the ideal imaging window for ischemia detection.

**Methods:** 25 patients with known reversible defects, as detected by nuclear perfusion imaging, underwent dipyridamole-stress CTMPI. Patients received 50cc of contrast and 50cc of saline at a flow rate of 6cc/s, followed by perfusion imaging with the CT. The perfusion CT scan yields full TACs, i.e. wash in and wash out of contrast, for the entire myocardium. TACs were computed for all 17 segments of the myocardium, and attenuation curves of healthy and ischemic segments were compared.

**Results:** The difference between healthy and ischemic myocardium ranged from 34HU at the optimal time for imaging to 12HU at a suboptimal (late) imaging time. Using maximum arterial enhancement as a reference time-point, there was a time delay of 0.35 seconds in the detection of ischemia.

**Conclusions:** 1) The window of 10s implies that there is some latitude of scanning in the detection of ischemic defects. 2) However this relatively broad window may result in variability of estimation of size of ischemic defect, the quantitation being affected by exact scan timing.

**P720**

**Myocardial perfusion at rest is higher in women than in men**

C.B. Bertelsen1, J.T. Kuhl1, M. Zacho2, B.G. Nordestgaard3, A. Fuchs1, D. Kouramaea1, L. Kober1, K.F. Kolbod1, Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark; 2Rigshospitalet - Copenhagen University Hospital, Department of Radiology, Copenhagen, Denmark; 3Herlev Hospital - Copenhagen University Hospital, Department of Clinical Biochemistry, Copenhagen, Denmark

**Background:** The clinical presentation of ischemic heart disease in women differs from men, which could reflect gender-related differences of normal physiology. With 320-multi detector computed tomography (MDCT) it has become possible to assess non-invasively regional and transmural myocardial perfusion in addition to coronary atherosclerosis. The aim of this study was to assess the usefulness of stress myocardial CT perfusion to detect functional coronary stenoses as determined by fractional flow reserve (FFR) in patients with calcified plaques.

**Methods:** In patients presenting with suspected coronary artery disease, the calcium scores were determined for each of the main coronary arteries before CT angiography. Patients who had at least one calcified vessel with Agatston score of ≥ 200 underwent 256 slice adenosine stress myocardial CT perfusion and CT angiography. The FFR was measured in the calcified vessels with ≥ 50% diameter stenosis on invasive angiography. FFR of 0.80 or less was considered hemodynamically significant.

**Results:** The FFR was measured in 58 calcified vessels (Agatston score 730.1±597.6) of 43 patients (Age 71.0±8.6 years, 74% male). Agatston score and FFR (0.80±0.12) were not significantly correlated (r = 0.03, p = 0.82). In the vessel-based analysis, CT perfusion had similar sensitivity (83% vs. 96%, p = 0.35), higher specificity (82% vs. 15%, p < 0.001), and higher diagnostic accuracy (83% vs. 48%, p < 0.001) for detection of hemodynamically significant stenosis as compared with CT angiography. The area under the receiver-operating characteristic curve for CT perfusion (0.83; 95% confidence interval [CI]: 0.71 to 0.94) was greater than that for CT angiography (0.55; 95% CI: 0.40 to 0.70).

**Conclusions:** Stress myocardial perfusion imaging with multidetector CT localizes calcified coronary plaques and offers feasible diagnostic performance in detecting functional coronary stenoses in asymptomatic women with coronary atherosclerosis.

**P721**

**Stress myocardial computed tomography perfusion imaging and fractional flow reserve in patients with coronary plaques**

H. Ueda, A. Kido, S. Matsuhashi, K. Asaawa, N. Yoshida, Y. Sasaki, Y. Kuga, M. Yamasaki, K. Ueda, Y. Nishida, KoseiKai Takai Hospital, Cardiovascular Center, Tenri, Japan

**Purpose:** Multidetector computed tomography (CT) angiography is limited in the ability to detect coronary stenosis with calcification. The objective of this study is to assess the usefulness of stress myocardial CT perfusion to detect functional coronary stenoses as determined by fractional flow reserve (FFR) in patients with calcified plaques.

**Methods:** In patients presenting with suspected coronary artery disease, the calcium scores were determined for each of the main coronary arteries before CT angiography. Patients who had at least one calcified vessel with Agatston score of ≥ 200 underwent 256 slice adenosine stress myocardial CT perfusion and CT angiography. The FFR was measured in the calcified vessels with ≥ 50% diameter stenosis on invasive angiography. FFR of 0.80 or less was considered hemodynamically significant.

**Results:** The FFR was measured in 58 calcified vessels (Agatston score 730.1±597.6) of 43 patients (Age 71.0±8.6 years, 74% male). Agatston score and FFR (0.80±0.12) were not significantly correlated (r = 0.03, p = 0.82). In the vessel-based analysis, CT perfusion had similar sensitivity (83% vs. 96%, p = 0.35), higher specificity (82% vs. 15%, p < 0.001), and higher diagnostic accuracy (83% vs. 48%, p < 0.001) for detection of hemodynamically significant stenosis as compared with CT angiography. The area under the receiver-operating characteristic curve for CT perfusion (0.83; 95% confidence interval [CI]: 0.71 to 0.94) was greater than that for CT angiography (0.55; 95% CI: 0.40 to 0.70).

**Conclusions:** Stress myocardial perfusion imaging with multidetector CT localizes calcified coronary plaques and offers feasible diagnostic performance in detecting functional coronary stenoses in asymptomatic women with coronary atherosclerosis.
The study compiled with the Declaration of Helsinki.

Results: The qualitative CT analysis of stress images had a sensitivity of 100%, a specificity of 93.3%, Positive predictive value (PPV) of 86.7%, and a negative predictive value (NPV) of 100% compared to the qualitative CMR stress analysis on a per patient basis, while the qualitative CT analysis of rest images had a sensitivity of 100%, a specificity of 96.7%, PPV of 90.0%, and NPV of 100% compared to the qualitative CMR rest analysis on a per patient basis to detect myocardial perfusion defects (Table 1).

Conclusions: Our study shows that 320-detector CT perfusion images can be used clinically with a high probability to detect myocardial perfusion defects compared to CMR both for the stress and rest images.

Feasibility of coronary CT angiography for predicting the functional significance of stenosis severity in patient with intermediate coronary artery disease

J.W. Kim, M.H. Yoon, S.J. Tahk, B.J. Choi, S.Y. Choi, H.S. Lim, H.M. Yang, K.W. Seo, S.M. Kim, E.J. Ahn, Ajou University School of Medicine, Suwon, Korea, Republic of

Purpose: Feasibility of coronary CT angiography (CCTA) in intermediate coronary artery disease (CAD) is not well elucidated. The purpose of this study was to evaluate the feasibility of CCTA in intermediate CAD by comparing with fractional flow reserve (FFR).

Methods: We enrolled 109 Patients (129 lesions) with intermediate CAD who underwent CCTA years with coronary angiography (CAG) with FFR retrospectively. Intermediate CAD was defined as 30–70% diameter stenosis (DS, %) assessed by CAG, and functionally significant stenosis was defined as FFR<0.8. Maximal hyperemia was induced by intravenous continuous adenosine infusion using microcather. CCTA measurements included diameter stenosis and agatston calcium score. We divided 2 groups according to agatston calcium score for evaluation of calcium score effect assessing stenosis severity (group A: calcium score<100, n= 64, group B: calcium score≥100, n=65).

Results: In intermediate coronary artery lesions, there was a weak negative correlation between FFR and DS assessed by CCTA (r=-0.248, p=0.005), whereas there was no positive correlation between FFR and DS assessed by CCTA was not different between 2 groups (group A: AUC= 0.576, 95% CI=0.483-0.660, p=0.005) and FFR versus minimal luminal diameter (MLD) assessed by CAG (r=-0.373, p=0.001) and FFR versus minimal luminal diameter (MLD) assessed by CAG (r=-0.400, p=0.001). The best cut-off value of DS assessed by CCTA to predict FFR<0.8 was >37.2% (74.7% sensitivity, 68.9% specificity, 55.1% positive predictive value, 59.7% accuracy, area under the ROC curve (AUC) = 0.573, 95% CI: 0.483-0.660). The accuracy of CCTA to predict FFR<0.8 was not different between 2 groups (group A: AUC= 0.576, 95% CI: 0.446-0.699 versus group B: AUC= 0.575, 95% CI: 0.466-0.687).

Conclusions: CCTA may not be useful to predict the functional significance of stenosis severity in patients with intermediate CAD.

Relationship between regional hyperaemic myocardial blood flow on dynamic dual-source computed tomography and coronary artery stenosis

F. Pugliese1, A. Wragg2, C. Anagnostopoulos3, L.C. Davies1, M.A. Westwood4, A.D. Timmins1, C. Parkin3, E. Klotz4, A.D. Mathur1, S.E. Petersen1, Bart's and The London NHS Trust, London, United Kingdom; 2Bart’s and The London NHS Trust, London, United Kingdom; 3Academy of Athens, Biomedical Research Foundation, Athens, Greece; 4Siemens Healthcare, Erlangen, Germany

Purpose: To evaluate the relationship between regional myocardial blood flow (MBF) estimated in absolute terms by computed tomography and coronary percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for the performance of hybrid SPECT/CTA. In selected cases indications for percutaneous and possibly surgical revascularization could be made prior to CA in all patients. The study outcome was the treatment decision categorized as: no revascularization, percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). These treatment decisions were made by a panel of two interventional cardiologists and one cardiothoracic surgeon in two steps: first based on the results of hybrid SPECT/CTA, and on a second occasion based on SPECT and CA. Percent agreement between the treatment decisions on both hybrid SPECT/CTA or SPECT and CA were calculated for all patients. Secondly three subgroups of patients were assessed: those with matched stenosis on CTA and corresponding ischemic myocardium on SPECT, with unmatched stenosis and CTA findings and those with normal findings on both SPECT and CTA.

Results: Revascularization (PCI or CABG) was necessary in 54 (50%) of patients based on SPECT and CA. Percent agreement between treatment decisions based on either hybrid SPECT/CTA or SPECT and CA were calculated first for all patients. Secondly three subgroups of patients were assessed: those with matched stenosis on CTA and corresponding ischemic myocardium on SPECT, those with unmatched stenosis and CTA findings and those with normal findings on both SPECT and CTA.

Conclusions: Panel evaluation shows that patients could be accurately indicated for and deferred from revascularization based on hybrid SPECT/CTA. In selected cases indications for percutaneous and possibly surgical revascularization could even be based on hybrid SPECT/CTA alone.
Usefulness of indirect quantitative approaches to aortic regurgitation severity by duplex sonography of proximal common carotid artery


Backgrounds: The evaluation of aortic regurgitation (AR) severity by trans-thoracic echocardiography (TTE) has some limitations especially in eccentric AR with non-circular vena-contracta. Diastolic reverse flow of aorta is known as a useful indirect index of AR. However, suboptimal image and increased arterial stiffness mislead to inaccurate evaluation. Thus, we evaluated the severity of AR by common carotid artery (CCA) flow.

Methods: Seventy patients (Age ≥11 y.o.) with mild to severe AR underwent TTE, duplex sonography of CCA and aortography. We used aortography as a reference method to define AR severity. As a recommended index of AR by TTE, we measured vena-contracta width (VCW) of AR from parasternal long-axis view. Then, proximal CCA flow was obtained by duplex sonography (Figure). We measured end-diastolic flow velocity (DFV) and maximum systolic flow velocity (SFV) and calculated resistive index (RI= SFV/DFV/SFV) as an index of AR severity.

Results: Severe AR was present in 48 patients (68%). We obtained optimal images of CCA flow in all cases. RI correlated better with AR severity by aortography than CCA flow (RI R=0.74, CCA R=0.70, p<0.001). Cut-off value of severe AR by RI was 0.89 (sensitivity 81%, specificity 82%, AUC=0.90). In patients with severe AR, eccentric AR was present in 18 patients. CCA of eccentric AR was smaller than that of central AR (5.3±2.7 vs. 8.5±3.9, mm, p<0.001). However, there were no significant differences between RI (0.96±0.07 vs. 0.96±0.09, NS) of eccentric AR and that of central AR.

Abstract P728 - Table 1. Aorta biomechanics

<table>
<thead>
<tr>
<th>Group</th>
<th>Control I</th>
<th>Control II</th>
<th>Marfan I</th>
<th>Marfan II</th>
<th>BAV I</th>
<th>BAV II</th>
<th>TAAD I</th>
<th>TAAD II</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>41</td>
<td>26</td>
<td>24</td>
<td>21</td>
<td>26</td>
<td>23</td>
<td>28</td>
<td>21</td>
</tr>
<tr>
<td>Age years</td>
<td>48±7</td>
<td>58±4</td>
<td>26±7</td>
<td>54±12</td>
<td>31±6</td>
<td>56±9</td>
<td>30±7</td>
<td>55±11</td>
</tr>
<tr>
<td>Aorta mm</td>
<td>29±1.4±3</td>
<td>31±4±3</td>
<td>40±5±6</td>
<td>44±3±4</td>
<td>42±7</td>
<td>46±5±4</td>
<td>39±6±4</td>
<td>44±1±4</td>
</tr>
<tr>
<td>BF mm²</td>
<td>98</td>
<td>83</td>
<td>87</td>
<td>89</td>
<td>90</td>
<td>83</td>
<td>89</td>
<td>96</td>
</tr>
<tr>
<td>Stiff</td>
<td>5±2±2</td>
<td>12±7±2</td>
<td>9±7±5</td>
<td>13±7±9</td>
<td>14±6±10</td>
<td>23±0±15</td>
<td>12±1±6</td>
<td>20±3±4</td>
</tr>
<tr>
<td>PWV m/s</td>
<td>5±6±4</td>
<td>8±3±2</td>
<td>8±3±2</td>
<td>8±3±2</td>
<td>8±3±2</td>
<td>11±3±3</td>
<td>8±2±2</td>
<td>10±3±3</td>
</tr>
</tbody>
</table>

Mean ± sd. §p<0.001 vs Control I; ¶p<0.001 vs Control II; *p<0.05 vs Marfan.

Figure 1. CCA flow by duplex sonography

Conclusions: Indirect quantitative approaches to AR severity by CCA flow were easy to measure and useful. AR assessments by CCA underestimated the severity of eccentric AR. However, CCA flow index accurately quantified the severity also in patients with eccentric AR.

P729 The bicuspid aortic valve: a correlation between phenotypic classification of leaflet morphology and valvular function

J. H. Kim1, S.-P. Lee1, H.-K. Kim1, Y.-J. Kim1, G.-Y. Cho2, D.-W. Sohn1, 2-Seoul National University Hospital, Department of Internal Medicine, Division of Cardiology, Seoul, Korea, Republic of; 2Seoul National University Bundang Hospital, Division of Cardiology, Seongnam, Korea, Republic of

Background: A bicuspid aortic valve (BAV) is common congenital heart disease, affecting about 0.5–2% of population, oftentimes causes aortic stenosis (AS) or regurgitation (AR). But, the proportion ophthephenotype and prevalence of steninsufficiency were evaluated in very limitednumber of patients and mainly reported in western country. Therefore, we evaluated the proportion of phenotype and the effect on stenosis orregurgitation in large Korean cohort.

Methods: From SNUH Echo database, 424 adult patients (mean age 55±5±15.0, 68.5% male) with BAV who underwent echocardiography between May 2007 and December 2010 were collected and reviewed. Aortic valve in echocardiography were reevaluated for appropriate classification of phenotype and the size of aortic root was measured approximately. At least moderate degree of stenosis orregurgitation is defined as a significant AS or AR.

Results: We identified three morphologies: type 1, fusion of right and left coronary cusp (N=236), type 2, right and non-coronary fusion (n=114); and type 3, left and...
Clinical efficacy of doppler-echocardiographic indices in asymptomatic moderate or severe aortic stenosis with preserved ejection fraction: a comparison between resting and low-dose dobutamine values

M. Barovc1, V. Vujacic-Tesic2, B. Bojic2, M. Petrovic3, I. Nedeljkovic1, D. Trifunovic1, D. Popovic2, P. Seferovic2. 1Clinical Center of Serbia, Clinic for Cardiology, Belgrade, Serbia; 2Institute for Statistics, Faculty of Organizational Sciences, University of Belgrade, Belgrade, Serbia

Purpose: In aortic stenosis (AS) symptoms usually occur during exercise and, furthermore, most Doppler-echocardiographic indices that are used for assessing AS severity are not validated in such patients. The aim of this study was to assess which hemodynamic parameter best accounts for the clinical outcome and to analyze the value of low-dose dobutamine testing (DT) in patients with moderate or severe AS with preserved ejection fraction (EF).

Method: A total of 126 asymptomatic patients with aortic valve area (AVA) ≤ 1.5cm² and EF > 50% were enrolled in this prospective study. The follow-up period was 13.1±3.2 months. Mean age was 66.47±10.53 (58.73% males), mean EF was 72.03±6.69%, mean pressure gradient (Pmean) 41.94±11.22 mmHg and average AVA 0.82±0.22cm². Patients with > 2+ valvular regurgitation or mild mitral stenosis were excluded. The low-dose dobutamine infusion protocol was begun at 5 μg/kg/min body weight up to 20 μg/kg/min, titrated upwards at steps of 5 μg/kg/min every 3 min. The composite outcome endpoint (MACE) was defined as cardiac death, aortic valve replacement and hospitalization caused by AS during follow-up. Univariate analysis was performed according to patient’s medical record or referring physician.

Results: No patient experienced a serious adverse event during or after DT. A total of 70 patients had MACE (55.5%), of which 9 patients (7.14%) have died during follow-up. Univariate analysis showed that resting mean values of Vmax (maximal velocity), Pmean, AVA, Zva (valvulo-arterial impedance), ELI (energy loss index), AVR (aortic valve resistance) and S’ were associated (p < 0.05) with MACE. The multivariate analysis revealed that only AVR (p = 0.007; HR = 1.001-1.006) was independently associated with MACE. Regarding death only, the univariate analysis showed that AVA, Zva, ELI, SWL (stroke work loss), AVR, S’ and SAC (systemic arterial compliance) were associated (p < 0.05) with death. However, only Zva was independent predictor of death according to multivariate analysis (p = 0.017; HR = 3.244; CI = 1.669-6.309). Parameters that were not predictors of MACE, or death only, did not become predictors after DT either.

Conclusion: The DT increased, but not significantly, the prognostic value of parameters that are determinants in such patients. Our aims were to assess MEC with the use of peak VO2 and identify its determinants in such patients.

Method: Asymptomatic patients with moderate or severe AS (n=65, aortic valve area ≤ 1.5 cm², 65±14 years, 66% men) and preserved left ventricular (LV) systolic function (LV ejection fraction > 50%) were prospectively referred for both comprehensive resting echocardiography and cardiopulmonary exercise test. Valvulo-arterial impedance (Zva), a marker of global LV hemodynamic load, was calculated as the sum of systolic blood pressure and mean trans-aortic gradient, divided by the indexed LV stroke volume, as previously validated.

Results: Baseline total VO2 was 19.5±5.7 mL/kg/min and varied widely among patients (median 19.62 mL/kg/min; range 7.2 - 33.12 mL/kg/min). According to the median of peak VO2, patients with reduced MEC were significantly older (p < 0.001) and had higher systolic blood pressure values (p = 0.02). There were no other significant differences between the 2 groups (reduced vs. preserved MEC) regarding demographic and clinical data. There was a significant correlation between peak VO2 and: age, body mass index, LV stroke volume, mean flow rate, cardiac output, S’ and E’ wave velocities, E/E’ ratio and LA diameter (all p < 0.05). Zva was the strongest univariate echocardiographic determinant of peak VO2 (r = 0.39, p = 0.002). In addition, patients with reduced MEC (peak VO2 mean value) had higher Zva values compared to those with preserved MEC (4.2±1.18 vs. 3.71±0.68 mmHg/mL/M²; p = 0.036). In multivariable analysis, older age (β = 0.24±0.05; p < 0.001) and higher Zva (β = 3.8±0.68; p = 0.048) were the only independent predictors (β < 0.40) of reduced peak VO2.

Conclusion: In asymptomatic patients with moderate or severe AS, MEC varies widely and is often lower than expected. Global LV hemodynamic load is the main Doppler-echocardiographic determinant of reduced MEC in these patients, further supporting the usefulness of this parameter for their clinical evaluation and management.
28% higher hazard of AS-related events (95% CI 1.04-1.57, p < 0.05) independent of changes in EF over time, severity of AS, and study treatment.

Conclusions: Combined assessment of EF and MWS improves risk stratification in asymptomatic AS by identifying patients with normal EF, low MWS and a significant increased CV risk over an average 4 to 5-year follow-up including faster progression of AS.

P734 Impact of atrial fibrillation on long-term clinical outcomes among patients with severe aortic stenosis undergoing transcatheter aortic valve implantation

S. Stortzek1, L. Buttlefeld1, P. Varenweser1, D. Hegi1, T. Pilgrimm1, A.A. Khatall1, S. Gloeckler1, C. Huber3, P. Jueni2, S. Windecker1.

1Bern University Hospital, Department of Cardiology, Bern, Switzerland;
2Institute of Social & Preventive Medicine & Clinical Trial Unit, University of Bern, Bern, Switzerland; 3Bern University Hospital, Department of Cardiothoracic Surgery, Bern, Switzerland

Background and Aim: Atrial fibrillation (Afib) impairs hemodynamic parameters by loss of atrio-ventricular synchrony and is a major risk factor for stroke. Degenerative aortic stenosis is the most common valvular heart disease and like Afib considered a disease of the elderly. Elderly patients considered high-risk for surgical aortic valve replacement are candidates for transcatheter aortic valve implantation (TAVI) with a prevalence of Afib in up to 50% of patients. The impact of Afib on long-term clinical outcomes in these patients is not well established. We therefore compared outcomes of patients with pre-existing or new-onset Afib with patients without Afib after TAVI.

Methods and Results: Between 2008/2007 and 2009/2010, 260 patients (age 83±6years) with symptomatic, severe aortic stenosis (mean NYHA functional class 2.6±0.8) were included into a prospective single-center registry. Sixty-eight patients (26.2%) presented with Afib at baseline, and 21 patients (8.1%) developed new-onset Afib after TAVI. Compared to patients without Afib, those with had similar baseline clinical characteristics including age (83±5 vs 82±7, p=0.66), gender (female 61% vs. 54%, p=0.29), arterial hypertension (82% vs. 77%, p=0.31), diabetes (27% vs. 23%, p=0.53), chronic renal failure (74% vs. 68%, p=0.11) and risk scores (STS-Score 6.4±7 vs. 6.8±5, p=0.76; Euroscore 25.7±15 vs. 24.8±15, p=0.64). Patients with Afib more frequently had revascularization for coronary artery disease by either coronary artery bypass grafting (12% vs. 26%, p=0.009) or percutaneous coronary intervention (16% vs. 26%, p=0.05) than those without Afib. At one year, all-cause mortality (31.5% versus 12.3%) was significantly higher in crude (HR 2.87, 95% CI 1.63-5.05, p=0.0003) and adjusted (HR 2.89, 95% CI 1.64-5.1, p=0.0002) analyses. Similarly, rates of cardiac death (8.6% vs. 22.5%, adjusted HR 2.84, 95% CI 1.45-5.55, p=0.002) were significantly increased among patients with as compared to those without Afib. Conversely, we recorded no differences with respect to major stroke (4.7% vs. 4.5%, adjusted HR 1.05, 95%CI 0.32-3.55, p=0.92) and life-threatening bleeding (11.7% vs. 11.2%, adjusted HR 0.94, 95% CI 0.42-2.12, p=0.68) between patients with and without Afib at one year of follow-up.

Conclusion: Afib frequently coexists with severe aortic stenosis in elderly patients who are candidates for TAVI. Although the risk of stroke and bleeding appears similar, Afib carries a nearly 3-fold increased risk of all-cause and cardiac mortality, which deserves further study.

P735 Abdominal visceral adiposity and left ventricular hypertrophy in patients with aortic stenosis - results from the progressa study

R. Capoulade, J.P Despres, P. Mathieu, M.-A. Clavel, A. Dahou, M. Arsenault, E. Bedard, F. Le Ven, J.G. Dumesnil, P. Pibarot. Quebec Heart and Lung Institute, Quebec, Canada

Background: We reported that metabolic syndrome (MeS) is associated with increased prevalence of LV concentric hypertrophy and impairment of LV systolic function, two risk factors for poor prognosis in AS patients. Excessive visceral fat accumulation could be one of the key causal factors underlying this association. The objective of this study was to examine the association between magnitude & distribution of adiposity and degree of LV hypertrophy and systolic dysfunction in AS patients.

Methods: 104 consecutive patients with AS were recruited in the PROGRESSA study and underwent Doppler-echocardiography and computed tomography (CT). As an estimate of the global LV hemodynamic load, we calculated the valu e of arterial impedance (Zva). Abdominal visceral fat (AFT), subcutaneous fat (ASF), and total fat (ATF=AFT+ASF) areas were measured by CT between L4 and L5 lumbar vertebrae spaces. The AFT/ATF ratio was calculated to assess the proportion of total fat deposited in the visceral compartment.

Results: Body mass index (BMI) correlated strongly with AVF, ASF and ATF (r=0.7, r=0.69 and r=0.86 respectively; p<0.0001) but weakly with AVF/ATF ratio (r=0.23; p=0.02). Patients with AVF/ATF ratio =0.4 (i.e. median value) had higher prevalence of MetS (48 vs. 20%, p=0.003), hypertension (HTN: 86 vs. 57%, p=0.001), diabetes (30 vs. 12%, p=0.02), hyperlipidemia (74 vs. 53%, p=0.03), and coronary artery disease (CAD: 56 vs. 25%, p=0.002) compared to those with AVF/ATF ratio <0.40. Peak aortic jet velocity was similar in both groups (Vpeak: 2.8±0.5 vs. 2.9±0.6m/s, p=NS). LV mass index was higher in patients with AVF/ATF ratio =0.40 (LMI: 53±12 vs. 46±8g/m2.7, p=0.0007). In a multinaviable model adjusted for age, gender, HTN, MetS, CAD, creatinin, valcular calcification, Vpeak, and Zva, the two most powerful predictors of higher LMI were larger BMI (p=0.0001) and higher AVF/ATF ratio (p=0.03). Patients with AVF/ATF ratio >0.40 also had a lower LVEF (64±7 vs. 67±5%, p=0.02). In multivariable model adjusted for age, gender, HTN, CAD, and Zva, higher AVF/ATF ratio was associated with lower LVEF (p=0.04).

Conclusion: This study reports that the degree of global adiposity (as reflected by BMI) as well as the more extensive distribution of this adiposity within the visceral compartment (as reflected by AVF/ATF ratio) are independently associated with more pronounced LV hypertrophy and reduced LV systolic function in AS patients. These findings provide impetus for elaboration of interventional studies aiming at the reduction of obesity, and particular visceral obesity, in AS population.
measurements, plasma BNP levels and clinical outcome were studied. Mean follow-up was 27.5±24.2 months; mortality was gathered from Social Security Death Index and a Cox proportional hazards model was used to explore the association of BNP with all-cause mortality.

Results: Average BNP was 415±588 pg/dl, and 85 pts (32%) had BNP ≥ 200 pg/dl. 137 pts (53%) were medically treated and 123 pts (47%) underwent AVR; over 27.5±24.2 months of follow-up, 105 pts (41%) underwent AVR had BNP ≥ 200 pg/dl and medically treated 50 pts (59%) had BNP ≥ 200 pg/dl (p=0.12). BNP showed a significant univariate association with all-cause mortality (HR: 1.001 [95% CI: 1.000-1.001], p=0.001), and a BNP cut off value of 200 pg/dl remained a strong predictor of mortality (see Figure 1) (HR: 1.83 [95% CI: 1.079-3.052], p=0.021), independent of age (HR: 1.021 [95% CI:0.991-1.052], p=0.16), gender (HR: 0.702 [95% CI: 0.422-1.166], p=0.17), LV EF (HR:0.993 [95% CI: 0.958-1.030], p=0.72) and valvular aortic impedance (Zva) (HR: 1.073 [95% CI: 0.884-1.303], p=0.48).

Conclusion: BNP cut off value of 200 pg/dl can help to predict adverse outcome in low gradient “severe” AS patients with preserved LVEF.

### Characteristics and prevalence of flow-gradient patterns in patients with severe aortic stenosis and preserved ejection fraction

M. Eleid, P. Sorajja, H. Michelena, J. Malouf, P. Pellikka. Mayo Clinic, Division of Cardiovascular Diseases and Internal Medicine, Rochester, United States of America

Background: Paradoxical low-flow (LF), low-gradient (LG) severe aortic stenosis (AS) with preserved ejection fraction (EF) is reported to be a common entity associated with an adverse prognosis. Potential causes of discordant valve area and mean gradient include measurement error, small body size and high afterload, but their prevalence is still under debate. We investigated population characteristics of consecutive patients with severe AS using the newly proposed flow-gradient classification.

Methods and Results: An analysis was performed at our institution of all patients ≥18 years undergoing 2-D and Doppler echocardiography between 2006 and 2011 with severe AS and preserved EF (EF ≥ 50% and aortic valve area <1.0 cm²) (n=3,422). Patients were compared in 4 groups using the flow-gradient classification (Table): LF (stroke volume index <35 mL/m²), LG (mean gradient <40 mm Hg) (LF/LG), HF, high-gradient (HG, mean gradient ≥ 40 mm Hg) (LF/HG), normal-flow (NF, stroke volume index ≥35 mL/m²), LG (NF/LG), and NF/HG.

Conclusions: LG severe AS with preserved EF is found in 30% of severe AS patients and is associated with female sex and small body size. However, paradoxical LF/LG severe AS characterized by high global afterload is less common and present in 5% of severe AS patients. Using the flow-gradient classification helps to further stratify groups according to hemodynamic findings that may have prognostic significance.

----

**Abstract P738 - Table 1. Flow Gradient Patterns in Severe AS**

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>LF/LG (n=112) (28%)</th>
<th>LF/LG (n=185) (28%)</th>
<th>NF/LG (n=870) (28%)</th>
<th>NF/HG (n=2255) (28%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>76±16</td>
<td>74±16</td>
<td>77±16</td>
<td>77±16</td>
<td>77±16</td>
<td>0.04</td>
</tr>
<tr>
<td>Female sex</td>
<td>56(50%)</td>
<td>100(54%)</td>
<td>601(65%)</td>
<td>1055(47%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>34±7.9</td>
<td>29±6.7</td>
<td>27±6.5</td>
<td>28±6.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body surface area (m²)</td>
<td>2.1±0.3</td>
<td>1.9±0.2</td>
<td>1.8±0.2</td>
<td>1.9±0.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Aortic valve area (cm²)</td>
<td>0.66±0.15</td>
<td>0.83±0.12</td>
<td>0.89±0.10</td>
<td>0.90±0.10</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Indexed aortic valve area (cm²/m²)</td>
<td>0.33±0.05</td>
<td>0.44±0.08</td>
<td>0.51±0.06</td>
<td>0.43±0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Left ventricular outflow tract diameter (cm)</td>
<td>2.09±0.30</td>
<td>2.05±0.20</td>
<td>2.08±0.15</td>
<td>2.20±0.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Stroke volume (mL)</td>
<td>64±14</td>
<td>60±11</td>
<td>79±12*</td>
<td>99±12*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Indexed stroke volume (mL/m²)</td>
<td>31±5</td>
<td>30±4</td>
<td>45±6*</td>
<td>49±4*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Valvular aortic impedance (mm Hg·mL⁻¹)</td>
<td>5.6±3.2</td>
<td>4.9±2.1</td>
<td>5.6±3.2</td>
<td>3.6±2.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*Significant difference (p<0.05) with low flow (LF)/high gradient (HG) group; † significant difference with low flow gradient (LG) group; ‡ significant difference with normal flow (NF/LG) group.
AVAP by preoperative transesophageal echocardiography (TEE) (Philips iE33) and analyzed quantitatively 3D measurements, such as coaptation height (CH), root area, cusp volume and leaflet length, by the 3D feature-tracking software (Siemens SC2000 eSeValves prototype).

Results: See figure.

Conclusions: Type I dysfunction was identified as the dilation of aortic root, particularly sinusotubular junction, and the increase of CH. Type II dysfunction was identified as the decrease of leaflet length. 3D quantitative analysis of AVAP by TEE is a new objective approach for elucidation of AR mechanism.

The distinctive temporal patterns in regression of Left Ventricular Hypertrophy and left atrial reverse remodeling after Aortic Valve Replacement in patients with severe aortic stenosis

T. Hatani, T. Kita, T. Tani, K. Kim, N. Ebara, A. Kobori, M. Kinoshiba, S. Kaji, A. Yamamura, Y. Furukawa. Kobe City Medical Center General Hospital, Kobe, Japan

Background: In patients with severe aortic stenosis (AS), chronic pressure overload induces left ventricular hypertrophy (LVH) and left atrial (LA) enlargement. Aortic valve replacement (AVR) remains the most effective treatment for severe AS, and a regression in LVH after AVR has been reported. However, few data exist regarding the association between regression of LVH and LA reverse remodeling after AVR.

Methods: We retrospectively reviewed 268 consecutive patients who underwent AVR in our institution between 2006 and 2010. Among them, 105 patients (age: 76±8 years) who underwent surgery for severe AS, without any prior cardiac surgery were analyzed. Echocardiographic data were obtained before surgery, 1 month, 1 year, and 3 years after surgery.

Results: A significant reduction in both LV mass index and LA volume index were observed over time after surgery (Figure, both P<0.001). LA dilatation was improved and reached plateau at 1 year after surgery, whereas LVH was improved and reached plateau at 1 year after surgery. There was no significant correlation between regression of LVH, defined as ≥20% reduction of LV mass, and LA reverse remodeling, defined as ≥35% reduction of LA volume (n=0.19, P=0.12).

Preoperative LVH was the independent predictor of regression of LVH (odds ratio, 3.76; P=0.004), and preoperative LA dilatation was the independent predictor of regression of LA dilatation (odds ratio, 20.1; P<0.001).

Conclusion: LA reverse remodeling and regression of LVH after AVR may be independent processes, although AVR imparted beneficial effects on LV and LA structures over time. LA reverse remodeling preceded regression of LVH.

Aortic valve replacement surgery in octogenarians: predictive value of euroSCORE I and II and 30-day and 1-year mortality


Background: Aortic valve replacement surgery (AVRS) is the preferred therapy option in symptomatic severe aortic stenosis. In octogenarians, the perioperative mortality can reach 15% in the presence of comorbidities.

Purpose: To assess the 30-day and 1-year mortality of AVRS and evaluate the predictive power of euroSCORE I and II in a population of octogenarians submitted to isolated AVRS.

Methods: Retrospective, single study, including 108 consecutive patients (pts) in the ninth decade of life, who underwent AVRS between July 2003 and November 2010. The predictive power was calculated by ROC (Receiver Operating Characteristic) curve, with a confidence interval (CI) of 95%.

Results: 108 pts were studied, mean age 83.1±2.2 years old, 62% females. 67.5% (66 pts) were in NYHA I and II and 37.0% (40 pts) had angina. 18.5% (20 pts) were diabetic. 67.6% (73) had creatinine clearance below 50 mL/min; extracardiac arteriopathy was found in 14.8% (16 pts), chronic obstructive pulmonary disease in 8.3% (9 pts). Left ventricular systolic dysfunction occurred in 25.8% (24 pts) and 4.6% (5 pts) had severe pulmonary hypertension. AVRS was elective in 91.7% (88 pts) of cases. Mean Euroscore I was 13.1±1.1% and mean euroSCORE II was 4.3±2.8%. 30-day mortality was 5.7% (6 pts) and 1-year mortality was 4.3±2.8% (6 pts). The ROC curve AUC was 0.655 (CI 95%, 0.433-0.876) for euroSCORE I and 0.585 (CI 95%, 0.302-0.818) for euroSCORE II.

Conclusions: Isolated AVRS in octogenarians can be performed with a low 30-day and 1-year mortality, despite the increased perioperative risk. In this population, euroSCORE II was the best mortality predictor.

Morti-mortality of biological aortic valve replacement in a monocentric cohort of 3507 patients operated on between 2002 and 2010

J.C. Roussel, S. Senage, R. Gaudin, M. Michel, A. Mugniot, C. Periguard, O. Habash, D. Duveau, P.H. Despins, O. Baron. Institute of the Thorax, University Hospital of Nantes, Nantes, France

Objective: The aim of this study was to evaluate the actual morbi-mortality rate in a series of biological aortic valve replacement (BAVR) in a same center.

Material and Method: Between 2002and 2010, 3535 aortic valve prosthesis were implanted in 3507 consecutive patients in a same center. Mean age was 74.7±7.6 years [19.4-94.5 years,median 75.8] 63.3% of the patients were male. Main indication for BAVR was aortic stenosis in 83.4% of the patients. Mean logistic euroscore was 8.4±8.3 [5.88-4].

Results: Mean CPB and cross-clamp times were 98±38 min and 67±30 min respectively. BAVR was isolated in 59.1% of the patients (n=2089) or associated to coronary artery bypass in 33.6% of the cases (n=1188). Hospital mortality rate was 3.8% (n=133) and main post-operative complications were: mental confusion (9.5%), stroke (1.9%; n=66), TIA (0.7%; n=25), pulmonary infections (4.6%; n=164),acute renal insufficiency (15.5%; n=550) requiring dialysis in 4.4% of the patients, episod of atrial fibrillation (38.3%; n=1355), atrioventricular blockrequiring PM implantation (4.3%; n=147), myocardial infarct (0.8%; n=23). Several statistical risk factors for earlymortality were found in univariate and multivariate analysis (see table).

Risk factors for hospital mortality

<table>
<thead>
<tr>
<th>Variable</th>
<th>p</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Euroscore Log</td>
<td>10^-7</td>
<td>1.0336</td>
<td>1.0181 to 1.0495</td>
</tr>
<tr>
<td>Dyspnea III or IV (NYHA)</td>
<td>0.001</td>
<td>2.1482</td>
<td>1.360 to 3.391</td>
</tr>
<tr>
<td>Pre-op. renal insufficiency</td>
<td>0.021</td>
<td>2.4278</td>
<td>1.3798 to 4.276</td>
</tr>
<tr>
<td>DM</td>
<td>0.008</td>
<td>2.6468</td>
<td>1.283 to 5.743</td>
</tr>
<tr>
<td>Mean aortic cross clamp time</td>
<td>10^-6</td>
<td>1.0154</td>
<td>1.01 to 1.019</td>
</tr>
<tr>
<td>Inotropes post-CPB</td>
<td>10^-6</td>
<td>5.5435</td>
<td>3.765 to 8.112</td>
</tr>
<tr>
<td>Rads surgery</td>
<td>10^-6</td>
<td>3.1067</td>
<td>1.829 to 5.276</td>
</tr>
<tr>
<td>Postoperative renal insufficiency</td>
<td>10^-6</td>
<td>6.4101</td>
<td>4.354 to 9.409</td>
</tr>
<tr>
<td>Prolonged intubation (&gt;48h)</td>
<td>10^-6</td>
<td>4.0582</td>
<td>2.569 to 6.410</td>
</tr>
</tbody>
</table>

Conclusion: Biological AVRs is currently safe and associated with an hospital mori-mortality rate <4% with abeter identification of patients at risk.

MITRAL VALVE DISEASE

Isovolumic myocardial acceleration, new index of right ventricular function after percutaneous mitral valvuloplasty

E.A. Khalifa1, W.A.E.L. Elnaggar2.1Dar Al Fouad Hospital, Cairo, Egypt; 2Cairo University, Faculty of Medicine, Cairo, Egypt

Objectives: In mitral stenosis, Right ventricular (RV) function may be affected either by rheumatic process or due to pulmonary vascular alterations. The aim of this study was to determin if isovolumic myocardial acceleration (IVA) measured by tissue Doppler imaging (DTI) of tricuspid annulus could be used in detection of RV function immediately after percutaneous mitral valvuloplasty (PMV).

Patients and methods: The current study enrolled 108 patients with chronic rheumatic mitral stenosis in sinus rhythm. Conventional echocardiographic parameters, mitral valve area (MVA), transmitial diastolic gradient, pulmonary artery pressure (PAP), RV fractional shortening (RVFS%), tricuspid annular plane systolic excursion (TAPSE), TDI-derived systolic velocities of tricuspid annulus, isovolumic myocardial acceleration (IVA), peak myocardial velocity during isovolumic contraction (IVV), peak systolic velocity during ejection period (Sm) and RV Tei index were calculated to all patients before and after (one day) PMV.

Results: TAPSE, RVFS% and Sm were relatively higher following PMV but did
not attain statistical significance. TDI-derived IVA, IVV index were found to be significantly increased after PMV from 1.71±0.54 m/s² to 3.27±0.22 m/s², and from 0.11±0.04 cm/s to 0.14±0.06 cm/s respectively with (P<0.001) for all. RV Tei index significantly decreased from 0.49±0.025 to 0.31±0.21 (P<0.001). Significant negative correlation could be established between IVA and PAP (before and after PMV) (r = -0.61, r=-0.58 respectively), Tei index (r = -0.72) and mean trans-mitral diastolic gradient (r = -0.74), whereas significant positive correlation was identified between IVA and MVA (r = 0.68) with p<0.0001 for all correlations.

Conclusion: TDI-derived IVA can be used as reliable, non-invasive parameter to detect early improvement of RV function following PMV.

**Repeat percutaneous mitral valvuloplasty for patients with mitral valve restenosis: comparison with initial procedure and predictors of outcomes**

Z. Frikha1, L. Abid2, S. Kalafi2, R. Bouhlal1, M.M. Abdenaderh1, D. Abid1, M. Akrouf1, M. Hentati1, A. Karouz1, S. Kammoun1, M. Cheker Hospital, Department of Cardiology, Sfax, Tunisia; 2Habib bourguiba hospital, Department of Anesthesiology, Sfax, Tunisia

**Background:** Only a few reports have been published into redo PMV and data regarding its long term safety and efficacy are scarce.

**Objectives:** To explore the immediate and long-term outcome of repeat (redo) percutaneous mitral valvuloplasty (PMV) in a series of patients with mitral restenosis in comparison with initial PMV in the same series and to determine predictors of outcome.

**Methods:** Our study is retrospective enrolling 354 patients, hospitalized in the cardiology department between January 1996 and January 2011. The study group consisted of 80 patients (mean age 47±10 years) who benefited from a redo PMV. All redo PMV procedures were performed using the Inoue balloon system. Procedural success was defined as 50% or more increase of mitral valve area (MVA) with a final MVA ≥1.5 cm², without major complications. Restenosis was defined as loss of ≥50% of the initial gain of MVA by the preceding PMV with a final MVA <1.5 cm².

**Results:** Successful procedural outcome was achieved in 81.1% of patients. There were no deaths and restenosis was noted in 40% (p=0.0032). The Procedural success and the gain of MVA were higher in the initial as compared to the redo procedure (P<0.05).

The only independent predictor of redo PMV success was an echocardiographic score >8. Early symptomatic improvement after redo PMV of ≥1 NYHA functional class was obtained in 95% of the patients. The mean follow-up was 64, 85±35 months. There were no deaths and restenosis was noted in 40%.Ten (12.5%) patients required mitral valve replacement (34.21 months after redo PMV) due to recurrent symptoms. The predictive factors of restenosis identified by the univariate analysis in our study were: previous surgical commissurotomy and a high echocardiographic score.

**Conclusions:** Repeat PMV is safe and provides good immediate results in patients with restenosis after successful first procedure. Long-term results of redo PMV are satisfactory and related mainly to the echo score.

**Quantification of mitral regurgitation by calculation of regurgitant volume: 3D left ventricular echocardiography versus PISA**

F. Arsac, N. Floris, P. Reant, M. Djop, R. Rouldaut, S. Lafitte on behalf of Hôpital Cardiologique, CIC à thématique cardiovasculaire CIC-005 INSERM, Université Victor Segalen, CHU de Bordeaux, Bordeaux, France. University Hospital of Bordeaux - Hospital Haut Leveque, Department of Cardiology, Bordeaux-Pessac, France

Quantification of mitral regurgitation (MR) by echocardiography is well established using several echocardiographic parameters in which effective regurgitation flow area (ERO) and regurgitant volume (RV) are the most commonly used. However, hemispheric assumptions allowing application of proximal isovelocity area (PISA) may be erroneous due to the complex mitral valve morphology (i.e. mitral valve prolapse).

We hypothesized that 3D left ventricular echocardiography combined with aortic pulsed Doppler could obtain RV with high reliability and will allow a comparison of 2 methods (3D vs PISA) in presence of mitral regurgitation.

**Methods:** First, in 50 patients without MR, we compared LV ejection volumes (LVEj) from a full volume 3D echocardiographic acquisition and 2D Simpson method to the aortic stroke volume (ASV) obtained by Pulsed Doppler for validation of the 3D approach. Second, we analyzed 50 patients with different degree MR for comparison of the two approaches and verification of PISA RV values.

**Results:** Serial 3D TEE based analysis of AROA during systole allows accurate definition of MVRV. Dynamic variation in MR is predominantly determined by changes in flow and less by changes in AROA.

**Conclusions:** Dynamic variation in mitral valve regurgitation is predominantly determined by alterations in flow velocity and less of regurgitant orifice area**

S. Hamada, E. Alliok, M. Frick, M. Becker, N. Mars, R. Hoffmann. University Hospital Aachen. RWTH, Internal Medicine I, Cardiology, Pulmonology & Vascular Medicine, Aachen, Germany

Background: Mitral valve regurgitant volume (MVRV) can be calculated as product of regurgitant orifice area and velocity time integral (VTI). Direct planimetry of anatomic regurgitant orifice area (AROA) can be accurately performed by 3D transesophageal echocardiography (3D TEE). To account for dynamic variations in mitral regurgitation (MR) during systole, serial planimetry and concordant analysis of flow during subintervals of systole may improve estimates of MVRV. We determined the impact of AROA and flow changes throughout systole on estimates of MVRV. MVRV derived by AROA and VT were compared with MVRV obtained by magnetic resonance imaging (MRI).

**Methods:** 3D TEE and MRI were performed in 43 patients (age 71±11 years) with grade 2-4 MR. Echilometry of MR was fail in 15 patients and functional in 28 patients. MVRV was defined as sum of five systolic subintervals of equal duration. For each subinterval the AROA and the corresponding regurgitant VTI using the CW-Doppler signal were determined. Planimetry of AROA was performed using QLAB-Software (Philips). MRI quantification of MVRV was performed by subtracting left ventricular stroke volume from aortic outflow volume.

**Results:** AROA derived MVRV correlated to MVRV determined by MRI (r= 0.439, p<0.0032). AROA determined at five consecutive time points throughout systole varied only by 18% in-hospital complications of the subinterval with the highest flow was 120% of the subinterval with the lowest flow. Considering the echilometry of MR, in both fail as well as functional MR greatest AROA and subinterval VT were reached in the third quintile of systole.

**Left atrial strain relates to surgical indication in patients with severe organic mitral regurgitation: a 2D-speckle tracking study**

P.J.M.R. Debonnaire1, D.P. Leong1, T.G. Witkowski2, I. Al Amri1, E.M. Joyce1, S. Katsanos1, M.J. Schalij1, J.J. Bax1, V. Delgado1, N.A. Marsan1, 1Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 2Military Hospital, Cardiology Department, Wroclaw, Poland

Purpose: To evaluate the effect of chronic severe organic mitral regurgitation (MR) on left atrial (LA) phasic function and its relationship with the presence of established criteria for surgical indication (SI).

**Methods:** 2D methods transesophageal echocardiography-derived strain indices for LA reservoir, conduit and contractile function were assessed in 121 patients with chronic severe organic MR and 20 healthy controls. MR patients were divided according to the presence of no (n=46) versus ≥1 (n=75) criteria for SI according
Mitral valve morphological abnormalities in severe aortic stenosis - a three-dimensional transesophageal echocardiographic study

Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands

Purpose: Mitral regurgitation has been reported to accompany severe aortic stenosis (AS) in a significant proportion of cases. However, the mechanism underlying this association remains unclear. The aim of this study was to characterize the mitral apparatus using 3-dimensional (3D) transesophageal echocardiography (TEE) in patients with severe AS.

Methods: Ninety-four patients undergoing 3D TEE prior to transcatheter aortic valve implantation and 21 individuals free of structural heart disease (controls) were studied. The 3D morphology of the mitral annulus and leaflets and the aortomital angle were measured offline using commercially available software.

Results: As summarized in the table, AS patients exhibited widening of the aortomital angle and anterior mitral leaflet angles, increased mitral valve tenting volume and reduction in mitral annular height compared with controls. Despite contrasting clinical characteristics between AS patients and controls, the differences between groups in aortomital angle and mitral annular height persisted after adjustment for age, coronary disease, left ventricular volume and mass, and relative wall thickness.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>AS cases (n=94)</th>
<th>Controls (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVEDVi mL/m² (lQR)</td>
<td>24 (19-39)</td>
<td>21 (13-22)</td>
<td>0.001</td>
</tr>
<tr>
<td>LVEF % = SD</td>
<td>53 ±14</td>
<td>65 ±6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>LV mass index, g/m² (lQR)</td>
<td>120 (100-139)</td>
<td>77 (68-90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Relative wall thickness, ± SD</td>
<td>0.41 ±0.10</td>
<td>0.34±0.06</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Mitral annular height (lQR)</td>
<td>6.3 (5.0-7.7)</td>
<td>8.1 (7.3-9.5)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Aortomital angle (°), ± SD</td>
<td>131 ±11</td>
<td>114 ±11</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Anterior mitral leaflet angle (°), ± SD</td>
<td>35 ±5.7</td>
<td>32 ±5.9</td>
<td>0.01</td>
</tr>
<tr>
<td>Posterior mitral leaflet angle (°), ± SD</td>
<td>43 ±8.4</td>
<td>42 ±7.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Non-planer (°), ± SD</td>
<td>103 ±12</td>
<td>106 ±10</td>
<td>0.2</td>
</tr>
<tr>
<td>Mitral tenting volume, ml (lQR)</td>
<td>2.8 (1.7-3.9)</td>
<td>1.8 (1.2-2.9)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusions: Severe AS is characterized by reduced mitral annular height and increased aortomital angle that may exert traction on the anterior mitral leaflet, increasing mitral tenting volume. These findings provide insight into mechanisms predisposing to mitral regurgitation.

The loss of dynamic deformation of mitral leaflet in functional mitral regurgitation

Q.S. Lin¹, A.P. Lee¹, Y.C. Zhang¹, F. Fang¹, W. Song², M.J. Underwood³, C.M. Yu⁴. ¹Div of Card, Dept of M&T, IVM, LIHS, SH Ho Cardio Disease & Stroke Ctr, PWH, CUHK, Hong Kong, China, People’s Republic of; ²Div of Cardiothoracic Surgery, Dept of Surgery, PWH, CUHK, Hong Kong, China, People’s Republic of

Purpose: The mitral leaflets (ML) in functional mitral regurgitation (FMR) has been considered structurally and functionally normal. We challenge this widely accepted concept using quantitative real-time three-dimensional echocardiography (RT3DE).

Methods: Transesophageal RT3DE of the mitral valve was acquired in 43 patients with FMR and 30 normal controls (NC). Leaflet thickness was measured in diastole. Dynamic changes of anterior and posterior leaflet surface area (AMLA and PMLA) were tracked in systolic valve closure using dedicated quantification software.

Results: In FMR, the ML was significantly thicker (2.71±0.03 vs 2.09±0.37mm, P<0.001) with significantly larger surface area (P<0.001) than normal. Dynamic deformation of the mitral leaflet surface area was evident in normal subjects. The mitral leaflet was stretched during systole with significantly increase by 25% in leaflet surface area from onset to end systole (AMLA 4.94±1.13 to 5.95±1.56cm², P=0.001), PMLA 3.51±0.97 to 4.56±1.13cm², respectively. P>0.001), but showed no dynamic deformation with increase only by 0.8% in FMR (AMLA 7.26±1.83 to 7.42±1.84 cm², PMLA 6.41±1.94 to 6.30±1.83 cm², respectively, P>NS. (Figure)

Conclusions: The MLs are abnormal in FMR: they are thicker, larger and less stretchable than normal mitral valve during systolic closure.

Management guidelines for severe mitral regurgitation: Is it time for three-dimensional LV volumes to replace LV dimensions?

T. Yingchoncharoen. Cleveland Clinic, Cleveland, United States of America

Purpose: Mitral regurgitation (MR) causes eccentric LV hypertrophy, and current guidelines propose an LV end-systolic dimension of <4 cm as an indication for mitral valve surgery in patients with severe MR. However, assessment of LV size using M-mode or 2D echo may be inaccurate. We sought the correlation and the discrepancy between standard and three-dimensional echocardiography (3DE) for accurate quantification of LV size in MR.

Methods: Conventional and 3D transthoracic echos were performed using standard equipment in 84 pts (age 61±11 years, male 73%) with organic severe MR. LV dimensions and 2D volumes were analyzed in accordance with ASE guidelines. 3D volumes were measured with dedicated software (TomTec Imaging Systems, Munich, Germany).

Results: All pts were successfully measured. The mean 3D LV end-diastolic volume index (LVEDVi) was 161.51±46.28 ml/m² and the mean LV end-systolic volume index (LVESVi) was 97.51±36.53 ml/m². LVEDVi from 3D is significantly greater than 2D (98±37 vs 38±10 ml/m², p<0.001). Although the 3D LVEDVi
was correlated with 2D-derived LV end-systolic dimension (r²=0.57 p<0.001) there are some discrepancies between the two measurement (Figure). The cut-off value of 4 cm of LV end-systolic dimension failed to diagnose LV dilatation in 64.3% (Figure).

Conclusion: Pts with MR show major discrepancies between conventional and 3D derived parameters. Use of guideline criteria for LV enlargement may not represent the true volume-loading of the LV.

**P752 Understanding of the etiology of degenerative mitral valve disease by echocardiography, surgeon and pathologist**

E. Malev², G. Kim³, L. Mitranova², M. Gordeev¹, E. Zemtsovsky³.¹Almazov Federal Heart, Blood and Endocrinology Centre, Saint Petersburg, Russian Federation; ²Saint-Petersburg State University, Saint-Petersburg, Russian Federation

**Purpose:** Degenerative mitral valve disease (DMVD) often results in severe mitral valve regurgitation due to leaflet prolapse or chordal rupture. To select the most appropriate repair technique a complete understanding of the underlying degenerative etiology (Barlow’s disease, BD or fibroelastic defect, FEĐ) is mandatory. The purpose of this study was to determine the capability of transesophageal echocardiography to distinguish BD and FEĐ compared with surgical and pathological findings.

**Results:** Transthoracic echocardiograms were retrospectively compared with microscopy in 233 patients (mean age: 53.8±12.9) undergoing surgery for severe mitral regurgitation due to degenerative mitral valve disease at Almazov Federal Heart, Blood and Endocrinology Centre between 2000 and 2011. The analyzed echocardiographic features of DMVD included valvular thickening (≥5 mm), valve prolapse, failed leaflet due to ruptured chordae tendineae, and valvular calcification.

**Conclusion:** There are some discrepancies between the two measurement (Figure). The cut-off value of 4 cm of LV end-systolic dimension failed to diagnose LV dilatation in 64.3% (Figure). The application of a series of new quantitative parameters in this study, including NPA, TVI, CI, may helpful to make up the appropriate FMR therapeutic plans and assess the prognosis.

**P753 Mitral valve remodelling caused by increased diastolic shear-stress mediated forces: observations in patients with a bicuspid aortic valve**


**Background:** Mitral valve (MV) leaflets enlarge as a response to increased systolic stress produced by leaflet tethering. However, flow-mediated shear-stress is the most important hemodynamic force responsible for physiological development of most vascular structures. Hypothesis: excentric aortic regurgitation (AR) in bicuspid aortic valve (BAV) patients rises diastolic shear-stress on the MV leaflet and could trigger leaflet remodelling.

**Methods and results:** We applied cardiovascular magnetic resonance to characterize MV geometry in 65 BAV patients (43±16 years old, 86% male) and 22 control subjects. Anterior leaflet length (ALL), leaflet coaptation pattern (% of anterior leaflet projection onto the mitral annular diameter), tenting area (TA) and LV volume were measured. AR was graded as non-significant (Group I:none AR or regurgitation fraction (RF) ≤25%) or moderate-severe (Group II:RF >25%). 23 patients had significant AR (Group II). Group II showed significantly higher values of ALL compared with Group I (3.6±0.5 cm vs 2.8±0.4 cm, p<0.001) with posterior displacement of the coaptation point (TA1.01±0.2 cm2 vs 1.9±0.2 cm2, p<0.05). ALL was significantly higher in Group II compared with control subjects (3.6±0.5 cm vs 2.5±0.4 cm, p<0.001), however no differences were found with Group I (2.5±0.4 cm vs 2.6±0.4 cm, p=0.4). By multivariate analysis ALL correlated with AR volume (p<0.001), but not with LV volume (p=0.6).

**Conclusion:** Diastolic shear-stress on the mitral valve is associated with remodelling changes in valve geometry. Diastolic jet impact and not LV dilatation seems to be related to anterior mitral leaflet enlargement and posterior displacement of the coaptation point.

**P754 Evaluation the alteration of mitral valve structures in functional mitral regurgitation using real-time three-dimensional transthoracic echocardiography**

W. Bai, H. Tang, L. Rao. West China Hospital, Sichuan University, Department of Cardiology, Chengdu, China, People’s Republic of China

**Objective:** To investigate the geometric alterations of the mitral leaflets (MV) and annulus (MA) using real-time three-dimensional transthoracic echocardiography (RT-3DTEE), and to clarify the effect of MV structures’ changes in FMR occurrence.

**Methods:** Twenty-five patients with paroxysmal supraventricular tachycardia, 25 isolated paroxysmal atrial fibrillation patients and 20 old myocardial infarction patients without functional mitral regurgitation (FMR) were enrolled as controls. Twenty ischemic cardiomyopathy cases with FMR were ICM group. Standard RT-3DTEE evaluations were performed. The quantification parameters include: anterior-posterior diameter (APD), anterolateral-posteromedial (ALPMD), three dimensional annulus circumference (3DAC), two dimensional annulus area (2DAA), three dimensional annulus area (3DAA), sphericity Index (SI), non-planar angle (NPA), two dimensional annulus area fraction (2DAAF), tenting height (TH); commissural diameter (CD), anterior leaflet area (ALA), posterior leaflet area (PLA), tenting volume index (TVI), tenting volume fraction (TVF), coaptation index (CI) (Fig. 1).

**Results:** There were significant difference of APD, ALPMD, NPA, AC, 2DAA, 3DAA, TV, TH, CD, ALA, PLA, TVI, CI, AAF in different groups ( F<3.84, P<0.05). Correlation analysis revealed significant negative correlations between left ventricular dimension, left atrial dimension, left ventricular ejection fraction and MA, MV parameters except for SI, TVF and NPA (p<0.05).

**Conclusions:** The geometric and function alteration of MA and MV not only the final way of FMR, but also make the FMR worsen. The application of a series of new quantitative parameters in this study, including NPA, TVI, CI, may helpful to make up the appropriate FMR therapeutic plans and assess the prognosis.

**P755 Acute hemodynamic effects following percutaneous mitral valve therapy assessed by pressure-volume analysis**


**Background:** Percutaneous mitral valve repair (PMVR) is anevolving therapeu-
tic alternative for patients with mitral regurgitation (MR) with favorable long-term efficacy in selected patients. The acute hemodynamic effects of this procedure are still incompletely understood. We hereinassessed changes of left ventricular hemodynamics during PMVR by pressure-volume relation analysis using a left ventricular conductance catheter.

Methods and results: Pressure-volume loops were recorded in 13 patients (age: 73±7y, 5 females) undergoing PMVR with the conductance catheter throughout the entire procedure. Patients with a baseline EF<30% (n=8, 3 functional MR, 5 degenerative MR) revealed acute ventricular unloading with a reduction of resting stroke volume (EDV; pre: 155±67, post: 143±62ml, p=0.14), pressure (EDP; pre: 11±2, post: 16±3 mmHg, p=0.03) and wall stress (WSED, pre: 36±9, post: 29±9 mmHg, p=0.03). Conversely, with an EF>30% (n=6, 5 functional MR, 1 showed significant increases in EDV (pre: 320±69, post: 348±67 ml, p=0.04), EDP (pre: 12±3, post: 16±3, p=0.02) and WSED (pre: 45±11, post: 67±8 mmHg, p=0.01). Simultaneous transesophagealechocardiographical assessment revealed normal forward stroke volume inpatients with EF<30%, which did not change after clip implantation. Incontrast, in patients with EF≥30% FSVs were reduced at baseline but showed asignificant increase following clip implantation.

Discussion: Our data suggest that changes in leftventricular hemodynamics following PMVR critically depend on on baseline leftventricular systolic function and may help to predict outcome in thesepatients.

**Three-dimensional echocardiography-guided assessment of vena contracta at rest predicts exercise-induced severe functional mitral regurgitation**

J. Vecera, J. Bartunek, M. Vanderheyden, P. Mertens, O. Bodea, M. Penicka. OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

**Purpose:** To assess the value of the three-dimensional (3D) echocardiography-guided assessment of vena contracta (3DVC) at rest to predict exercise-induced changes in functional mitral regurgitation (FMR) in systolic heart failure patients.

**Methods:** The study population consisted of 42 patients (age 69±11y, 84% males, ejection fraction 30±9%) with chronic systolic heart failure and mild-to-moderate FMR (≤2/4) at rest. All patients underwent Doppler 3D echocardiography at rest and during semi-supine bicycle exercise. Vena contracta area and its longest diameter (3DVC) were assessed at mid-systole.

**Results:** A total of 18 (43%) individuals showed a significant (≥20mm²) exercise-induced increase of FMR (effective regurgitant orifice rest vs. exercise; 17±5mm² vs. 42±10mm², p<0.001) (FMR increase) while 24 (57%) individuals did not (12±4mm² vs. 16±7mm², NS) (FMR stable). At rest, the FMR increase versus stable group had significantly larger 3DVC (7.6±1.8mm vs. 3.9±2.2mm, p<0.0001), higher prevalence of multiple jets (44% vs. 8%, p<0.01) and larger electromechanical dysynchrony between the papillary muscles (87±46 ms vs.45±35 ms, p<0.002). In contrast, degree of left ventricular remodeling and mitral valve deformation were similar. The resting 3DVC ≥ 6.5 mm had the highest accuracy (AUC=0.84) to identify patients with significant exercise-induced FMR with a sensitivity of 88% and a specificity of 83% (Figure). The presence of multiple jets showed fair positive predictive value of 80% to predict exercise-induced increase in FMR.

**Conclusions:** The behavior of FMR during exercise can be accurately predicted from the assessment of the resting 3DVC.

**Ischemic mitral regurgitation - myocardial scarring and left ventricular dilatation independently cause geometric change of mitral valve: Configuration analysis of functional mitral regurgitation by three-dimensional echocardiography**


**Backgrounds:** Functional mitral regurgitation (FMR) is related to several overlapping factors. In some studies, tethered mitral valve because of left ventricular (LV) dilatation and dysfunction was recognized as a primary cause of FMR. However, FMR exists also in patients with normal LV size or ejection fraction (EF). Thus, we evaluated mitral valve configurations in patients with LV regardless of LV size and EF by three-dimensional trans-esophageal echocardiography (3DTEE).

**Methods:** Forty-three patients with moderate or severe non-generative FMR and 24 normal subjects underwent trans-oesophageal echocardiography for LV regardless of left atrial (LA) volume measurements and 3DTEE for the assessments of mitral valve configuration and FMR severity. We three-dimensionally measured mitral annulus area (MAA) and tenting volume (MTV) by MVQ (Philips) software. Moreover, we directly measured vena-contracta area (VCA) as an index of FMR severity by three-dimensional color Doppler. In FMR, EF was under 50% in 22 patients and left ventricular end-diastolic diameter was less than 55mm in 12 patients.

**Results:** VCA correlated with MAA (r=0.67, p<0.001) and MTV (r=0.37, p=0.002), which were independent predictor of severe FMR. MTV positively correlated with left ventricular end-systolic volume (LVESV) (r=0.726, p<0.001) and not with left atrial volume (LAV) (r=0.003, NS). On the other hand, MAA positively correlated with LAV (r=0.695, p=0.001) and not with LVESV (r=0.236, NS) (Figure). LV dilatation was independent predictor of MTV increase and LA dilatation was that of MAA dilatation by multivariable analysis.

**Conclusions:** LV dilatation caused mitral leaflet tenting, while LA dilatation did mitral annulus dilatation. LV and LA dilatation independently changed mitral valve geometry and worsened FMR.
Comparison of mitral annular calcification and coronary artery disease

1Gaziantep Education Hospital, Gaziantep, Turkey; 2Gaziantep University, Department of Radiology, Gaziantep, Turkey; 3Gaziantep University Department of Emergency Medicine, Gaziantep, Turkey; 4Gaziantep University, Faculty of Medical Sciences, Department of Physiology, Gaziantep, Turkey.

Purpose: We tried to evaluate: 1) the value of the annulus calcification measured by using echocardiography in predicting the presence and extent of coronary artery disease (CAD) and relation with other measures of subclinical atherosclerosis, namely carotid brachial artery intima-media thickness (IMT) in patients with suspected CAD; 2) the relationship between MAC and traditional CAD risk factors including high sensitive CRP, lipoprotein (a), homocyctein.

Methods: We enrolled 146 consecutive patients with proven or suspected CAD who were referred for coronary angiography at our institution have been selected. The study is comprised of 63% men and 37% women aged 26-80 years (mean age 52.74±9.93). All patients underwent echocardiographic examination and Carotid and brachial arteries Duplex sonography before underwent coronary angiography. MAC was considered when the thickness of the intense echo-producing structure was ≥ 5 mm as measured with echocardiography. We used the Gensini score for this study to test the burden of atherosclerosis.

Results: Patients with MAC were more likely to be older than those without MAC (p=0.020). From all coronary traditional risk factors only diabetes mellitus was associated with MAC (p=0.017). The common carotid artery (CC-IMT) and brachial artery-IMT values were significantly higher in the MAC subjects than without MAC (p=0.006, p=0.003, respectively). MAC was found to have higher Gensini score (46.22 vs 23.03, p=0.002), Plasma level of h-CRP, lipoprotein (a) and homocyctein values were not related with MAC. Presence of MAC was associated with multivessel CAD (p=0.002). Multivariate analysis identified women gender (p=0.035, p=0.23), BA-IMT (p=0.004, p=0.29), multivessel CAD (p=0.002, p=0.73) and component predictors of MAC.

Conclusion: The presence of MAC by echocardiography is highly associated with pericardiac atherosclerosis and presence and extent of coronary atherosclerosis. Therefore identification should be accepted a manifestation of later stage of atherosclerosis and thus, aggressive preventive approach, independent from the presence of risk factors, may be warranted to retard the atherosclerosis process.

Novel equations to calculate mitral valve area by mitral leaflet separation index

E. Mahmoud Abdel Fathah1, S. Mohamed2, H. Younan1, Z. Ashra2, K. Al Khashab3, S. Ghareeb3. 
1Cardiology department-fayoum university, Fayoum, Egypt; 2Cardiology surgery department- Fayoum University, Fayoum, Egypt; 3cardiology department-Cairo university. Cairo, Egypt.

Aim of this study is evaluation of the MLS index as a novel method for assessment of mitral valve area.

Methods: 2D Echocardiography was done in 50 patients with MS in this study: 
- Group1 consisted of 25 patients in sinus rhythm with mean age was 28.6±5.5 years. Four of the patients were male (16%), and 21 were female (84%). Six patients had mild, 13 had moderate and 6 had severe Mitral stenosis. Group II consisted of 25 patients suffering from atrial fibrillation. The mean age was 37.2±9.8 years. Twelve of the patients were male (48%), 13 were female (52%). Three patients had mild, 14 had moderate and 8 had severe Mitral stenosis.

Patients with significant other valvular lesions or heavily calcified Mitral valve were excluded from the study. The MVA was assessed half time. MLS index was measured in end diastole, as the maximal separation at the tips of mitral leaflets in the parasternal long axis (PLX) and apical 4 chamber (A4C) views.

Results:ROC curves for group I demonstrated that: In the PLX view, severe Mitral stenosis was predicted by a MVA of 8.05 mm or less and there was a 82% sensitivity and 100% specificity for planimetry (MVA = -0.167 (0.162×MVA+0.835, p<0.001) and MLS of 8.25 mm or less with a 85% sensitivity and 100% specificity for PHT (MVA ≤ -0.122 + (0.155×MVA) ≤ -0.753, p<0.001). In the apical 4chamber view, severe Mitral stenosis was predicted by a MVA of 7.9 mm or less with a 82% sensitivity and 86% specificity for planimetry (MVA = -0.268 + (0.176×MVA) ≤ -0.837, p<0.001), and 8.25 mm with a 81% sensitivity and 90% specificity for PHT (MVA ≤ -0.103 + (0.177×MVA) ≤ -0.799, p<0.001).

ROC curves for Group II demonstrated that: In the PLX view, severe Mitral stenosis was predicted by a MVA of 7.25 mm or less with a 89% sensitivity and 90% specificity for planimetry (MVA ≤ -0.133 + (0.139×MVA) ≤ -0.611, p<0.001) and MLS of 7.75 mm or less with a 84% sensitivity and 100% specificity for PHT (MVA ≤ -0.203 + (0.168×MVA) ≤ -0.710, p<0.001). In the apical 4chamber view, severe Mitral stenosis was predicted by a MVA of 7.65 mm or less with a 89% sensitivity and 100% specificity for planimetry (MVA ≤ -0.122 + (0.152×MVA) ≤ -0.759, p≤0.001), and 7.9 mm with a 84% sensitivity and 100% specificity for PHT (MVA ≤ -0.261 + (0.174×MVA) ≤ -0.840, p≤0.001).

Conclusion: The MLS index is a new easy and practical method for assessment of mitral stenosis severity and mitral valve area.
Mitral valve disease

A cut-off value of left atrial remodeling parameters may predict the recurrence of atrial fibrillation after radiofrequency ablation concomitant to mitral valve surgery

A. Olasinska-Wisniewska, T. Mularek-Kubzdela, A. Marszalek, W. Sarnowski, M. Jemielity, W. Seniuk, B. Perek, S. Grajek, Poznan University of Medical Sciences, Poznan, Poland

Though the benefit from the concomitant radiofrequency ablation and mitral valve surgery is high, the atrial fibrillation recurrence is possible in follow-up. The purpose of this study was to investigate the left atrial remodeling in patients undergoing ablation and mitral valve replacement and to determine the appropriate cut-off value of remodeling parameters to predict atrial fibrillation recurrence.

Methods: 66 consecutive patients with of atrial fibrillation (AF) and mitral valve disease underwent radiofrequency ablation and mitral valve surgery. Heart rhythm was evaluated before and 12 months post surgery. Biopsies of the posterior wall of the left atrium were obtained during the operation. The extent of fibrosis, myocyte diameter, intensity of inflammatory infiltrates, degree of myocytolysis and capillary density were determined. Transthoracic echocardiography was performed, and valvular disease and left atrial dimension were evaluated. A potential relationship between left atrial remodeling and these parameters was investigated, and a receiver-operating characteristic (ROC) curve was designed thereafter to identify a cut-off value of important variables that best predicted the recurrence of atrial fibrillation.

Results: Ten patients died and 1 patient was lost to follow-up. Heart rhythm at 12 months was used to divide the remaining 55 patients into two groups: group I, 34 with sinus rhythm; group II, 21 with AF. There was a significant difference in ROC curve in myocardium (17.9±3.5 μm vs 20.3±4.6 μm, p<0.04), percentage of fibrosis (38.7±11.2% vs 47.6±12.3%, p<0.009), inflammatory infiltrates (p<0.02) and preoperative atrial diameter (5.03±0.7 cm vs 5.5±0.8 cm, p<0.04) between groups I and II. No differences were found in capillary density (797.9±500.6 mm² vs 946.0±372.7 mm², p=0.3) and myocytolysis (p=0.4). According to the ROC curve cut-off values at 38.1% for fibrosis (p<0.003) and at 17.9 μm for myocyte diameter (p<0.01) predicted procedure failure (area under the curve 0.7). Cut-off value at 54.9 mm for left atrial size predicted procedure failure (area under the ROC curve 0.7, p=0.036).

Conclusions: These results suggest that a atrial fibrillation recurrence is strongly associated with a left atrial remodelling in patients with mitral valve disease and atrial fibrillation undergoing RF ablation concomitant to valvular surgery. The values of 38.1% for fibrosis, 17.9 μm for myocyte diameter and 5.49 cm for left atrial size allow us to predict the risk of atrial fibrillation recurrence in these patients.

Predicting post-operative outcomes after mitral valve surgery: additive value of three-dimensional echocardiography

T. Yingchoncharoen, T.H. Marwick, Cleveland Clinic, Cleveland, United States of America

Purpose: Mitral regurgitation (MR) causes eccentric LV hypertrophy, therefore assessment of LV size using M-mode or 2D echo may be inaccurate. We sought the value of three-dimensional echocardiography (3DE) in predicting post-operative outcomes after mitral valve surgery.

Methods: We prospectively followed 84 cases with severe organic MR (73% men, age 61±11 years, 96% mitral valve prolapse, 4% ischemic MR) who underwent mitral valve surgery from Jan 2010 to Dec 2011. In addition to standard 2D echocardiography, three-dimensional echocardiography (3DE) was performed for accurate quantification of LV size. Patients were followed for post-operative development of atrial fibrillation (AF) and LV dysfunction (LVEF<50%) as an outcome.

A multivariable regression analysis was performed to identify associations with events. Results: Over 4.0±0.9 months, 23 patients had post-operative AF (22.5%) and 23 patients had post-operative LVEF dysfunction (24.7%). LVEF decreased from 57.4±6.1 to 50.7±7.7 by 12 months post-operatively (p<0.001). Post-operative AF and LV dysfunction were predicted (R2=0.76) by mean 3D LV end-systolic volume index (LVESVI) (HR 1.19 [95%CI 1.07-1.20], p<0.001), independent of age, gender, pre-operative AF, NYHA functional class, and LVEF. LVESVI > 100 ml/m² was the best cut-off value to predict post-operative events (sensitivity 90.9%, specificity 85.2%). After adding the LVESVI to a model containing clinical and echocardiographic parameters, net reclassification improvement was 0.48 (95% CI 0.38 to 0.52, p<0.001). The additive value of LVESVI was shown in Figure.

Conclusion: LVESVI from 3DE is not only an independent predictor of post-operative outcomes in patients with severe mitral regurgitation but also incremental to other clinical and echocardiographic variables.

The predictive value of echocardiographic parameters in efficacy of percutaneous mitral annuloplasty for the treatment of functional mitral regurgitation

O. Jerzykowska, P. Kalmucki, L. Kramer, M. Wołoszyńska, A. Baszkó, T. Simiński, University of Medical Sciences, HCP Medical Center, Poznan, Poland

Background: The clinical importance of functional mitral regurgitation (FMR) is to search for novel therapeutic options with improved efficacy of percutaneous mitral annuloplasty. We have previously reported that percutaneous implantation of Carillon device into the coronary venous system results in the reduction in FMR as well as to functional improvement, but it is not clear which patients would benefit the most.

Aim: We thought to investigate which echo parameters may help in prediction of the efficacy of percutaneous mitral annuloplasty in patients with FMR.

Methods: A post-hoc analysis of baseline and 1 month follow-up echo recordings in 22 consecutive pts with FMR, who underwent successful percutaneous mitral annuloplasty with the CARILLON device was performed. The baseline inclusion criteria for the procedure were: dilated ischemic or non-ischemic cardiomyopathy, moderate to severe FMR, no option for revascularization, LVEF~40%, NYHA Class II-IV, and 6 minute walk distance (6MWD) 150-450 meters.

Results: The acute significant reduction of FMR measured by vena contracta (VC), EROA and regurgitant volume (RV) maintained throughout 1 month follow-up, but the improvement did not correlate with baseline anulus diameter (AD), LV diameters or with the left atrial diameter (LAD) - table. However, the baseline mitral tenting area correlated negatively with the relative improvement (% difference) of EROA (r=0.5898) and RV (r=0.4363), but not with VC (r=0.1341). In addition, the baseline mitral tenting area significantly correlated with the 1 month change in ejection fraction (r=0.5946) and stroke volume (r=0.6513).

The correlation between baseline echo anatomic values and relative change (% difference) in FMR values:

<table>
<thead>
<tr>
<th>AD</th>
<th>LVEV</th>
<th>LVESS</th>
<th>LAD</th>
<th>VC</th>
<th>EROA</th>
<th>RV</th>
<th>EROA</th>
<th>RV</th>
<th>LVEV</th>
<th>LVESS</th>
<th>LAD</th>
<th>VC</th>
<th>EROA</th>
<th>RV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.3485</td>
<td>0.1521</td>
<td>0.2249</td>
<td>0.1669</td>
<td>0.0007</td>
<td>0.2656</td>
<td>-0.0603</td>
<td>0.0447</td>
<td>0.0964</td>
<td>-0.3696</td>
<td>-0.2092</td>
<td>-0.0253</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: The degree of hemodynamic improvement after percutaneous FMR treatment with the CARILLON® Mitral Contour System™ is dependent on baseline increase of heart diameters. Mitral tenting area seems to be an important echo parameter in the prediction of benefit from percutaneous mitral annuloplasty.
between the concentration of TGF-β1/2 and the progression of valve myxomatous and heart chambers’ remodeling after reconstructive surgery in MVP.

**Methods:** We examined 35 patients undergoing reconstructive surgery due to MVP complicated by severe mitral insufficiency (mean age 62.5±7.9 years, 46% men). Additional group was formed from the 11 subjects with MVP (32.5±11.3 years, 64% men), have been the first generation offsprings of the ten operated patients. All echocardiographic measurements were performed using an ultrasound system Vivid 7 Dimension (GE Healthcare). The levels of TGF-1 and TGF-β2 in serum were determined by enzyme-linked immunosorbent assay using a test system Human Platinum ELISA (Bender MedSystems).

**Results:** High level of TGF-1 (>14.75 ng/ml) and/or TGF-β2 (>2.0 ng/ml) was detected in majority (65%) of cases and correlated with the thickness of posterior leaflet (r=0.67, p=0.016), residual valve prolapase (r=0.68, p=0.007) and residual MR (r=0.56, p=0.01). In patients with high TGF-1/2 level a significant decrease in LV longitudinal systolic (-13.5±2.2% vs. -16.6±3.3%, p=0.008) and diastolic (11.4±0.20±1 vs 13±0.18±1, p=0.04) strain and SR (0.89±0.15±1 vs. -1.14±0.16±1, p=0.002).

In the nonoperated offsprings’ group high level of TGF-1/2 observed in 73% (8 subjects). The concentration of TGF-1 was strongly correlated with the thickness of the posterior valve (r=0.77, p=0.01), with the thickening of the valves (r=0.68; p=0.021) and severity of mitral retraction (r=0.69; p=0.018).

**Conclusions:** TGF-β1 has a significant impact on the progression of valve myxomatous after reconstructive surgery. The high activity of TGF-β1 signaling pathway also results in reduction in LV function, probably due to TGF-β1 profibrotic activity.
Percutaneous double-valve treatment of patients with coexisting aortic stenosis and mitral regurgitation

V. Rudolph1, J. Schirmer1, O.W. Franzen2, M. Schlueter2, M. Seifert1, H. Treede1, H. Reichenspurner1, S. Blankenberg3, M. Gohrbandt1, C. Baumbach1
1University Heart Center Hamburg, Hamburg, Germany; 2Rigshospitalet - Copenhagen University Hospital, Heart Centre, Copenhagen, Denmark

Background: Percutaneous techniques to treat severe aortic stenosis (AS) or significant mitral regurgitation (MR) in patients deemed at high surgical risk have shown to be safe and efficacious in either clinical entity. For AS, transcatheter aortic valve replacement (TAVR) using the Sapien/Sapien XT prosthesis (Edwards Lifesciences) via transapical (TF) or transaortic (TA) access or the CoreValve (Medtronic) via TF access has become a viable therapeutic option, whereas in MR, considerable clinical experience has gained with transvenous/transapical implantation of the MitraClip (MC) device (Abbott Vascular).

To date, little information is available on transcatheter treatment for both AS and MR in the same patient.

Methods and Results: By March 2011, 285 TAVR and 233 MC procedures had been performed at our center. Eleven patients (78 ± 6 years, 9 men [82%]) underwent both TAVR and MC implantation. In the first 8 patients treated, TAVR (5 TA, 3 TF) preceded MC by a median of 684 (range, 4 to 348) days, whereas in the last 3 patients (3 TA, 2 TF), TAVR followed MC. Subsequently, MC was performed in a single session. All TAVR procedures (7 Sapien [n=4]/Sapien XT [n=3]) and 4 CoreValve procedures were successfully completed, resulting in a large increase in ejection fraction (9.1 ± 3.8 vs. 17.5 ± 2.3) in the first 3 patients. Paravalvular AR was present at discharge in 8 patients. At a median of 203.5 days, 2 patients needed conventional heart surgery due to MR progress. 6 patients needed conventional heart surgery despite MC. In 5 patients the implantation procedures were successful. In 1 patient severe MR remained at discharge and no TC was placed in 2 patients. Permanent pacemaker implantation was required in 5 patients (4 Sapien/Sapien XT, 1 CoreValve); 1 patient suffered a stroke 19 days after double-valvuloplasty in a single session. Post TAVR, no patient had transvalvular aortic regurgitation (AR); minor (grade 1) paravalvular AR was present at discharge in 8 patients. At a median of 208 days, 2 patients were in NYHA functional class II, with only 1 patient improved from before TAVR, and 6 patients were in class III (improvement in 1).

Conclusions: Percutaneous double-valve treatment of patients with coexisting aortic stenosis and MR is technically feasible, even in a single session. Given the low prevalence of combined AS and MR, a postulated learning curve (cases 1-49) preceded MC by a median of 84 (range, 4 to 348) days, whereas in the last 3 patients, the interval the last 3 patients was 0.12 to 1.82 years. It is therefore evident that transcatheter double-valve treatment provides significant clinical benefits in selected patients with severe heart failure and significantly reduced LVEF.

Mid-term outcome after percutaneous mitral valve repair in patients with severe mitral regurgitation and significantly reduced left ventricular function

German Heart Center, Munich, Germany

Background: The percutaneous MitraClip edge-to-edge treatment has been established as a promising alternative for patients with symptomatic mitral regurgitation (MR). The clinical outcome of patients with severe heart failure and significantly reduced left ventricular ejection fraction (LVEF < 30%) undergoing such treatment is not well known. The current study compares mid-term outcome of patients with LVEFs ≤ 30% after percutaneous mitral valve repair.

Method: 98 consecutive patients (62 male and 36 female patients; age 73 ± 9.8 years) with symptomatic mitral regurgitation (MR) were enrolled. Transthoracic echocardiography was used to grade MR, to non-invasively evaluate pulmonary hypertension (PAPsys) as well as left ventricular (LV) dimensions; whereas clinical impact was assessed by NYHA classification and 6 minute walking test (6mWT).

Results: 21 pts displayed an EF ≤ 30% - group 1 (EuroScore: 30.2 ± 25.2%; 16 pts with functional MR), whereas 77 pts had an EF > 30% before clipping – group 2 (EuroScore: 15.2 ± 16.3%; 22 pts with functional MR). At follow-up (451 ± 203.5 days), survival free of repeat mitral intervention/surgery did not differ between groups (76% vs. 84%; p=NS). NYHA class improved in group 1 from 3.0 ± 0.6 to 1.9 ± 1.2 (p < 0.01) and in group 2 from 3.0 ± 0.5 to 1.3 ± 1.1 (p < 0.01). The 6mWT showed a trend to longer walking distances (248 ± 115 to 347 ± 123m; vs. 304 ± 118 to 389 ± 125m; p=NS). MR grade improved from 3.2 ± 0.5 to 1.8 ± 0.8 (p < 0.01) and from 3.4 ± 0.5 to 1.8 ± 1.0 (p < 0.01), respectively. PAPsys decreased in group 1 to 38 ± 7 mmHg in patients ≤ 58.7 ± 15.2 years, and in group 2 from 40.8 ± 12.9 to 37.2 ± 10.8 mmHg (p < 0.01) in group 2. The LV dimensions and volumes demonstrated a trend to smaller dimensions at follow-up.

Conclusion: At mid-term follow-up, the percutaneous MitraClip edge-to-edge treatment provided significant clinical benefits in selected patients with severe heart failure and significantly reduced LVEF. The obtained results are comparable to results achieved in patients with preserved LVEF. Therefore, percutaneous mitral valve repair represents a treatment option in patients with significant MR and low LVEF.
SIRT3 deficiency impairs cardiac function but not contractile recovery following ischemia-reperfusion

C. Koentges, K. Pfeil, C. Bode, H. Bugger. Albert-Ludwig University of Freiburg, Department of Cardiology and Angiology, Freiburg, Germany

Sirtuin 3 (SIRT3) is a mitochondrial NAD+–dependent deacetylase which is highly expressed in the heart, and which increases mitochondrial ATP production in various tissues. In rodent models of heart failure, myocardial mitochondrial dysfunction contributes to contractile deficits and is associated with reduced SIRT3 expression. Thus, we hypothesized that reduced SIRT3 expression may contribute to contractile dysfunction in failing hearts. In 8 week-old mice lacking SIRT3 (SIRT3 KO), heart weight-to-tibia length ratios were significantly increased (+18%; p<0.05) compared to wildtype (WT) mice, indicating cardiac hypertrophy. In isolated working hearts, left ventricular developed pressure (LVDevP; 14.7±0.7 vs. 16.9±0.6 mmHg; p<0.05) and cardiac efficiency (CE; cardiac work/oxygen consumption; 4.4±0.5 vs. 6.0±0.4%; p<0.05) were decreased in SIRT3 KO. These alterations were associated with a 48% increase in coronary flow (p<0.05). Since SIRT3 deficiency increases mitochondrial ROS accumulation and opening of the mitochondrial permeability transition pore, we hypothesized that lack of SIRT3 may also impair recovery following ischemia-reperfusion and subjected hearts to 17.5 min of global no-flow ischemia during working heart perfusion. LVDevP was decreased before and after ischemia in SIRT3 KO compared to WT; however, percental recovery of LVDevP following ischemia-reperfusion was similar in WT and SIRT3 KO (LVDevP 88±16 vs. 87.3±2%; n.s.). Similarly, CE and coronary flow showed equal rates of recovery. Thus, lack of SIRT3 causes cardiac hypertrophy and may impair contractile function in the heart, suggesting that reduced expression of SIRT3 in failing hearts may contribute to cardiac dysfunction. In contrast, SIRT3 may be expendable for contractile recovery following ischemia-reperfusion.

Concomitant phosphodiesterase 5-inhibition enhances myocardial protection of inhaled nitric oxide after ischemia-reperfusion injury

A. Lux1, P. Pokrezs2, M. Swirnen1, E. Catuwe1, H. Gillijns2, Z. Szendi1, B. Morley1, S. Janssens2. Semmelweis University Heart Center, Budapest, Hungary; 1Catholic University of Leuven, Leuven, Belgium

Purpose: Enhanced nitric oxide (NO) cGMP signaling attenuates LV functional deterioration after myocardial infarction (MI). We studied phosphodiesterase-5 (PDE5) expression after mPTP (mitochondrial permeability transition pore) injury (I/R) and tested the effect of concomitant inhaled NO (INO); tadafali (TA), a selective PDE5 inhibitor, or the combination (INO+TA) on MI size, LV remodeling and function.

Methods: In C57Bl/6J mice, ischemia was induced by 60 min proximal LAD ligation followed by reperfusion. Animals were randomized into non-treated (CON), INO, TA and INO+TA groups (n=20 per group), circulating and cardiac cGMP levels were determined at baseline and PDE5 expression levels (real time qPCR) determined at baseline, 3d and 4d after I/R. Plasma troponin I (TRI) was measured using ELISA at 0, 4, 24, and 72 hours after I/R. TAD (4 mg/kg) was administered orally 60 min before ischemia and NO inhalation (80 ppm) started 30 min before and continued 20 min during reperfusion. After 3d, MI size was measured using planimetry on TTC-stained LV sections and infiltrating myeloperoxidase–positive (MPO) cells were counted in perfused territories. After 4w, LV function and remodeling were assessed and analyzed using TTE (30 MHz VisualAonics) and pressure-volume (PV) catheterization.

Results: In intact mice, myocardial PDE5 expression was similar in all groups while circulating and cardiac cGMP levels increased significantly in INO-TAD (n=7; each, P<0.01 vs CON, P<0.05 vs NO or TA), with either therapy alone having a modest effect. In contrast, myocardial PDE5 expression at 3d and 4w after I/R was 2.5 and 4.3 fold increased in CON. After 4w, peak TRI levels were significantly reduced by 30% in INO and TAD (P<0.05); and by 50% in INO+TAD (n=10 for each group, P<0.05 vs CON). MI size, relative to area-at-risk, was significantly smaller at 3d in INO, TAD, and INO+TAD (35±3, 24±3, 4±4 vs 44±2% in CON; resp. P<0.05). All treatments tend to reduce MPO-cell infiltration to similar extent compared to CON (P<0.05 for each). After 4w, TTE revealed better-preserved fractional shortening and less LV dilatation in all treated groups with greatest benefit for INO+TAD (41±1 vs 33±2% and 3.0±0.2 mm in CON, resp. P<0.001 for both). Similarly, INO+TAD showed a better contractile function recovery during PV measurements than either treatment alone.

Conclusion: Combined treatment with INO and selective PDE5 inhibitor during acute myocardial ischemia is safe, synergistically protects the myocardium from early ischemic injury, and promotes LV functional recovery over time. Combination therapy may represent a promising strategy to reduce ischemic damage and enhance myocardial repair.

Protection of cardiomyocytes against reperfusion-injury through inhibition of glycogen synthase kinase 3-beta is mediated by delayed pHi-recovery during reperfusion via Inhibition of Na+/H+ exchanger

W. Tass1, M. Aslan2, H.M. Peyer1, Y. Abdallah1, J. Waltenberger1. 1University Hospital Muenster, Department of Cardiology and Angiology, Muenster, Germany; 2Institute of Physiology, Justus Liebig University, Giessen, Germany; 3University Hospital Giessen and Marburg, Medical Clinic I, Cardiology and Angiology, Giessen, Germany

Previously we have shown that inhibition of glycogen synthase kinase-3 (GSK-3β) at the beginning of reperfusion protects cardiomyocytes against reperfusion injury. The aim of the present study was to investigate whether inhibition of GSK-3β modifies the intracellular pH during reperfusion, and to analyze whether the activity of the Na+/H+ exchanger can be affected by GSK-3β-inhibition. First, isolated adult rat cardiomyocytes were superfused anoxically (60 min 37°C, no glucose; pH 6.4) and then reperfused with a normoxic buffer (25 min 21% O2, 2.5 mM glucose; pH 7.4). In the second set, the activity of the Na+/H+ exchanger was measured by the ammonium-pulse method. BCGF5-inh. cargiomyocytes were perfused normoxically (10 min) and then exposed to 10 mM NH4Cl (NH4Cl-pulse) for 30 min, before they were perfused for 45 min with normoxic buffer lacking NH4Cl (NH4Cl washout). Cellular pH was measured by the fluorescence indicator BCECF. Two specific inhibitors of GSK-3β, SB216763 [9 μM] and GSK-3β-inhibitor XI [300 nM] were applied during reperfusion in the first set and during the whole second set.

Injury in ischemia, cardiomyocytes developed an acidosis of pH 6.40±0.07 pH (under normoxic conditions: 7.20±0.08). During reperfusion, cellular pH recovered to a maximum of 87.62±1.08% of the normoxic value within 12 min of reperfusion in control. In the presence of SB216763, the cellular pH recovered slower and achieved a higher maximum of 99.45±2.25% of the normoxic value after 25 min of reperfusion (n=12; p<0.05). In the second set, NH4Cl washout led in the first contribute to an acidosis under all three conditions (control: 73.11±1.01% of the normoxic value, SB216763: 73.75±2.47%, GSK-3β-inhibitor XI: 73.93±2.39%). After 10 minutes of NH4Cl washout, pH in control cardiomyocytes recovered to a maximum of 94.07±1.79% (vs. SB216763: 76.31±2.41% and GSK-3β-inhibitor XI: 83.52±2.51%, n=6; p<0.05). In presence of the GSK-3β-inhibitor, 30 minutes of NH4Cl washout were needed to achieve the same maximum (control: 95.47±0.60%, SB216763: 97.24±2.15%, GSK-3β-inhibitor XI: 94.36±1.81%). In conclusion, the inhibition of GSK-3β delayed the cellular alkalisation at the be-
gaining of reperfusion and achieved a better recovery of pH during further reper-
fusion. In the presence of both GSK-3β-inhibitors during the application of NH4Cl
and its washout, the pH recovery was 3-fold delayed compared to controls indi-
cating an inhibition of the Na+/H+ exchanger. These data suggest a major role of Na+/H+
exchanger in the delayed pH-recovery in cardiomyocytes through GSK-
3β-inhibition.

RNAse1 protects against cardiac ischemia/reperfusion injury

H.A. Cabrera Fuentes1, J.A. Sanchez2, S. Fischer1, O.N. linskaya3, K.D. Schütte4, K.T. Preissner1 on behalf of IRTG - 1566 PROMISE.
1Justus-Liebig University Giessen, Institute for Biochemistry, Giessen, Germany;
2Graduate School of Medicine, Department of Cardiology, Nagoya, Japan
3Department of Microbiology, Kazan Federal University, Kazan, Russian Federation;
4Justus-Liebig University Giessen, Institute of Physiology, Giessen, Germany

Propose: Extracellular RNA (eRNA), exposed after tissue trauma, ischemia or damage, has been shown to exert prothrombotic and hyperpermeability-inducing functions, which are prevented by Ribonuclease1 (RNAse1) treatment in vivo. Following ischemia and myocardial necrosis during reperfusion, the presence of eRNA (as collector for cytokines and coagulation proteases) might potentiate the development of rigor contracture. Here, we report the contribution of RNAse1 on myocardial ischemia/reperfusion (I/R) injury was investigated in isolated rat hearts in a Langendorf system.

Methods: Dihydrogenase (LDH) release, a marker of cell damage/necrosis, as well as eRNA and RNAse activity were determined in the perfu-
satue before and during reperfusion (120 min) following 45 min of ischemia. To study the effects of RNAse1 on physiological parameters, left ventricular pressure was continuously recorded. RNAse1 was added in different concentra-
tions to the perfusion buffer, starting 3 min before the ischemic phase and main-
tained for the whole duration of the experiment.

Results: In the initial period of reperfusion (following the ischemia phase) there was a sharp increase in LDH release (32.83±0.5 U/g dry tissue), a prominent initial peak of eRNA (52.9±3.3 ng/ml) followed by a prolonged high level of eRNA between 15 and 60 min of reperfusion. Only very low endogenous RNAse1-activity was found in the perfusate. Treatment with RNAse1 in a concentration-
dependent manner induced a lower and delayed increase in diastolic pressure during reperfusion, indicating a less severe rigor contracture. In addition, functional recovery of heart tissue after 30 min reperfusion was preserved as indicated by elevated increase of LV developed pressure (I/R: 83±5% vs. baseline; RNAse1- treatment:83±13%, n=6, baseline:80±5%). Finally, RNAse1 reduced the severity of the maximal hypercontracture (I/R: 67±8 mmHg; RNAse1-treatment:19±3
mmHg; p<0.05) during the initial reperfusion phase and prevented the initial LDH release (16.31±2 U/g dry tissue, 30 min after reperfusion), indicating less myo-
cardial damage and protection against necrosis.

Conclusion: eRNA is released from the rat heart during I/R and may contribute to the outcome of injury. RNAse1 intervention appears be a new potential ther-
ipotential for the treatment of I/R injury, whereby the underlying mechanisms deserve further investigation.

Role of the parasympathetic nervous system in cardioprotection by remote hindlimb ischemic preconditioning

B. Buchholz1, M. Donat1, M. Rodriguez1, V. Perez1, J. Inserte2, D. Garcia-Dorado2, R.J. Gelpi1. 1University of Buenos Aires, Faculty of Medicine, Institute of Cardiovascular Physiopathology, Buenos Aires, Argentina; 2Institute of Research Hospitals Vall d’Hebron, Laboratory Cardiology Experimental, Barcelona, Spain

Purpose: The mechanisms underlying remote ischemic preconditioning (r-IPC) have not been fully elucidated and still unknown how the signal is transmitted from the remote organ to the heart. Our aim was to determine the participation of the vagus nerve and muscarinic receptors in the r-IPC mechanisms.

Methods: New Zealand rabbits (non-r-IPC, n=8) were anesthetized and the femoral artery dissected. After 30 min of follow up, the hearts were isolated, perfused according to the Langendorff technique and subjected to 30 min of global ischemia followed by 180 min of reperfusion. In a second group (r-IPC group, n=8), the animals were remotely preconditioned by three-cycles hindlimb ischemia (5 min) and reperfusion (5 min) by femoral artery occlusion. After that, they received the same protocol as in non-r-IPC group. In a third group (n=8), the same pro-
tocol as in r-IPC group was performed but the left and right vagus nerves were sectioned at the middle cervical level before r-IPC protocol. In a fourth group (n=6) the same protocol as in r-IPC group was performed but atropine sulfate was administered during the r-IPC protocol. In a fifth group we evaluated the ef-
effect of r-IPC following 20 min of ischemia (n=6). For this, the right vagus nerve was sectioned at the middle cervical level and its distal end electrically stimulated by 10 min followed by 5 min of recovery without stimulation. Then, they received the same protocol as in non-r-IPC group. In a sixth group (n=10), the same protocol as in r-IPC group was performed but the femoral and sciatic nerves were sectioned before the r-IPC protocol. Finally, (n=4) in a new set of experiments the same protocol as in r-IPC group was performed but the spinal cord between T9-T10 was sectioned before the r-IPC protocol.

Results: In the non-r-IPC, infarct size was 40.8±3.1%, r-IPC decreased infarct size to 16.4±3.5% (p<0.05). The section of vagus nerves or the atropine ad-
mistration during r-IPC protocol abolished the effect of r-IPC on infarct size (43.2±3.4% and 37.7±3.1%, respectively). Vagal stimulation mimicked the effect of r-IPC, decreasing infarct size to 15.2±4.7% (p<0.05). The femoral and sci-
itac nerves section only partially abolished the effect of r-IPC (p<NS). However, the spinal cord section (T9-T10) completely abrogated the effect of r-IPC on the infarct size (44.2±5.4% ; p<0.05).

Conclusion: Hindlimb ischemia in r-IPC activates a neural afferent pathway that reaches the heart via the vagus nerves (afferent pathway) and contributes to car-
dioprotection. The beneficial effect of r-IPC may be mediated by acetylcholine, since that it was blocked by atropine.

Mitochondrial remodelling and increased Mfn1 expression in a mouse model of coronary heart disease

S.M.J. Duggan, A.P. Halestrap, G.D. Angelini, M.-S. Suleiman. Bristol Heart Institute, Bristol Royal Infirmary, Bristol, United Kingdom

Background: Mitochondria are dynamic organelles whose function can be reg-
ulated by changes in their shape through the processes of fusion and fission. Dysfunction of these processes has been implicated in cardiac pathologies.

Aim: To investigate the mitochondrial morphodynamics and expression of fusion and fission proteins in a model of chronic coronary heart disease (CHD).

Methods: Male apolipoprotein E knockout mice (ApoeE/-) were fed either a high-
fat diet (21% lard & 0.15% cholesterol) or Chow diet for 24 weeks from weaning. High-fat diet ApoeE/- mice develop atherosclerosis including in their coronary ar-
teries (CHD). In contrast, ApoeE/- litter mates fed a chow diet exhibit no disease (control).

Excised hearts from each disease group were perfused on a Langendorff ap-
paratus with oxygenated Krebs solution. After 10 minutes of stabilization (pre-
ischemia, n=3/group) or after 10 minutes of stabilization followed by 30 minutes of global ischemia (n=3/group), hearts were perfused with a fixative solution. Quantification of interfibrillar mitochondrial morphology by electron microscopy was determined by number of mitochondria per unit area (density), individual mitochondria area and fibres per unit area and subjected to 30 min of global ischemia (<1.8±1.8-2.0 ± 2 um. For each heart >900-1000 interfibrillar mitochondria were assessed.

Expression of two fusion-related proteins mitofusin (Mfn) 1, Mfn2, and two fission-
related proteins, dynamin-related protein 1 (pDrp1) and Anti-Fis 1 was determined by western blotting in the pre-ischemia hearts (n=5/group) and the post-ischemia hearts (n=4/group) and the post-ischemia hearts (n=5/group) and the post-ischemia hearts (n=5/group) and the post-ischemia hearts (n=5/group)

Results: In the pre-ischemia hearts, mitochondria from CHD mice are signifi-
cantly smaller in area (control,1.37 μm²±0.23; CHD, 0.45 μm²±0.02; p<0.01, n=3), appearing more fragmented and shorter (p=0.0185, n=3).

Mfn1 protein levels were significantly decreased in pre-ischemia coronary heart disease tissue compared with non-diseased control mice (p<0.05, n=5). There was no difference in protein levels of Mfn2, pDrp1, or Fis1.

Following 30 minutes of global ischemia, CHD hearts show an increase in mitochondrial size (p<0.008) and a lead a decrease in their density (p<0.064) compared to pre-ischemic diseased hearts. There is no significant change in the mitochondrial length.

In contrast, there was a decrease in mean mitochondrial size (p=0.04), increase
A method of studying the course of myocardial ischemia and reperfusion in rats in vivo

D. O. H.-L., T. Dietrich, T. Kuehne, D. Messroghli, German Heart Center Berlin, Unit of Cardiac Molecular Imaging, Dept of Cardiac Heart Disease, Berlin, Germany. 2 German Heart Center Berlin, Department of Cardiology, Berlin, Germany

Background: The use of MRI for the study of ischemia and its consequences in small animals has been limited by the need for a thoracotomy and operative occlusion of the coronary arteries. The trauma of the surgery may be an important confounder in this open-chest model. The closure of the coronaries with a suture would not allow multiple occlusion-reperfusion cycles, and has limited the study of ischemia-reperfusion in small animals.

Objective: To develop a “closed chest” model of ischemia-reperfusion, which would allow ischemia and infarction to be studied in real-time while the rat is in vivo MRI environment.

Materials and Methods: We developed a method of implanting a balloon occluder to the left coronary artery. Male Sprague Dawley rats (n=12, weight 363±10 g) were anesthetized and then intubated. The heart was exposed by an incision in the fourth rib space. The occluder was then secured loosely to the myocardium with a 6-0 non-absorbable suture. Occlusion and reperfusion of the coronary artery was confirmed by visual inspection (blanching of the left ventricle) and by ECG (ST-segment elevation and normalization) on brief inflation and deflation of the balloon. The tubing of the occluder was then tunneled to the back of the rat and exposed in the infra scapular area. The animals were then allowed to recover from the operation for at least 5 days.

For coronary occlusion and MRI scanning, rats were again anaesthetized, the tubing was connected to a syringe, and animals were placed in the MRI scanner. Rats were placed in a supine position on the scanner bed, which was inclined to 45°. A transverse slice 1.5 cm thick, 1.5 cm long, and 1.5 cm wide was positioned in the middle of the heart. Rats were placed in a heated and ventilated chamber, and standard scans were obtained with an in-plane resolution of 0.5×0.5 mm and a slice thickness of 3.0 mm.

Results: There was a very low mortality rate for the implantation of the coronary occluder (8.3%). Inflation of the occluder on the MRI table resulted in myocardial ischemia in all animals as documented by ECG, and allowed the effects of ischemia and reperfusion on myocardial edema and function to be studied serially before, during, and after coronary occlusion. The changes in ECG were visible on the standard Philips console. There was no visible artifact from the occluder on any of the images.

Conclusions: The use of a pre-implanted balloon occluder allows for studying the effects of single or repeated myocardial ischemia and reperfusion with MRI in real-time in a closed-chest rat model. As the current treatment of myocardial infarction is urgent revascularization, this model is more clinically relevant than a simple infarction model. A more physiologically suitable model should aid the study of the complex mechanisms involved.

N-acetylcysteine effects on major adverse cardiac events and markers of cardiac remodeling in patients with acute myocardial infarction in one year follow up

A.H. Talazay, Y. Jenab, H. Khali, Tehran University of Medical Sciences, Tehran, Iran (Islamic Republic of)

Purpose: Ischemia and infarction affect the oxidative stress markers such as reactions of peroxynitrous acid and increased levels of pro-inflammatory cytokines. The treatment of acute myocardial infarction (AMI) by N-acetylcysteine (NAC) has some beneficial effects, but long-term effects of NAC on cardiac remodeling in patients with AMI are not known. This study evaluated the effects of NAC on clinical outcomes and markers of cardiac remodeling in patients with acute myocardial infarction in one year follow-up.

Methods: Following confirmation of AMI, 123 patients randomly administered NAC 600 mg (Flumucil®, Zambon, Swiss) or placebo twice daily for three days in a prospective double blind placebo controlled study. For quantification of serum markers after 24 and 72 hours of NAC or placebo administration, peripheral venous blood samples were collected at these time points. We followed up patients for one year for major adverse cardiac events (MACE) including the occurrence of recurrent MI, death and need for target vessel revascularization.

Results: After hospitalization, patients received NAC, transforming growth factor (TGF-β) levels in placebo group increased significantly over time (p=0.042). In patients who received NAC the serum levels of matrix metalloproteases (MMPs) including MMP-9 and MMP-2 after 72 hours were significantly lower than those in placebo group (p=0.014 and p=0.045, respectively). With respect to MACE, there was a significant difference between those received NAC (14.3%) compared to patients on placebo (24.5%). Risk re-infarction took place in 3% of patients in NAC group as compared to 17% in patients received placebo.

Conclusions: NAC administration could be helpful in preventing early remodeling by reducing the level of MMP-2 and MMP-9. Furthermore, NAC could prevent TGF-β levels, as pro-fibrotic cytokine, from increasing after 72 hours. By decreasing MACE, NAC could possibly be introduced as a magic bullet in the pharmacotherapy of patients with AMI. Further studies are needed to elucidate NAC role in this population.

N-acetylcysteine ameliorates infarction-induced myocardial fibrosis

T.-M. Lee, C.C.C. Chang on behalf of nil. 1 Chi Mei Medical Center, Taichung, Taiwan; 2 Division of Cardiovascular Surgery, Chi-yi Christian Hospital, Chi-yi, Taiwan

Purpose: Excessive production and deposition of extracellular matrix proteins is a feature after myocardial infarction. Excessive fibrosis is an important substrate for ventricular vulnerability. Reactive oxygen species contributes to collagen synthesis through the activation of RhoA. We assessed whether the antioxidant N-acetylcysteine could attenuate myocardial fibrosis after myocardial infarction, evaluating connective tissue growth factor signal transduction mechanism that is responsible for extracellular matrix deposition and arrhythmia.

Methods: Male Wistar rats after ligation coronary artery were randomized to either vehicle, or N-acetylcysteine for 4 weeks.

Results: Post-infarction was associated with increased oxidant release, as measured by myocardial glutathione and superoxide, and dihydroethidium fluorescent staining. RhoA/ROCK activation after myocardial infarction was observed in increasing RhoA localization from the cytosol to the membrane and phosphorylation of the ROCK substrate myosin phosphatase target subunit 1. N-acetylcysteine diminished myocardial fibrosis by inhibiting RhoA/ROCK activation without alteration of TGF-β1 proteins. A Rho inhibitor, C3 exoenzyme, and 2 ROCK inhibitors, Y-27632 and Y-27766, abolished N-acetylcysteine treated connective tissue growth factor expression. Arrhythmic scores during programmed stimulation in the vehicle-treated infarcted rats were significantly higher than that in those treated with N-acetylcysteine. The expression of connective tissue growth factor were abolished by administering L-buthionine sulfoximine, an inhibitor of γ-glutamylcysteine ligase.

Conclusions: These results indicate that N-acetylcysteine as a glutathione precursor can expedite the attenuation of infarction-induced myocardial fibrosis probably through the inhibition of TGF-β1-independent RhoA/ROCK activity and thus plays a critical role in the beneficial effect on arrhythmogenic response to programmed electrical stimulation.

Dynamic regulation of myocardial telomere biology in the infarcted mouse heart

C. Werner, C. Arendt, C. Bakogianis, M. Boehm, U. Laufs. Universitätsklinikum des Saarlandes - Klinik für Innere Medizin III, Homburg, Germany

Introduction: The incidence of cardiovascular disease rises with age. The aging process on the level of organs and cells is finely regulated and involves the accumulation of irreversible DNA damage and the erosion of telomeres. Oxidative stress-induced DNA damage may induce premature stress-induced senescence of ischemic cardiomyocytes. Telomerase has been shown to protect cardiovascular cells from mitochondrial oxidative stress. In this study, we analyzed whether myocardial ischemia impacts on telomere biology and cellular senescence in the infarcted mouse heart.

Methods and results: C57Bl/6 mice (male, 10 weeks old, n=6-8 per group) were exposed to anterior myocardial ischemia induced by proximal ligation of the left anterior descending (LAD) coronary artery or sham operation. Infarct size and localization were verified by cardiac MRI. Sham-operated and mice with myocardial infarction were analyzed 3 days, 7 days, 4 or 7 days after LAD ligation and myocardial infarct zone and remote zone were compared on age-related telomere activity as measured by telomere repeat amplification protocols. A standard dilution curve of Human Embryonic Kidney (HEK) cells with high telomerase activity was used as positive control. The experiment revealed that 3 days after LAD ligation, telomerase activity was elevated in the infarct zone, but not in the remote zone of the hearts. 7 days after myocardial infarction, telomerase was up-regulated both, in the infarct zone and the remote zone. This effect was even more pronounced 4 weeks after LAD ligation. Corresponding to telomerase activation, telomere repeat binding factor (TRF) 2 protein expression was up-regulated in the infarct zone after three days and in both areas at 7 days and 4 weeks. At the same time, apoptosis regulators (p53, CHK2 and bax) and senescence regulators (p16) were up-regulated in the injured hearts as an indicator of a complex cellular remodelling process, which involves the cellular ageing signalling machinery.

Conclusion: Our data show that myocardial telomerase is up-regulated in a time- and region-specific fashion in the infarcted heart. We speculate that this regulatory process is compensated to cope with oxidative stress in myocardial ischemia and inflammation. The hypothesis of cell- and organ-specific aging represents a new paradigm in cardiovascular research with the ultimate goal on designing novel therapeutic strategies aimed specifically at cellular aging in the heart and vasculature. Future experiments will examine the causal role of telomerase in post-ischemic myocardial remodelling and cell-type specific contributions to these effects.
Combined of cilostazol and clopidogrel markedly attenuates rat critical limb ischemia

J.J. Sheu1, S. Chua2, T.H. TSAI1, Y.L. Chien1, H.K. Yip1. 1Kaohsiung Chang Gung Memorial Hospital, Kaohsiung, Taiwan; 2Kaohsiung Chang Gung University, Kaohsiung, Taiwan

Purpose: This study tested the superiority of combined cilostazol and clopidogrel therapy compared with either one in attenuating rat critical limb ischemia (CLI) and improving blood flow in CLI region.

Methods: Male Sprague-Dawley rats (n=40) were equally divided into group 1 (control), group 2 (CLI only), group 3 (CLI + cilostazol (12.0 mg/kg/day)), group 4 (CLI + clopidogrel (8.0 mg/kg/day)), and group 5 (combined cilostazol-clopidogrel) after CLI induction.

Results: By day 21 prior to sacrifice the animals, Laser Doppler showed lower ratio of ischemic/normal blood flow in group 2 compared with other groups (p<0.001). The inflammatory biomarkers (protein expressions: VCAM-1, oxidative stress: mRNA expressions: PAI-1, MMP-9, TNF-α, immunofluorescent (IF) staining: CD68+ cells) were lower in group 5 compared with groups 2 to 4, and lower in groups 3 and 4 than in group 2 (all p<0.001). The angiogenic biomarkers (protein expression: ENOS; IF staining: CD31+ and vWF+ cells; small number of vessels in CLI region) were higher in group 5 than in groups 2 to 4, and higher in groups 3 and 4 than in group 2 (all p<0.001).

Conclusion: Combined cilostazol-clopidogrel therapy is superior to either one alone in improving ischemia in rodent CLI.

The apoptotic [protein expressions: Bax, cleaved caspase-3 and PARP; mRNA expression: Bax, caspase-3] and muscle damaged [protein expressions: cytosolic cytochrome-C; mRNA expressions: serum and muscle micro-RNA-206] biomarkers were lower in group 5 than in groups 2 to 4, lower in groups 3 and 4 than in group 2 (all p<0.001). The angiogenic biomarkers [protein expression: ENOS; IF staining: CD31+ and vWF+ cells; small number of vessels in CLI region] were higher in group 5 than in groups 2 to 4, and higher in groups 3 and 4 than in group 2 (all p<0.001).

Conclusion: Combined cilostazol-clopidogrel therapy is superior to either one alone in improving ischemia in rodent CLI.

RIP-1 inhibition reduces infarct size and improves cardiac function in a porcine model of myocardial reperfusion injury


Purpose: As our understanding of key molecular events increases regarding reperfusion injury, new therapeutic approaches modulating these pathways could exert cardioprotective properties. The kinase activity of RIP-1, a central regulator in programmed necrosis, has been shown to be effectively silenced by a RIP-1 dominant-negative (DN) form, Necrostatin-1 (Nec-1), which prevents the occurrence of necrotic cell death after ischemia/reperfusion (IR) injury in rodents. Here, we sought to investigate the cardioprotective effects of Necrostatin-1 treatment after IR in pigs, which gave the path for future clinical applications.

Methods: In 20 pigs (weighting 70±2 kg), acute ischemia/reperfusion injury was induced by a 75 min surgical ligation of the left circumflex artery (LCA), 10 min prior to reperfusion, pigs were randomly allocated to receive Nec-1 intravenously in two different doses (1 mg/kg and 3.3 mg/kg respectively) or vehicle treatment. Cardiac function was measured with echocardiography and LV contractility was assessed as T100 (the end-systolic elastance at 100 mmHg) by pressure volume-loop analysis before occlusion and 24 hours after reperfusion. Infarct size (IS) was expressed as a percentage of the area at risk (AAR) using 1% Evans blue and triphenyl tetrazolium chloride (TTC).

Results: Administration of 3.3 mg/kg of Nec-1 (n=5) significantly reduced infarct size compared to 1.0 mg/kg Nec-1 (n=4) or vehicle treatment (n=6) (18.4±11.9 vs 54.8±24.2 vs 38.2±12.4, P<0.0196). Declined cardiac function following IR displayed a consistent trend towards a preserved systolic function in the high dose...
Cardiovascular Pathology

Cardiac morphology and function in migfilin deficient mice due to experimental pressure overload

M. Reiner1, K. Strelli1, B.J. Haubner2, K. Bader1, D.V. Moik3, R. Faessler4, O. Pachinger2, B. Metzler1, Innsbruck Medical University, Department of Internal Medicine III, Cardiology, Innsbruck, Austria; 1Institute of Molecular Biotechnology of the Austrian Academy of Sciences, Vienna, Austria; 2Max Planck Institute of Biochemistry, Martinsried, Germany

Background: Migfilin, a protein associated with cell adhesions and the cytoskeleton, is markedly reduced in the cardiomyocyte. Moreover, overexpression of Migfilin interacts with the transcription factor Csx/Nkx2-5, which is involved in cardiac development and hypertrophy by inducing gene expression of atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP), among others. The in vivo role of migfilin in cardiac hypertrophy and function is unknown.

Methods: Migfilin wild type (WT) and knockout (KO) mice were examined at baseline and further after one and three weeks of pressure overload, induced by transverse aortic constriction (TAC). TAC assesses cardiac morphology and function, transhilar echocardiography was performed, mean cross-sectional area of cardiomyocytes was measured in histological sections and mRNA of the cardiac hypertrophy genes ANP and BNP were assayed by rt-PCR.

Results: Echocardiography at baseline showed significantly smaller hearts but normal cardiac function in migfilin KO mice. After one and three weeks of TAC, cardiac function was reduced in KO mice (FS, 1 week: 51.99% vs. 52.21%, p<0.01; 3 weeks: 49.79% vs. 51.93%, p=0.02) and murine hearts appeared to be more dilated after three weeks of pressure overload (End Diastolic Diameter, 3.95 mm vs. 3.75 mm, p>0.005). Mean cross-sectional area of cardiomyocytes after one and three weeks of TAC was significantly decreased in KO compared to WT mice (both, p<0.05). Additionally, migfilin deficient mice showed decreased mRNA levels of ANP and BNP at baseline and after TAC (both, p<0.05).

Conclusion: These data suggest that migfilin plays an essential role in cardiac hypertrophy since loss of migfilin in mice results in smaller hearts at baseline and reduced myocardial hypertrophy and function in association to pressure overload.

Cardiac overexpression of JDP2 prevents processes of cardiac remodeling

G. Euler, A. Wuerfel, C. Hill, J. Heger, R. Schulz, Justus-Liebig University Giessen, Institute of Physiology, Giessen, Germany

Cardiac remodeling is often accompanied by enhanced expression of the transcription factor AP-1. Involvement of this transcription factor in processes of cardiac remodeling, like hypertrophic growth and apoptosis, has already been demonstrated on the level of ventricular cardiomyocytes in vitro. Now, we analysed the influence of AP-1 on processes of cardiac remodeling in mice with unilateral kidney stenosis by overexpression of the AP-1 inhibitor JDP2 in transgenic mice.

In 4 – 5 week old mice renal artery of left kidney was clipped. As control sham operated animals were used (sham). After 4 weeks mice were sacrificed and found in JDP2-mice blood pressure was reduced by 120±6 to 142±16 mmHg and from 126±5 to 156±9 mmHg, respectively (p<0.05). Hypertrophic growth, however, was seen in WT-animals only: Heart/body weight increased 4 weeks after stenosis to 111.6±3.4% compared to sham WT-mice (p<0.05). Furthermore, BNP-mRNA expression was enhanced 6.0±1.7-times vs. sham WT-mice (p<0.05). None of these hypertrophic parameters was increased in JDP2-mice after stenosis. Expression of TGFβ1, that is known to be regulated by AP-1, was enhanced 3.4-times after stenosis in WT-mice (p<0.05). At the same time, mRNA of SMAD7, which is an inhibitor of TGFβ1-signaling, was enhanced 5.4-fold in WT-mice (p<0.05). Thus, at this disease state hearts of WT mice seem to respond to increased –fibrotic action of TGFβ1 by enhanced –antifibrotic action of SMAD7. This response is reflected in enhanced expression of anti-apoptotic Bcl-2 mRNA and absence of changes in fibrotic marker genes like collagen I, elastin and loricrin. In JDP2 mice neither TGFβ1 expression nor Bcl-2 and SMAD7 expression was influenced by kidney stenosis. Concerning genes controlling calcium content and thus contractility of cardiomyocytes, SERCA-mRNA was reduced by 84% vs. sham WT-mice (p<0.05). In JDP2-mice reduction of SERCA-mRNA was also visible after kidney stenosis (p=0.41-fold; p<0.05).

Furthermore, JDP2-mice showed no signs of apoptosis. This is reflected by Annexin-V staining and Western blot analysis, which was characterized by Western blotting. The expression of paraffin-embedded p-TGFβ1 in cardiac tissue was lower in JDP2-mice compared to WT-mice. However, the expression of paraffin-embedded p-TGFβ1 in cardiac tissue was higher in JDP2-mice compared to WT-mice. This difference was statistically significant (p<0.05).

Conclusion: Four weeks after kidney stenosis hypertrophic growth is induced in WT-mice. Overexpression of the AP-1 inhibitor JDP2 prevents this hypertrophic growth response. In addition, JDP2 overexpression prevents induction of the pro-apoptotic –fibrotic growth factor TGFβ1. Furthermore, in WT mice SERCA-mRNA is reduced, which indicates an impairment of contractile heart function after not prevent the development of RV hypertrophy. This decline in SERCA-mRNA could not be prevented by JDP2 overexpression.
Inhibition of GSK-3β augments 5-HT2B receptor blockade induced protection in angiotensin-II-induced cardiac hypertrophy in rats

S. Bharati, D.S. Arya. All India Institute of Medical Sciences, New Delhi, India

Glycogen synthase kinase-3β (GSK-3β) is a multifunctional Serine/Threonine kinase that performs a crucial role in regulating cardiac hypertrophy. The purpose of the current study was to identify and dissect the intracellular signaling mechanisms that link 5-HT2B receptor (5-HT2B-R) blockade and GSK-3β pathway in angiotensin-II-induced cardiac hypertrophy. 5-HT2B-R antagonist, SB-204741 (1 mg/kg, i.p.) or GSK-3β inhibitor, SB-216763 (0.6 mg/kg, i.p.) plus SB-204741 were administered in angiotensin-II (100 ng/kg/min, s.c.) treated rats for 28 days. SB-204741, treatment significantly (P < 0.05) alleviated all killed cardiovascular function as revealed by improvement in mean arterial pressure, left ventricular end diastolic pressure (LVdP/dt min pre-load), ±LVdP/dt max, contractility (inotropic state), ±LVdP/dt max, relaxability (lupotropic state) and without affecting the heart rate in angiotensin-II infused rats. Additionally, SB-204741 significantly (P < 0.05) attenuated the cardiac hypertrophic injury markers (creatinine kinase-MB, c-reactive protein, brain natriuretic peptide and malondialdehyde).

Mechanical stretch via transforming growth factor- β1 activates microRNA-208a to regulate hypertrophy in cultured rat cardiomyocytes

G. Shyu, B.W. Wang. Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan

Purpose: MicroRNAs (miRs) and mechanical stress play a key role in cardiac hypertrophy. MiR208a is essential for expression of the genes involved in cardiac hypertrophic growth. The relationship between miR208a and mechanical stress in cultured cardiomyocytes has not been investigated yet. The molecular mechanisms underlying miR208a involved hypertrophy of cardiomyocytes by mechanical stress is poorly understood. We sought to investigate whether miR208a is a critical regulator in cardiomyocyte hypertrophy under mechanical stretch.

Methods: Neonatal rat cardiomyocytes grown on a flexible membrane base were stretched via vacuum to 20% of maximum elongation at 60 cycles/min. TaqMan® microRNA real-time quantitative RT-PCR assay was used to quantify microRNA expression. Western blot was used to measure hypertrophic protein expression. Quantitative enzyme immunoassay was used to measure transforming growth factor-beta1 (TGF-β1) in the culture medium. Protein synthesis of cultured cardiomyocytes was measured by 3H-proline incorporation assay.

Results: Mechanical stretch significantly enhanced miR208a expression after 4 h of stretch. Stretch significantly increased cardiomyocyte hypertrophic protein expression such as ANP, BNP, MHCβ and phosphorylated Akt/GSK-3β. Moreover the stretch-induced miR208a expression was significantly reduced upon treatment with silencing miR208a siRNA. Therefore, mechanical stretch significantly increased miR208a expression and pretreatment with TGF-β1 antibody attenuated the miR208a expression induced by stretch. Stretch combined with overexpression of miR208a increased protein synthesis significantly while 5HT2B-R antagonist did not. Our results provide the first direct evidence that GSK-3β phosphorylation/inhibition regulates 5-HT2B receptor blockade mediated anti-hypertrophic effect not only by preserving cardiac functions but also, importantly, through modulating apoptosis, oxidative stress and inflammatory pathways.

Mechanical stretch via transforming growth factor-beta1 activates microRNA-208a to regulate hypertrophy in cultured rat cardiomyocytes

Mechanical stretch via transforming growth factor-beta1 activates microRNA-208a to regulate hypertrophy in cultured rat cardiomyocytes

G-alpha-13 mediates pressure overload-induced cardiac remodeling and heart failure

M. Takefuji, S. Offermanns, N. Wettswsche. Max Planck Institute for Heart and Lung Research, Bad Nauheim, Germany

Purpose: Myocardial hypertrophy is the adaptive response of the heart to pressure overload. A variety of in vivo studies indicated that G-protein coupled receptors (GPCRs) agonists induce heart remodeling through heterotrimeric G-proteins of the Gq/11 family. However, these GPCRs can also activate the G12/13 family which has been shown to regulate vascular smooth muscle contraction in a Ras-related manner. We examine in this study whether Gα13/Gq/11 contributes to cardiac remodeling.

Methods: To circumvent this embryonic lethality in Gα13-deficient mice, we generated tamoxifen-inducible, cardiomyocyte-specific knockouts of Gα13 (Gα13-KO). As a pressure-overload model, transverse aortic constriction (TAC) surgery was performed in Gα13-KO mice. Cardiac function was measured left ventricular function (LVFW and LVFW/LVIB length (TL) and quantified ejection fraction (EF) by magnetic resonance imaging analysis.

Results: To investigate how RhoA is activated in cardiomyocyte in response to TAC, we performed siRNA-mediated knockdown of the two major alpha-subunits of the Gα11 family and Gα12 family in neonatal rat ventricular myocytes. RhoA activity assay showed that the ET-1 or stretch induced RhoA activation was significantly reduced after knockdown of Gα13, but not on Gα11. The ET-1 or stretch induced expression of ANP and β-MHC was reduced by knockdown of Gα12/13.

The study role of Gα13-dependent RhoA activation for hypertrophy in vivo, we performed TAC in cGα13-KO mice. Four weeks after TAC, control hearts showed increased LVFW/TL and this response was reduced in cGα13-KO mice. To determine the mechanisms underlying the reduced TAC in Gα13-KO compared with controls, EF was preserved compared to wildtype mice. In order to understand how Gα13-mediated RhoA activation affects the growth of cardiomyocytes, we performed siRNA-mediated knockdown of the major alpha-subunits of the Gα11 family and Gα12 family in neonatal rat ventricular myocytes. RhoA activity assay showed that the ET-1 or stretch induced RhoA activation was significantly reduced after knockdown of Gα13, but not on Gα11. The ET-1 or stretch induced expression of ANP and β-MHC was reduced by knockdown of Gα12/13.

Conclusion: The signaling cascade Gα13-RhoA-MRTF-A is crucial for pressure overload-induced cardiac remodeling and plays a central role in the transition to heart failure.
Micro-RNA 146a: a new kid on the block in the post-infarct treatment with G-CSF and active cardiac F16618, an antagonist of the protease activated receptor signalling mediated in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising target in the treatment of cardiac hypertrophy upon a pressure overload stimulus.

Methods: MiR-146a knockout (KO), wild-type (WT) and miR-146a cardiomyocyte-specific overexpressing transgene (TG) CSTB/ShN mice were exposed to angiotensin-II 2.5 mg/kg/day during 4 weeks. Next, miR-146a was pharmacologically blocked by administering specific miR-146a antagonists. Functional analysis with echocardiography was performed. All mice were sacrificed and hearts were dissected for further histological and molecular analysis.

Results: Upon pressure overload, miR-146a expression levels decrease both in mice submitted to 4 weeks of Ang-II, and in cardiomyocytes in vitro stimulated with endothelin-1. Ang-II infusion significantly increased the heart weight (normalized to tibia length) in the WT mice (HW/TL = 7), but not in the KO (HW/TL = 6), where the hypertrophic response was severely blunted (p<0.05).

Conclusions: Absence or inhibition of microRNA-146a blunts the hypertrophic response and cardiac failure upon pressure overload, whereas its overexpression in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising therapeutic target in hypertensive heart disease.

The forkhead-transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

F16618, an antagonist of the protease activated receptor 1 reduces the atrial remodeling in a rat model of chronic heart failure.

Micro-RNA 146a: a new kid on the block in the post-pathophysiology of cardiac hypertrophy and hypertensive heart failure, and a promising therapeutic target in hypertensive heart failure.

Conclusions: Absence or inhibition of microRNA-146a blunts the hypertrophic response and cardiac failure upon pressure overload, whereas its overexpression in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising therapeutic target in hypertensive heart disease.

The forkhead transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

The forkhead transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

Methods: MiR-146a knockout (KO), wild-type (WT) and miR-146a cardiomyocyte-specific overexpressing transgene (TG) CSTB/ShN mice were exposed to angiotensin-II 2.5 mg/kg/day during 4 weeks. Next, miR-146a was pharmacologically blocked by administering specific miR-146a antagonists. Functional analysis with echocardiography was performed. All mice were sacrificed and hearts were dissected for further histological and molecular analysis.

Results: Upon pressure overload, miR-146a expression levels decrease both in mice submitted to 4 weeks of Ang-II, and in cardiomyocytes in vitro stimulated with endothelin-1. Ang-II infusion significantly increased the heart weight (normalized to tibia length) in the WT mice (HW/TL = 7), but not in the KO (HW/TL = 6), where the hypertrophic response was severely blunted (p<0.05).

Conclusions: Absence or inhibition of microRNA-146a blunts the hypertrophic response and cardiac failure upon pressure overload, whereas its overexpression in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising therapeutic target in hypertensive heart disease.

The forkhead transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

Methods: MiR-146a knockout (KO), wild-type (WT) and miR-146a cardiomyocyte-specific overexpressing transgene (TG) CSTB/ShN mice were exposed to angiotensin-II 2.5 mg/kg/day during 4 weeks. Next, miR-146a was pharmacologically blocked by administering specific miR-146a antagonists. Functional analysis with echocardiography was performed. All mice were sacrificed and hearts were dissected for further histological and molecular analysis.

Results: Upon pressure overload, miR-146a expression levels decrease both in mice submitted to 4 weeks of Ang-II, and in cardiomyocytes in vitro stimulated with endothelin-1. Ang-II infusion significantly increased the heart weight (normalized to tibia length) in the WT mice (HW/TL = 7), but not in the KO (HW/TL = 6), where the hypertrophic response was severely blunted (p<0.05).

Conclusions: Absence or inhibition of microRNA-146a blunts the hypertrophic response and cardiac failure upon pressure overload, whereas its overexpression in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising therapeutic target in hypertensive heart disease.

The forkhead transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

Micro-RNA 146a: a new kid on the block in the post-pathophysiology of cardiac hypertrophy and hypertensive heart failure, and a promising therapeutic target in hypertensive heart failure.

Conclusions: Absence or inhibition of microRNA-146a blunts the hypertrophic response and cardiac failure upon pressure overload, whereas its overexpression in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising therapeutic target in hypertensive heart disease.

The forkhead transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

Methods: MiR-146a knockout (KO), wild-type (WT) and miR-146a cardiomyocyte-specific overexpressing transgene (TG) CSTB/ShN mice were exposed to angiotensin-II 2.5 mg/kg/day during 4 weeks. Next, miR-146a was pharmacologically blocked by administering specific miR-146a antagonists. Functional analysis with echocardiography was performed. All mice were sacrificed and hearts were dissected for further histological and molecular analysis.

Results: Upon pressure overload, miR-146a expression levels decrease both in mice submitted to 4 weeks of Ang-II, and in cardiomyocytes in vitro stimulated with endothelin-1. Ang-II infusion significantly increased the heart weight (normalized to tibia length) in the WT mice (HW/TL = 7), but not in the KO (HW/TL = 6), where the hypertrophic response was severely blunted (p<0.05).

Conclusions: Absence or inhibition of microRNA-146a blunts the hypertrophic response and cardiac failure upon pressure overload, whereas its overexpression in cardiomyocytes increases hypertrophy. MicroRNA-146a thus represents a promising therapeutic target in hypertensive heart disease.

The forkhead transcription factor FoxO3a regulates MMP-13 expression, implications for cardiac myofibroblasts.

Micro-RNA 146a: a new kid on the block in the post-pathophysiology of cardiac hypertrophy and hypertensive heart failure, and a promising therapeutic target in hypertensive heart failure.
Conclusion: In conclusion our results implicate FOXO3a directly in the regulation of MMP13 expression. FOXO3a might play an important role in controlling extracellular matrix remodeling processes under cardiovascular stress and injury such as inflammation and myocardial infarction. Thus, targeting FOXO3a might have therapeutic potential.

P802

Eya4 mediates the development of acquired cardiac hypertrophy

T. Williams1, D. Kraemer1, J. Schoernerberger1, P. Nordbeck1, S. Voli1, M. Czolbe1, V. Pekarek1, O. Ritter1. 1University Hospital of Wurzburg, Medical Clinic I, Wurzburg, Germany; 2University of Wurzburg, Department of Experimental Physics V (Biophysics), Wurzburg, Germany

Introduction: We previously showed that a mutation in the transcription cofactor “Eyes absent” (Eya4) leads to late-onset familial dilated cardiomyopathy and heart failure. A precise role for Eya4 in the myocardium has not yet been identified. It appears to be a negative regulator of the protein kinase inhibitor p27kip1 (p27), a protein shown to regulate hypertrophic responses in the adult cardiomyocyte. This study was aimed to explore the role of Eya4 in angiotensin II (ATII)-induced cardiac hypertrophy.

Methods and results: We constructed a transgenic mouse model with a constitutive myocardial overexpression of HA-tagged Eya4. Wildtype and Eya4 overexpressing mice were challenged with ATII via osmotic minipumps for four weeks to induce cardiac hypertrophy. First analysis of these animals using magnetic resonance imaging to visualize cardiac structures in detail showed that in response to the sustained ATII stimulation, the Eya4 overexpressing mice exhibited a phenotype with significantly increased parameters of hypertrophy. LV free wall diameter as measured in 7T MRI was 1.7±0.2 mm in Eya4 mice with ATII compared to 1.3±0.2 mm in WT mice with ATII. This was also confirmed by HW/BW ratio, hemodynamic measurements and cell size measurements. Histology also affirmed the results of the MR imaging. Moreover, Eya4 overexpression induced a significant suppression of p27 protein expression which is in agreement with our in vitro data. This confirmed our hypothesis, that Eya4 suppresses p27 expression which facilitates development of myocardial hypertrophy.

Conclusion: In summary, we previously identified a mutation in Eya4 to disturb cardiac physiology. We now provide evidence that Eya4 is also involved in forms of acquired heart disease. It seems to suppress p27, thereby augmenting ATII induced cardiac hypertrophy.

P803

The transcription cofactor Eya4 is crucial in the development of heart disease

T. Williams1, D. Kraemer1, J. Schoernerberger1, P. Nordbeck1, S. Voli1, M. Czolbe1, V. Pekarek1, O. Ritter1. 1University Hospital of Wurzburg, Medical Clinic I, Wurzburg, Germany; 2University of Wurzburg, Department of Experimental Physics V (Biophysics), Wurzburg, Germany

Introduction: We identified a mutation in the human transcription cofactor Eya4 (E193) to cause terminal heart failure preceded by sensorineural hearing loss. Eya proteins lack DNA-binding and nuclear translocation sequences and therefore must interact with real transcription factors, including Six family members. The cyclin-dependent kinase inhibitor p27kip1 (p27), which inhibits hypertrophic function in the heart, at least in part due to impaired AMPK/SIRT1/PGC-1alpha signaling. In the heart, both lack of adiponectin receptor 1 but not adiponectin receptor 2 impairs mitochondrial function. Therefore, we examined the correlation of Eya4 and the mutant E193 overexpression upon p27 in permanent mammalian cell lines and primary cardiac myocytes. Westernblot analysis demonstrated that an overexpression of Eya4 led to a significant suppression of p27, whereas E193 had no effect on p27 levels; knockdown of Eya4 via siRNA exerted opposing effects. Promoter studies using a p27 promoter fragment including Six1 consensus sites revealed that the constitutive suppression of p27 by Eya4 was released after targeting one of the Six1 consensus sequences. This study was aimed to explore the role of Eya4 in angiotensin II (ATII)-induced cardiac hypertrophy.

Methods and results: We examined the correlation of Eya4 and the mutant E193 overexpression upon p27 in permanent mammalian cell lines and primary cardiac myocytes. Westernblot analysis demonstrated that an overexpression of Eya4 led to a significant suppression of p27, whereas E193 had no effect on p27 levels; knockdown of Eya4 via siRNA exerted opposing effects. Promoter studies using a p27 promoter fragment including Six1 consensus sites revealed that the constitutive suppression of p27 by Eya4 was released after targeting one of the Six1 consensus sequences. This study was aimed to explore the role of Eya4 in angiotensin II (ATII)-induced cardiac hypertrophy.

Conclusion: In summary, we previously identified a mutation in Eya4 to cause terminal heart failure preceded by sensorineural hearing loss. Eya proteins lack DNA-binding and nuclear translocation sequences and therefore must interact with real transcription factors, including Six family members. The cyclin-dependent kinase inhibitor p27kip1 (p27), which inhibits hypertrophic function in the heart, at least in part due to impaired AMPK/SIRT1/PGC-1alpha signaling. In the heart, both lack of adiponectin receptor 1 but not adiponectin receptor 2 impairs mitochondrial function. Therefore, we examined the correlation of Eya4 and the mutant E193 overexpression upon p27 in permanent mammalian cell lines and primary cardiac myocytes. Westernblot analysis demonstrated that an overexpression of Eya4 led to a significant suppression of p27, whereas E193 had no effect on p27 levels; knockdown of Eya4 via siRNA exerted opposing effects. Promoter studies using a p27 promoter fragment including Six1 consensus sites revealed that the constitutive suppression of p27 by Eya4 was released after targeting one of the Six1 consensus sequences. This study was aimed to explore the role of Eya4 in angiotensin II (ATII)-induced cardiac hypertrophy.

P804

Alogliptin reverses cardiac remodeling and dysfunction induced by pressure overload through the GLP-1/cAMP-mediated mitophagy

M. Aoyama, Y. Kunishi Bando, T. Shigeta, A. Moriyi, T. Mitsuji, T. Murakura, Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Purpose: Dipeptidyl peptidase-4 (DPP4) inactivation protects heart from pathological remodeling and higher mortality induced by acute myocardial infarction. However, the impact of DPP4 inhibition on the chronic heart failure induced by pressure overload (TAC) remains uncertain.

Methods and Results: Male 10-week-old C57BL/6 mice were randomly allocated into 6 groups: sham and TAC treated with (sham/ALO, TAC/ALO) or without (sham/CTL, TAC/CTL) alogliptin (10 mg/kg/day) or exendin-4, a potent GLP-1 receptor agonist (24 nmole/kg/day) (n=5–6). Echocardiogram revealed that TAC/CTL exhibited cardiac hypertrophy and their systolic and diastolic left ventricular functions were impaired 4 week after exposure to pressure overload, which were reversed by alogliptin treatment. Alogliptin increased circulating GLP-1 levels, which induced cardiac elevation of cyclic AMP levels. Administration of exendin-4 consistently reversed the left-ventricular dysfunction induced by pressure-overload via increase in cardiac cyclic AMP concentration. Of note, both alogliptin and exendin-4 had no effect on cardiac angiogenesis. PINK/Parkin accumulations occurred in response to increased pressure overload, which were reversed by alogliptin treatment. Alogliptin increased autophagy by enhancing expression of Atg5 and Bnip3, two autophagic markers.

Conclusion: The present study demonstrates that the GLP-1/cAMP axis protects heart from pressure-overload-induced chronic heart failure via activation of mitophagy.
The effect of estrogen receptor agonists on hypertension-induced oxidative stress of cardiac and renal tissue in rats

M. Kolgazi1, Z.N. Ozdemir Kurna1, O. Kasimay1, G. Sener2*
1Department of Physiology, Istanbul, Turkey; 2Marmara University, School of Pharmacy, Department of Pharmacology, Istanbul, Turkey

Although endogenous ovarian estrogen is known to offer cardiac benefit and vascular protection in pre-menopausal women, there is still a debate in the literature whether hormone replacement therapy decreases or even increases the risk of cardiovascular disease. We aimed to investigate the effects of the estrogen receptor agonists on the cardiovascular and renal functions of 2 kidney-1 clip (2K1C) hypertensive rats.

Female Sprague-Dawley rats (250-300 g) were divided into 2K1C and 2K1C+ovariectomy (OVX) groups. Both groups received either estrogen receptor-α (ER-α) agonist diarylpropionic acid (DPN; 1 mg/kg/day) or estrogen receptor-β (ER-β) agonist propylpyrazole triol (PPT; 1 mg/kg/day) starting at the third week following the surgery and continuing for 6 weeks. Indirect blood pressure (BP) recordings were obtained to verify hypertension. At the end of the 9th week, the animals were decapitated. In the kidney and cardiac samples, malondialdehyde (MDA) and glutathione (GSH) levels, superoxide dismutase (SOD), catalase (CAT) and total antioxidant activity (TAA) measurements were performed. Statistical analysis was carried out using Mann-Whitney U test and Student’s t test.

2K1C hypertension resulted in increased BP and caused significant decreases in cardiac (CAT) superoxide dismutase activity and GSH contents, while ISO + vildagliptin (Vehicle: 43.9 ± 0.9, ISO: 11.1 ± 0.5 mmHg, p < 0.05) and prolonged time constant of LV relaxation (Tα) improvement (ISO: 4.43 ± 0.39, ISO + vildagliptin: 4.14 ± 0.29, p < 0.05).

Conclusion: These findings demonstrate that administration of vildagliptin exerts a therapeutic effect on the development of LV hypertrophy and diastolic dysfunction.

YP087
Evidence for a reciprocal down-regulation between beta-1-adrenergic receptor and sphingosine-1-phosphate receptor 1

A. Carnavo1, G. Rengo2, D. Icardo1, C. zincarel1, M.C. De Angelis1, E. De Pietro, R. Puglia1, W.J. Koch1, D. Leoc糄1, A. Rapaccio1
1University of Naples Federico II, Dept of Clinical Medicine, Cardiovascular & Immunological Science, Naples, Italy; 2Salvatore Maugeri Foundation, IRCCS, Scientific Institute of Rehabilitation of Telese, Telese Terme, Italy

Purpose: Sphingosine-1-phosphate receptor 1 (S1P1) and β1-adrenergic receptor (β1AR) belong to the superfamily of G-protein coupled receptors (GPCRs), whose function is regulated by the G-protein coupled receptor kinase-2 (GRK2), whose function is regulated by the G-protein coupled receptor kinase-2 (GRK2). We used HEK293 cells overexpressing mouse wild type β1AR (WT/1AR) or 2 mutants lacking, respectively, the putative PKA (PKA-WT1AR) or GRK2 (GRK2-1AR) phosphorylation sites. All cells were transiently transfected with S1P1. By confocal microscopy experiments we evaluated receptor-receptor interaction following isoproterenol (ISO; [α]AR agonist) or sphingosine (SIP; [α]AR agonist) stimulation. Our data in WT/1AR cells showed that both receptors mDA levels and MPO activities were increased in both tissues of the OVX and non-OVX groups. PPT treatment reduced BP in both OXV (p < 0.01) and non-OXV (p < 0.01) groups. PPT and DPN treatments had no effect on BP and MDA levels.

The findings demonstrate that hypertension-induced oxidative damage of the cardiac and renal tissue was reduced by both ER-α and ER-β agonists, while ER-α agonist was more efficient in ameliorating cardiac oxidative stress. Thus, in the absence of cardiac protective effects of endogenous ovarian hormones, the agonists that mimic the cardioprotection via the ER receptors, or in part via the ER-β receptors, have the potential to reduce the risk of cardiovascular disease.

YP089
Conclusions: These results provide a biochemical and functional evidence of a direct connection between S1P1 and β1AR that appears to be GRK2 dependent. Importantly, this reciprocal down-regulation was observed also in vivo both after chronic β1AR hyperstimulation or in a clinically relevant experimental model of HF, which is known to be characterized by sympathetic nervous system overdrive.

YP089
Vildagliptin, a dipeptidyl peptidase-4 inhibitor, prevents cardiac hypertrophy and diastolic dysfunction induced by chronic beta-1 adrenergic stimulation in adult rat hearts


Background: Congestive heart failure with left ventricular (LV) diastolic dysfunction and preserved ejection fraction is often observed in hypertensive patients; however, the effective treatment of diastolic heart failure has not been established. Recent studies showed that dipeptidyl peptidase-4 (DPP4) inhibitors, which increase circulating GLP1 level, have cardio-protective effects. Accordingly, the current study elucidated whether vildagliptin prevents the development of LV hypertrophy and diastolic dysfunction in isoproterenol (ISO)-induced hypertrophied rat hearts.

Methods: Male Wistar rats (9 weeks old) received a vehicle (control, n=5), ISO subcutaneously (2.4 mg/kg/day, n=20) or ISO subcutaneously + vildagliptin with oral administration (30mg/kg/day, n=20) for 7 days. Cardiac catheterization and echocardiography were performed after ISO treatment to evaluate LV diastolic functions.

Results: After 7 days, LV hypertrophy in ISO + vildagliptin was significantly decreased compared with those in ISO (Heart weight/body weight, Vehicle: 3.19±0.42, ISO: 4.43±0.39, ISO + vildagliptin: 4.14±0.29, p<0.05). Cardiac hypertrophy (J. Heger, C. Harjung, S. Partsch, R. Schulz, G. Euler. Justus-Liebig University, Giessen, Germany

Question: Apoptosis and hypertrophy are processes that both contribute to heart failure progression. The transcription factor Y-box binding protein 1 (YB-1) functions as a regulator of transcription and is capable to interact with AP-1 as well as SMAD proteins. Therefore, the question arises whether YB-1 is able to influence apoptosis and/or hypertrophy in adult cardiomyocytes and thus would counteract the development of heart failure.

Methods and Results: To answer this question we infected adult cardiomyocytes of rat and H9C2 cells with adenovirus overexpressing YB-1 (AdYB-1). To analyze the influence of YB-1 on hypertrophic growth we stimulated cardiomyocytes with a β-adrenergic agonist phenylephrine (10 μM, PE). PE increased protein synthesis rate and cross sectional area (CSA). Hypertrophic growth was completely inhibited when cells were infected additionally with AdYB-1. PE stimulation of AdYB-1-infected cardiomyocytes revealed a significant increase in RGS5 mRNA. The up-regulation of this cardiac Gq signalling inhibitor might prevent PE-induced hypertrophy. Additionally, we stimulated cardiomyocytes with GDF-15 (3 ng/ml), another stimulator of hypertrophic growth. In contrast to PE, infection of cardiomyocytes with AdYB-1 did not block GDF-15 induced hypertrophy, since receptor for CSA nor the relative rate of CSA was increased in AdYB-1-infected cardiomyocytes. Furthermore, influence of YB-1 on apoptosis induction was analyzed. YB-1 overexpression also inhibited TGFβ1-induced apoptosis. TGFβ1 (1 ng/ml) stimulation increased mRNA expression of the AP-1 subunits JunB and JunD in wild-type cardiomyocytes but not in YB-1-overexpressing cardiomyocytes. Additionally, increase in SMAD4 mRNA expression was reduced upon AdYB-1 infection in TGFβ1-stimulated cardiomyocytes. Thus, YB-1 inhibits upregulation of the transcription factors AP-1 and SMAD4, both of which are nec-
Influence of angiotensin-II type 1 receptor blockade on cardioprotection through S-nitros(yl)ation of male Wistar-Kyoto rats (n=40) were subjected to standard rat chow (C: 3.2kcal/g) or hypercaloric diet (OB: 4.9kcal/g) for 30 weeks and then assigned to three groups: C; OB, and OBL. OBL received losartan in drinking water (30mg/kg/day). After five weeks, body weight (BW), adiposity, tracycylic glycerol (TC), and serum leptin concentration were analyzed. Cardiac structure and left ventricular diastolic posterior wall thickness; E-wave, early diastolic mitral inflow ratio; *p < 0.05; one-way ANOVA, Bonferroni post-hoc test. Results: OB presented higher values of BW, adiposity, TG, and leptin than C (p < 0.05). Losartan treatment decreased TG concentration (C: 56±28; OB: 125±35; OBL: 73±20, * p < 0.05). Interstitial collagen and MyHC isoforms were analyzed by Western blot. Statistical analysis: ANOVA and Bonferroni test. Evaluation of the site of S-nitros(yl)ation confirmed that MIF was S-nitros(yl)ated of post-ischemic hearts using the biotin-switch technique and mass spectrometry identified cysteine 81 to be site-specifically modified by S-nitros(yl)ation, whereas the CXXC-derived cysteine residues of MIF remained unaffected. SNO detection in the CXXC-derived cysteine residues of MIF remained unaffected. SNO detection in vivo model. In conclusion, we have identified S-nitrosylation of the A1-R as a site-specifically modified by S-nitrosylation, whereas the CXXC-derived cysteine residues of MIF remained unaffected. SNO detection in vivo model. In conclusion, we have identified S-nitrosylation of the A1-R as a site-specifically modified by S-nitrosylation, whereas the CXXC-derived cysteine residues of MIF remained unaffected. SNO detection in vivo model. In conclusion, we have identified S-nitrosylation of the A1-R as a site-specifically modified by S-nitrosylation, whereas the CXXC-derived cysteine residues of MIF remained unaffected. SNO detection in vivo model. In conclusion, we have identified S-nitrosylation of the A1-R as a
Cytodines and hormones in cardiomyopathy


Background: It has been shown that cardiac myocyte apoptosis is an important mechanism for ventricular remodeling after myocardial infarction. Present data showed an upraising formation of reactive oxygen species (ROS) in nonischemic myocardium. Uncoupling of eNOS seems to be one of the key mechanisms in this process of reperfusion damage and myocardial remodeling after infarction. It remains unclear if eNOS uncoupling with upraising ROS-formation leads to reduced myocardial remodeling.

Methods: Wistar rats were treated with the BH4-analogue Sapatroperi dine-dihy drochloride (5 mg/kg i.p.) or saline (NaCl). Animals were subjected to MI by LAD ligation in situ under general anesthesia. Westernblots for pro- and antiapoptotic pathways and histological sections were performed.

Results: Two days after MI, animals treated with saline showed significant higher antiapoptotic protein levels as a result of increased nitrosylation in contrast to sham-operated animals (LIG +12%, p=0.0003). Animals also showed a significant increased activation of proapoptotic signalling pathways (cleaved caspase 3: LIG +214%, p=0.002; reduced of bcl-2/bax-ratio to proapoptotic box: LIG -30%, p=0.002, decrease of procaspase 3: LIG -13%, p=0.004). Also significant increases in TUNEL- and M30-antibody-positive apoptotic cardiomyocytes were found in the ischemic posterior myocardial wall of LIG-animals. Pretreatment with BH4-analogue leads to a stabilisation of eNOS with reduced nitrosylation as an indicator for reduced ROS-production (LIG +4% vs. Sham, p=n.s.). Activation of caspase 3 was totally inhibited through pretreatment and bcl-2/bax-ratio was increased up to the level of sham-operated animals. Furthermore, the antiapoptotic protein kinase B/ AKT was significantly more phosphorylated in pre-treated animals after myocardial infarction (LIG +49%, p=0.001), showing an activation of antiapoptotic pathways in pre-treated animals. M30 and TUNEL-staining indicated a reduced number of apoptotic cardiomyocytes in nonischemic myocardium.

Conclusion: Inhibition of eNOS-uncoupling with resulting reduced ROS-formation leads to an inhibition of apoptosis in the nonischemic area with the counterbalance of a reduced activation of proapoptotic pathways versus an activation of antiapoptotic pathways are possible mechanisms. It is postulated, that the reduction of apoptotic myocardial results in increased survival of cardiomyocytes contributing to a reduction of remodeling in the nonischemic myocardium.

P817

Antibody against oncostatin M receptor-beta attenuates left ventricular remodeling in an inflammatory cardiomyopathy

P. Poelung1, P. Gajawada2, H. Loercher2, S. Schimankii2, W. Pees3, S. Kostin4, T. Kubin5, H. Warnecke1, T. Braun2, 1Schuchtermann Clinic, Bad Rothenfelde, Germany; 2Max-Planck-Institute, Bad Nauheim, Germany

Purpose: Heart failure (HF) is often the consequence of damage to the myocardium during which remodelling and de-differentiation of cardiomyocytes is observed. During the course of the disease the infiltration of the myocardium with inflammatory cells is well recognized and becomes nowadays a major focus of research. We hypothesized that oncostatin M (OSM) a cytokine mainly restricted in its expression to infiltrating macrophages is a major contributor to heart failure. In addition, the exceptionally high level of the OSM receptor-1 (OIR) on cardiomyocytes is described to be upregulated in heart failure.

Methods: We used a mouse model of cardiomyopathy based on the heart specific expression of monocyte chemoattractant protein-1 (MCP-1) leading to massive infiltration by macrophages and HF after 6 months. Samples from mice and from patients with endstage HF were analyzed by Western blot (WB), confocal microscopy, ZDE-analysis combined with mass spectrometry (2DE-MS) and immunofluorescence (IF) at various time points. Functional analysis was performed by cine MRI. The role of OSM was assessed by blocking OIR by in vivo in MCP-1 mice.

Results: Mice showed ventricular dilatation and heart failure as well as massive infiltration of the myocardium with macrophages. 2-DE-MS and WB analysis revealed more than 10 re-expressed proteins such as ANP, desmin and α-smooth muscle actin. Confocal microscopy showed clear localization of re-expressed proteins to cardiomyocytes. We found upregulation of the OSM receptor on the OIR axis coinciding with de-differentiation and remodeling of cardiomyocytes in failing hearts. Activation of the OSM signaling pathway correlated with enhanced MEK/Erk signaling. Blockade of OIR with a neutralizing antibody or genetic deletion of the

CME. In addition, collagen volume fraction in glucocorticoid therapy group was markedly lower than that in CME group.

**Conclusions:** Glucocorticoid therapy could improve early cardiac function after CME, and its mechanism could be associated with TGF-β1/Smad3 and DTGF suppression.

P818

The association between different monocyte subsets and coronary collateral development

U. Arslan1, I. Kogacoglu2, M.Y. Falay3, M.M. Balcı3, S. Duygu4, A. Korkmaz2. 1Samsun Education and Research Hospital, Samsun, Turkey; 2Samsun Education and Research Hospital, Samsun, Turkey; 3Ankara Numune Education and Research Hospital, Ankara, Turkey

Purpose: Increased circulating monocyte count has been found to be related with glycemic control and cardiovascular disease. The purpose of the present study was to find out any possible relationship between the levels of circulating monocyte subsets and coronary collateral development.

Methods: Patients who had >95% stenosis of at least one major coronary artery in their first coronary angiogram were included consecutively in this study. Coronary collateral development was graded as good and poor according to Cohen-Rentrop method. Blood samples underwent cytometric analysis for determination of monocyte subsets.

Results: Out of 105 patients; 55 had good, 50 had poor coronary collateral development. When the baseline characteristics were compared, the monocyte subset distribution was significantly higher in the good collateral group (p=0.01). When multivariate analysis was performed, increased CD14+CD16– monocytes (per mm3) was still significantly associated with good collateral development.

**Conclusions:** Our present results are the first to show a significant association between increased circulating CD14+CD16– monocyte levels and good coronary collateral development. Further studies are needed to better understand the relationship between different subsets of monocytes and collateralization.
Oligo-improved LV function and attenuated progressive LV chamber dilatation. De-differentiation and remodeling was markedly reduced demonstrating the key role of the OSAM/QO axis. In HF patients we observed a significant increase of OSAM and OSAM in parallel with a re-expression of de-differentiation markers in cardiomyocytes.

**Background and objectives:** Inflammatory cells and cytokines contribute to myocardial and vascular remodeling. The role of TRIF-domain-containing adapter-inducing interferon-λ (TRIF) and interferon regulator factor-3 (IRF3)-dependent inflammatory signaling during myocardial hypertrophy is incompletely understood.

**Methods and results:** Afterload-induced myocardial remodeling induced by trans-aortic constriction (TAC) in C57Bl/6J wildtype (WT) and in C57Bl/6J TRIF−/− mice was compared to sham surgery (sham). mRNA-expression of TRIF-dependent cytokines TNFa, IL6 and MCP1 was persistently increased in WT mice after 16 h, 3 d, 7 d and 35 d following TAC. Similarly, gene expression of TRIF-dependent cytokines (Ccl2, Ccl11, CXCL10, F4/80 macrophage) was enhanced compared to sham-operated controls. In contrast, in TRIF−/− mice, expression of Ccl2, Ccl11 and F4/80 macrophage was unchanged 7 d after TAC, while myD88-dependent cytokines increased similarly to WT. TRIF−/− mice showed reduced CD3 T-cell (8.1±1.3-fold vs. sham, p<0.001) and F4/80 macrophage (10.4±2.0-fold vs. sham, p<0.001) infiltration following TAC, compared to WT mice (12.0±3.0-fold p<0.001), and 24±4.0-fold (p<0.001) in WT vs. p<0.005 TRIF−/− vs. WT. Cardiomyocyte size increased similarly in TRIF−/− (130±6%, p<0.01) and in WT animals (119±5%, p<0.05) relative to sham mice. However, left ventricular (LV) posterior wall thickness (echocardiography) afterload-induced left ventricular hypertrophy (LVHT) (130±9%, p<0.05, and 131±11%, respectively) was significantly reduced in TAC-WT mice (74±2%, p<0.01 compared to their sham controls). The number of cardiomyocytes/mm² was reduced in WT following TAC (54±6%, p<0.005, but not in TRIF−/− mice (83±1%, p=ns), but significantly reduced in TAC-WT mice (74±2%, p<0.01 compared to their sham controls). The number of cardiomyocytes/mm² was reduced in WT following TAC (54±6%, p<0.005, but not in TRIF−/− mice (83±1%, p=ns), but significantly reduced in TAC-WT mice (74±2%, p<0.01 compared to their sham controls). The number of cardiomyocytes/mm² was reduced in WT following TAC (54±6%, p<0.005, but not in TRIF−/− mice (83±1%, p=ns), but significantly reduced in TAC-WT mice (74±2%, p<0.01 compared to their sham controls). The number of cardiomyocytes/mm² was reduced in WT following TAC (54±6%, p<0.005, but not in TRIF−/− mice (83±1%, p=ns), but significantly reduced in TAC-WT mice (74±2%, p<0.01 compared to their sham controls). The number of cardiomyocytes/mm² was reduced in WT following TAC (54±6%, p<0.005, but not in TRIF−/− mice (83±1%, p=ns), but significantly reduced in TAC-WT mice (74±2%, p<0.01 compared to their sham controls).

**Conclusion:** TRIF-dependent inflammatory signaling plays an important role in the regulation of fibrosis and capillarisation during pressure overload-dependent cardiac hypertrophy.

**P818**

**STIMULATING ANTI-ß1-RECEPTOR ANTIBODIES AND KIDNEY FUNCTION: RENO-CARDIAC CROSS TALK AND ITS RELEVANCE FOR WORSENING CARDIAC FUNCTION**

S. Hartmann1, R. Schneider2, C. Held2, C. Zechmeister1, C. Bitterer1, M.J. Lohse1, G. Erit2, R. Jahns1, V. Bovin1, 1Institute of Pharmacology and Toxicology, Wuerzburg, Germany; 2Department of Internal Medicine I, Nephrology, Wuerzburg, Germany; 3Department of Internal Medicine I, Cardiology, Wuerzburg, Germany.

Stimulating antibodies directed against the beta1-adrenocceptor (beta1-ABs) induce cardiac dilatation and failure in rats. After immunization, antibody-positive animals in the first 6 months develop a hypertensive phenotype (increase in blood pressure, hypertrophy), which then evolves into a dilated cardiomyopathic phenotype. As beta1-receptors (beta1-AR) are also highly expressed in the kidneys, we hypothesized that the early hypertensive phenotype might -in part- also rely on a stimulation of renal beta1-AR.

**Methods:** Cardiomyopathy was induced in n=40 Lewis rats by monthly immunization with beta1-ECII/GST fusion proteins. Antibody-titers & cardiac function were followed every 3 months by ELISA and by echocardiography, respectively. In HF patients we observed a significant increased levels of MSH-OE on physiological age-related cardiac growth in mice. Second, we examined the effects of a stable melanocortin analogue (MT-II) on pressure-overload-induced cardiac hypertrophy. We subjected 8-week-old C57Bl/6J mice to pressure-overload by transverse aortic constriction (TAC) and randomly assigned the mice to receive daily i.p. injections of either saline or MT-II (0.3 mg/kg) for 6 weeks starting 2 weeks after surgery.

**Results:** At the age of 6 months, MSH-OE mice had lower heart weight (n=11) with maintained cardiac function compared to their age-matched wild-type littermates (n=15) while no differences in heart weight were noted at the age of 3 months, indicating that melanocortin overactivity restrains age-related cardiac growth. Eight weeks of pressure-overload induced significant left ventricular (LV) hypertrophy in saline-treated TAC mice (n=15) compared to sham-operated con-
Evaluation of the national institute for clinical excellence mini-GRACE risk scores for acute myocardial infarction: the myocardial ischaemia national audit project (MINAP) 2003 to 2009

A.D. Simms1, S. Reynolds1, P.D. Baxter1, J.R. Pearson2, P.D. Batin2, J.I. Wilson3, H.M. West1, K.A.A. Fox1, A.S. Hall1, C.P. Gale1. 1University of Leeds, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; 2Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; 3Pinderfields General Hospital, Wakefield, United Kingdom; 4University of Edinburgh, Centre for Cardiovascular Science, Edinburgh, United Kingdom

Purpose: Comparative provider performance for acute coronary syndromes often requires patient level adjustment. The GRACE risk score considers case mix; however, national registers, such as the Myocardial Ischaemia National Audit Project (MINAP) do not collect all 8 GRACE variables. We investigated performance of the mini-GRACE (MG) and adjusted mini-GRACE (AMG) models, developed by the National Institute for Clinical Excellence (NICE), for use in MINAP.

Methods: In-hospital and 6-month all-cause mortality was regressed on predictors using scoring system and coefficients described by the GRACE investigators to generate the MG and AMG models. The MG model predictors included age, admission systolic blood pressure and heart rate; cardiac arrest, elevated troponin and ST deviation on presenting ECG. The AMG model in addition included an estimation of renal failure and heart failure. For this, a creatinine below 200 μmol/L was given a score of 5, and a creatinine above 200 μmol/L a score of 20, and patients who were prescribed a loop diuretic scored 20 points. Calibration, accuracy, discrimination and clinical reclassification for in-hospital and 6-month all-cause mortality models MG and AMG were studied in 462650 patients hospitalized with acute cardiac infarction (AMI) from 1 January 2003 to 30 September 2009.

Results: There were 308324 MG and 134304 AMG complete cases. In-hospital mortality model calibration, Hosmer-Lemeshow goodness of fit test (H-L), for MG and AMG was: STEMI P=0.25 and, P=0.03; NSTEMI P=0.96 and, respectively. MG and AMG model accuracy, Brier score: STEMI 0.05 and 0.05, NSTEMI 0.05 and 0.05; and discrimination, C-statistic (95%CI): STEMI 0.90 (0.89-0.91), NSTEMI 0.86 (0.85-0.86) and 0.87 (0.86-0.87), respectively. Net reclassification index (NRI) for AMI: 7.5%. Six month mortality MG and AMG model calibration: STEMI, P=0.01 and P=0.04 and, P=0.01, respectively. MG and AMG model accuracy: STEMI 0.09 and 0.08, NSTEMI 0.12 and 0.10; and discrimination: STEMI 0.84 (0.83-0.84) and 0.85 (0.85-0.86), NSTEMI 0.80 (0.79-0.80) and 0.82 (0.81-0.82), NRI for AMI: 12.5%.

Conclusions: The MG and AMG risk scores for in-hospital and 6-month mortality show good performance in the wider spectrum of AMI phenotypes and clinical subgroups. Overall the AMG model performed better across performance indices, but was limited by the number of complete cases.

P823 Inverse relationship between treated cardiovascular risk factors and mortality among patients with first-time myocardial infarction - a nationwide study

A.M. Olsen1, M. Lamberts1, J. Lindhardsen1, C. Andresson1, F. Folke1, S. Abitz Winther1, E. Kolber1, C. Torp-Pedersen1, G. Gislason1. 1Department of Cardiology, Copenhagen University Hospital, Gentofte, Denmark, Hellerup, Denmark; 2Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark

Purpose: Diabetes, hypertension and dyslipidaemia are known risk factors for a poor prognosis following myocardial infarction (MI). However, with more efficient treatment these risk factors may not be prognostic important. We conducted this study to investigate the association between the number of treated cardiovascular disease (CHD) risk factors and the prognosis among a population of patients with first-time MI.

Methods: Patients aged ≥30 years admitted with first-time MI during 1997-2007 were identified by individual-level-linkage of nationwide registers in Denmark. Use of antidiabetic drugs, statins and antihypertensive drugs 180 days before MI was used as proxy for prevalent diabetes mellitus, dyslipidaemia and hypertension, respectively. The association between number of treated CHD risk factors and 30 days mortality were estimated by age stratified logistic regression analyses.

Results: A total of 128,418 patients were admitted with first-time MI, 31.6% had at least 1 of the 3 risk factors. There was an inverse relationship between number of CHD risk factors and 30 days mortality (Odds Ratio (OR), 95% confidence intervals [95% CI] – 1 risk factor, OR 0.75 [0.72-0.77], 2 risk factors, OR 0.63 [0.59-0.66] and 3 risk factors, OR 0.43 [0.38-0.49]). We stratified the analyses due to interaction with age (figure).

INTERESTING NEWS FROM LARGE EPIDEMIOLOGICAL STUDIES AND REGISTRIES

P822 Clockwise rotation was positively and counter-clockwise rotation was inversely associated with cardiovascular mortality in Japanese (24 year follow-up of nippon data80)

Y. Nakamura1, T. Okamura2, A. Higashiyama3, M. Watanabe4, A. Kadota5, T. OhiKubo5, K. Mura5, F. Kasagi6, A. Okayama7, H. Ueshima8 on behalf of NIPPON DATA 80 Research Group. 1Kyoto Women’s University, Kyoto, Japan; 2Keio University, Tokyo, Japan; 3Hyogo College of Medicine, Nishinomiya, Japan; 4National Cardiovascular Center, Suita, Osaka, Japan; 5Shiga University of Medical Science, Otsu, Japan; 6Radiation Effects Association, Tokyo, Japan; 7First Institute for Health Promotion and Health Care, Tokyo, Japan

Purpose: Although clockwise (CW) and counter-clockwise rotation (CCW) are distinct findings of ECG, their prognostic significance is almost never studied.

Methods: We studied prognostic values of CW and CCW on total, cardiovascular disease (CVD) and subtype mortality using the NIPPON DATA80 database with a 24-year follow-up. At the baseline in 1986, data were collected on study participants, ages 30 years and over, from randomly selected areas in Japan. We followed 9,067 participants (44% men, mean age 51).

Results: During the 24-year follow-up, there were 2,581 total, 887 CVD, 173 CHD, 173 HF, and 411 stroke mortality. The multivariate-adjusted hazard ratio (HR) using the Cox model including biochemical and other ECG variables revealed that CW was significantly positively associated with heart failure (HF) in men and women combined (HR=1.79, 95% confidence intervals [CI]: 1.13-2.83, P=0.013), CVD in men and combined (HR=1.49 [1.12-1.98], P=0.007 in men; HR=1.28 [1.02-1.59], P=0.030 in combined), and total mortality in men and combined (HR=1.19 [1.00-1.49], P=0.049 in men; HR=1.15 [1.01-1.32], P=0.045 in combined). CCW was significantly inversely associated stroke combined in (HR=0.77 [0.62-0.98], P=0.017), CVD in men and combined (HR=0.74 [0.59-0.94], P=0.011 in men; HR=0.81 [0.70-0.94], P=0.006 in combined), and total mortality in women (HR=0.87 [0.77-0.98], P=0.023).

Conclusions: We found a significant positive association of CW, and a significant inverse association of CCW with CVD mortality in men, and women combined, independent of confounding factors including other ECG changes.

P824 Pulse wave velocity as a determinant of coronary artery disease in patients with essential hypertension: Data from a Greek 6-year-follow-up study

K. Dimtriadis1, C. Tsiofou2, A. Kasiakogias, M. Giakoumis, I. Batsakis, K. Kintis, V. Tzamou, I. Andrikou, C. Pitsavos, C. Stefanadis. 1First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece

Purpose: Although arterial stiffening is related to atherosclerosis progression, its prognostic role in hypertension is not fully elucidated, while augmented left ventricular mass index (LVMI) is linked to adverse outcome. The aim of the present study was to compare the predictive role of arterial stiffness and LVMI for the in-
Multiple siblings or mother with myocardial infarction are primarily responsible for familial clustering - a nationwide study

M. Nielsen, C. Andersson, C. Törp-Pedersen. Gentofte hospital, department of cardiology, Gentofte, Denmark

Purpose: The importance of parents and siblings in familial clustering of myocardial infarction (MI) is controversial. We performed the hitherto largest study of familial clustering of MI in first-degree relatives.

Methods: This is a nationwide register-based cohort study. The study population was combined from two large databases, the Danish civil registration system and The Danish National Registry on Patients. For siblings the first sibling to have a MI would be defined as the proband. The date of the MI of the proband would be the start of risk time for the rest of the siblings. If more than 1 sibling in a sibship had a MI, a new analysis was made (without including the first proband) and the second sibling to have a MI would be the new proband and the rest of the siblings in the sibship would start a new risk time, from the date of the new proband’s MI. Further when a parent was the proband the children’s risk time would start on the date of the parent’s MI. We used the Poisson model to calculate the relative risks for siblings or children of the proband. The date of the MI of the proband was compared to the date of the MI of the proband.

Results: We identified 10181 siblings to 7254 cases of MI. For 101 sibships more than one sibling had a MI. Furthermore we identified 54164 offspring of 29147 maternal MI cases (see table).

Conclusion: Familial clustering of MI is particularly strong in the presence of a maternal MI and multiple siblings with MI.

Evidence for obesity paradox in patients with acute coronary syndromes - a report from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR)

O. Angerås1, P. Albertsson1, K. Karason1, T. Ramunddal1, G. Matejka2, S. James2, B. Lagerqvist2, A. Rosengren1, E. Omerod1, on behalf of SCAAR-registry.1 Sahlgrenska Academy, University of Gothenburg, Dept. of Molecular & Clinical Medicine/Cardiology, Gothenburg, Sweden, 2Uppsala Clinical Research Center, Department of Medical Sciences, Uppsala, Sweden

Background: The ‘obesity paradox’ (OP) refers to epidemiological evidence that obesity, as compared to normal weight, is associated with contrainuitive improvement in health in a variety of disease conditions. The aim of this study was to investigate the relationship between body mass index (BMI) and mortality in patients with acute coronary syndromes (ACS).

Methods: We extracted data from the Swedish Coronary Angiography and Angioplasty Registry (SCAAR) and identified 64436 patients who underwent coronary angiography due to acute coronary syndrome. In 54419 (84.4%) patients a significant coronary stenosis was identified while 1017 (15.6%) patients had no significant stenosis. Patients were divided into nine different BMI-categories, with the group with significant stenosis further subdivided according to treatment i.e. medical therapy, percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG). Mortality for the different subgroups during a maximum of 3 years was compared using Cox proportional hazards regression with the leanBMI category (21.0 kg/m² – 23.5 kg/m²) as the reference group.

Results: Regardless of angiographic findings (significant or no significant CAD) and treatment decision the overweight group (BMI >18.5 kg/m²) had the greatest risk for mortality. In medical therapy and PCI treated patients with modest overweight (BMI-category 26.5–28 kg/m²) had the lowest risk of mortality (HR 0.52; 95% CI 0.34–0.80 and HR 0.64; 95% CI 0.50–0.81, respectively). When studying BMI as a continuous variable in patients with significant CAD the adjusted risk for mortality decreased with increasing BMI up to ~35 kg/m² and then increased. In patients with significant CAD undergoing CABG and in patients with no significant CAD there was no difference in mortality risk in the overweight groups compared to the normal weight group.

Conclusions: In this large and unselected group of ACS patients the relation between BMI and mortality was U-shaped, with the nadir among overweight or obese patients, and underweight patients having the highest risk. These data strengthens the concept of OP substantially.
Effect modification of dietary n-3 fatty acids on cardiovascular mortality risk by resting heart rate in Japanese general population: NIPPON DATA80

T. Hisamatsu1, K. Miura2, T. Ohtsuki2, N. Okuda2, Y. Murakami2, N. Miyagawa2, M. Hori3, T. Okamura4, A. Okayama3, H. Ueshima4 on behalf of NIPPON DATA80 Research Group. Cardiovascular and Respiratory Medicine, Shiga University of Medical Science, Otsu, Japan; 2Health Science, Shiga University of Medical Science, Otsu, Japan; 3First Institute for Health Promotion and Health Care, Tokyo, Japan; 4Preventive Medicine and Public Health, Keio University, Tokyo, Japan

Purpose: Multiple lines of evidence have shown that a higher dietary intake of n-3 fatty acids (FAs) reduces the risk of cardiovascular diseases (CVDs). Meanwhile, increased resting heart rate (RHR) has been reported to be an independent predictor of CVDs. Identification of measures for preventing CVD risk associated with increased RHR is therefore of considerable clinical and public health importance. We assessed the hypothesis that a higher n-3 FAs intake would attenuate the elevated cardiovascular mortality risk by increased RHR.

Methods: A total of 8,807 community-dwelling individuals (55.7% women, mean age of 48.3 years), none of whom had anti-hypertensive drugs and prior CVDs, from a rural area in central Japan were included in the analysis. The primary endpoint was cardiovascular mortality, and secondary endpoint was cardiac mortality during a mean follow-up of 20.4±6.1 years. Dietary n-3 FAs intake was estimated using a modified household food weighing method. The RHR measurement was obtained from 3 consecutive intervals between R waves on 12-lead electrocardiography (ECG). Cox models were used to calculate hazard ratios (HRs) per 10 beats per minute of RHR (95% confidence interval [95% CI]) adjusted for potential confounders, including ECG findings (left ventricular hypertrophy, suspected coronary heart disease) and nutritional parameters (saturated FAs, sodium and potassium intake, and fiber intake).

Results: During a median follow-up of 19.4 years, 617 individuals died from CVDs, and of these, 314 were from cardiac causes. Among men, in the lowest (<0.93/100 kcal) tertile of n-3 FAs group, increased RHR was associated with elevated cardiovascular mortality (HR, 1.19; 95% CI, 1.02–1.39), and cardiac RHR (HR, 1.29; 95% CI, 1.01–1.63). In contrast, in the medium (0.93–1.19/100 kcal) and high (1.20–2.00/100 kcal) tertiles, both HRs did not show statistically significant for CVD (HR, 0.74–1.14 and HR, 0.91; 95% CI, 0.72–1.15, respectively), and cardiac mortality (HR, 0.90; 95% CI, 0.56–1.21 and HR, 0.99; 95% CI, 0.69–1.43, respectively). For interaction between n-3 FAs and RHR was significant in cardiovascular mortality (P=0.029) and marginally significant in cardiac mortality (P=0.069), including the first 5 years of follow-up did not substantially alter the results. Among women, those relationships were not observed.

Conclusions: An elevated risk of CVD, and cardiac mortality related to increased RHR would be attenuated in individuals with higher dietary intake of n-3 FAs in Japanese men, suggesting that a higher n-3 FAs intake may prevent long-term mortality risk associated with increased RHR.

P831 Clinical predictors of the risk of AF - implications for monitoring

K.J. Brunner1, T.J. Burch2, C.M. Mullin3, S. Mahaptra3, 1St Jude Medical, St. Paul, United States of America; 2Intermountain Medical Center, Murray, United States of America; 3The Integra Group, Brooklyn Park, United States of America

Purpose: Asymptomatic atrial fibrillation (AF) can be a risk factor for stroke. Screening for AF with long-term monitoring to identify patients for stroke prevention may not be cost effective. We sought to create a risk score based on understood risk factors for predicting AF that could be considered for use in determining who to screen for AF.

Methods: Analysis was based on the literature cited in the 3rd Atrial Fibrillation Competence Network/European Heart Rhythm Association consensus conference. Validated risk factors for AF as defined there included age, coronary artery disease, diabetes, gender, heart failure, hypertension, and valvular disease. 17 manuscripts were reviewed of which 16 are included in the analysis.

The log odds ratio (OR) for AF from each study was used as the summary statistic in a meta-analysis, fit separately for each factor; from which a risk score was created and prospectively tested against a cardiac database.

Results: The risk score was derived from a total of 116,601 participants (61.9% female). The overall incidence of AF was 6.9%. In univariate analysis the largest risk factor was age. The meta-analytic OR of the risk factors for AF were all significant (all p<0.001) and are listed in the table below.

The risk score was validated against 34,788 patients’ records. Over 2142±1602 days, a total of 4402 (12.7%) patients had AF. A risk analysis, the risk score for AF was 1.70, 2.48, 3.41, 4.48 and 7.43 (all p<0.001) with risk scores of 1, 2, 3, 4, 5, 6, 7 respectively.

P832 Subclinical target organ damage and cardiovascular risk: can the subscORE?

D. Terentes-Printzios1, C. Vlachopoulos2, G. Vrysovalis1, K. Zafiriou3, N. Katsanos1, I. Skorda4, I. Andreakos5, I. Papatheodorou5, A. Ioannidis6, I. Vlachos7, C. Koutoudis8, I. Myaichou8, 1Department of Cardiology, Athens University, Athens, Greece; 2Department of Cardiology, University of Athens, Athens, Greece; 3Department of Cardiology, Athens University, Athens, Greece

Purpose: Hypertension is associated with higher cardiovascular risk as well as several markers of subclinical target organ damage (TOD). The present study investigated the relationship between Systolic Coronary Risk Evaluation (SCORE) and subclinical markers of TOD in never-treated hypertensives.

Methods: We enrolled 1223 consecutive essential hypertensives (mean age 53±0.3, 56.6% males, 726 males) without known cardiovascular disease (CVD). Markers of subclinical TOD were assessed by electrocardiography, echocardiography, ankle-brachial index (ABI), funduscopy, and auscultation. In univariate analysis, the risk score for AF was calculated using a composite score for AF in these high-risk patients will help reduce the risk of stroke.

Conclusions: Common risk factors can easily identify people at risk of AF who are thus at risk for stroke. Future studies should identify if long-term monitoring in these high-risk patients will help reduce the risk of stroke.

P833 Subclinical target organ damage and cardiovascular risk: can the subscORE?

D. Terentes-Printzios1, C. Vlachopoulos2, G. Vrysovalis1, K. Zafiriou3, N. Katsanos1, I. Skorda4, I. Andreakos5, I. Papatheodorou5, A. Ioannidis6, I. Vlachos7, C. Koutoudis8, I. Myaichou8, 1Department of Cardiology, Athens University, Athens, Greece; 2Department of Cardiology, University of Athens, Athens, Greece; 3Department of Cardiology, Athens University, Athens, Greece

Purpose: Hypertension is associated with higher cardiovascular risk as well as several markers of subclinical target organ damage (TOD). The present study investigated the relationship between Systolic Coronary Risk Evaluation (SCORE) and subclinical markers of TOD in never-treated hypertensives.

Methods: We enrolled 1223 consecutive essential hypertensives (mean age 53±0.3, 56.6% males, 726 males) without known cardiovascular disease (CVD). Markers of subclinical TOD were assessed by electrocardiography, echocardiography, ankle-brachial index (ABI), funduscopy, and auscultation. In univariate analysis, the risk score for AF was calculated using a composite score for AF in these high-risk patients will help reduce the risk of stroke.

Conclusions: Common risk factors can easily identify people at risk of AF who are thus at risk for stroke. Future studies should identify if long-term monitoring in these high-risk patients will help reduce the risk of stroke.

Conclusions: Our findings support the close relationship between SCORE and TOD in hypertension, as well as, the predictive ability of SCORE for TOD. Moreover, they highlight the significance of PWV in prediction of cardiovascular risk.
Investigation of sex differences in noninvasive vascular function

R. Schnabel1, P.M. Biener1, S. Wilde1, C.R. Simning1, F.M. Ojeda1, E. Lobis1, A. Warnholz1, T. Munzler1, S. Blankenberg1, P.S. Wilde1,2

1University Heart Center Hamburg, Clinic for General & Interventional Cardiology, Hamburg, Germany; 2Johannes Gutenberg University Mainz (University Hospital of Mainz), Mainz, Germany

Background: Sex differences in cardiovascular disease susceptibility have been reported, however, the relation of noninvasive vascular function measures to sex, female sex hormones, menopausal status and reproductive history is little understood.

Methods: We assessed menstrual cycle, reproductive history and simultaneous measurement of flow-mediated dilation (FMD) of the brachial artery and peripheral arterial tonometry in 454 women (mean age 40.4 ± 16.1 years) and 100 men (mean age 44.7 ± 15.3 years). Plasma estradiol, progesterone, luteinizing hormone, and follicle stimulating hormone were measured.

Results: In regression analyses, endothelial function was blunted in men compared to women irrespective of menopausal status and adjustment for classical cardiovascular risk factors and sex hormone concentrations. In women, vascular reactivity changed during the menstrual cycle with a mid-cycle peak and correlated with estradiol concentrations for FMD, r=0.13, P=0.066, and inversely with progesterone for baseline pulse amplitude, r=−0.14, P=0.035 and brachial artery diameter. Age at menarche was related to brachial artery diameter, r=−0.10, P=0.035. Multivariable-adjusted regression models showed a relation of estradiol with FMD, beta 0.658, 95% CI 0.084 to 1.232, P=0.025 in women. Age at menarche (beta 0.070, 95% CI 0.039 to 0.101, P=0.001) and breastfeeding duration (beta -0.006, 95% CI -0.011 to -0.001, P=0.036) were related to brachial artery diameter. Age at menarche was related to FMD (beta -0.455, 95% CI -0.886 to -0.023, P=0.039).

Conclusions: We observed sex differences for noninvasive conduit artery and peripheral arterial function with better vascular reactivity in women. Differences were not fully explained by female sex hormones and menopausal status. Age at menarche and duration of breastfeeding were also related to vascular function.

Genetic polymorphisms associated with coronary artery disease in women with previous low cardiovascular risk by traditional risk factors

A. Pereira1, R. Palma Dos Reis2, B. Silva1, S. Gomes1, H. Cafe1, S. Freitas1, A.I. Freitas1, A. Brehm1, J.J. Araújo1, M. Mendonca1

1Hospital Universitário de Santa Maria, Porto, Portugal; 2New University of Lisbon, Faculty of Medical Sciences, Lisbon, Portugal; 3Madeira University, Funchal, Portugal

Several studies have attempted to link genetic polymorphisms with the onset of coronary artery disease (CAD). The added risk from each polymorphism is relatively low, with an Odds Ratio (OR) of about 1.1 or 1.2, much lower than the usually associated with traditional risk factors (TRF). Therefore, it becomes relevant to understand the cause of vascular disease, in patients without TRF and try to assess genetic factors associated with these situations.

Objective: The aim of this study was to evaluate genetic factors associated with vascular disease development in patients without TRF.

Methods: A case-control study was performed. This study included 1032 individuals. 195 consecutive coronary patients without major cardiovascular risk factors (without diabetes, smoking habits, hypertension or severe dyslipidemia), as previously described, were used as cases. A control group was included, to represent the major traditional risk factors. The control group was selected according to sex, age and sex hormone status to match the case group.

Results: In patients with low cardiovascular risk, only three polymorphisms, namely: PCSK9 AA (OR=1.94, p=0.011); rs11330349 CC (OR=1.49, p=0.017) and PON 55 MM (OR=1.49, p=0.050) have shown an increased risk of CAD. The homoyguous wild genotypes were protective. On the other hand, the polymorphism normally associated with CAD, ACE DD genotype, was found to be not associated with CAD, suggesting that its mechanism of action may depend on the traditional risk factors.

Conclusions: The present study discloses some polymorphic variants associated with CAD in women without previous cardiovascular disease, in patients without major traditional risk factors and, apparently, low risk. In these really high risk patients, it will be important, in the future, to define early intervention preventive programs.

Who is at low risk for cardiovascular disease? An assessment of different definitions

A. Gabioud1, G. Waebber1, P. Vollenweider1, P. Marques-Vidal1

1University Institute of Social and Preventive Medicine Lausanne (IUMSP), Lausanne, Switzerland; 2University Hospital Center Vaudois (CHUV), Lausanne, Switzerland

Purpose: To assess the prevalence and trends of low cardiovascular risk factor (RF) profiles in the Swiss population according to different definitions.

Methods: Population-based cross-sectional study of 6170 subjects (3241 women) aged 35-75 years living in Lausanne, Switzerland. Trends were assessed using data from the Swiss MONICA population surveys conducted in 1984-6 (N=3300), 1988-9 (N=3331) and 1992-3 (N=3133) and restricted to the same age group. Seven different definitions of low RF profile were used.

Results: Prevalence of low RF profile varied between 6.5% (95% confidence interval 5.9-7.1) and 9.7% (9.0-10.5) depending on the definition used. The prevalence was inversely related to the number of criteria used and higher than in other countries. Irrespective of the definition used, the prevalence of low RF profile was higher in women and in physically active participants, and decreased with increasing age or in the presence of a family history of cardiovascular disease (table). The prevalence of low RF profile increased from 3.8% (3.1-4.5) in 1984-6 to 6.7% (6.1-7.3) in 2003-6; using another definition, the results were 5.9% (5.1-6.8) and 9.7% (9.0-10.5), respectively.

Prevalence of low CVD risk

<table>
<thead>
<tr>
<th>Definition</th>
<th>1984-6</th>
<th>1992-3</th>
<th>2003-6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low RF</td>
<td>6.7</td>
<td>6.6</td>
<td>9.3</td>
</tr>
<tr>
<td>Low RF</td>
<td>9.4</td>
<td>9.5</td>
<td>9.7</td>
</tr>
<tr>
<td>Low RF</td>
<td>7.6</td>
<td>7.6</td>
<td>9.3</td>
</tr>
<tr>
<td>Low RF</td>
<td>6.6</td>
<td>6.6</td>
<td>9.7</td>
</tr>
</tbody>
</table>

Conclusions: The prevalence of low RF profile varies according to the criteria used; this prevalence is relatively high and increasing in the Swiss population, which might partly explain the low and decreasing trend in cardiovascular mortality rates.

Comparison of different cardiac risk scores for coronary artery disease in women: do female-specific risk factors matter?

A.A.E.M. Rademaker1, I. Danad1, J.G.J. Groothuis2, M.W. Heymans3, C.B. Marcu1, P. Knaapen4, Y.E.A. Appelman5, V.U. University Medical Center, Department of Cardiology, Amsterdam, 1VU University Medical Center, Department of Epidemiology and Biostatistics, Amsterdam, Netherlands

Background: The estimation of the pre-test probability of coronary artery disease (CAD) in women is often difficult, due to a different clinical presentation compared to men. Meanwhile, cardiovascular diseases remain the leading cause of death in women, urging the need for more accurate risk assessment scores. The aims of our study were to compare the accuracy of several widely used cardiac risk assessment scores in predicting the likelihood of obstructive CAD on CT coronary angiography (CTCA) in women and to explore which female-specific risk factors were independent predictors for obstructive CAD on CTCA, and if adding these factors to usual risk assessment scores would improve their accuracy.

Methods: Data was obtained from a cohort of 228 female patients undergoing clinical CAD evaluation for CT and referred for CTCA. Obstructive CAD was defined as ≥50% luminal stenosis on CTCA. Pre-test probability for CAD was calculated according to the Diamond and Forrester score, New Score, Duke Clinical Score, and the updated Diamond and Forrester score. Female specific factors were obtained using a written questionnaire. Pre-test probability scores were compared with ROC analysis.

Results: ROC analysis showed that only the New Score and the extended Diamond & Forrester model were significant predictors of obstructive CAD on CTCA in women (area under the curve [AUC] 0.67, p < 0.01; AUC 0.61, p < 0.04, respectively). Multivariable logistic regression analysis identified that gestational diabetes mellitus (GDM) and estrogen status were independent predictors of obstructive CAD when adjusted for the pre-test probability scores. The updated Diamond and Forrester score was used for Net Reclassification Improvement (NRI) analyses, since the New Score already accounts for estrogen status. Adding GDM and estrogen status to the updated Diamond and Forrester score resulted in a significant NRI (p = 0.04).

Conclusion: Adding female-specific risk factors to the cardiac pre-test probability scores significantly improves their accuracy in predicting the presence of symptomatic CAD in women.

C-Reactive Protein (CRP) and mortality to cardiovascular diseases

A. Kesaniemi1, M. Santaniemi2, O. Ukkola1

1Institute of Clinical Medicine, Department of Internal Medicine, University of Oulu; 2Oulu University, Department of Clinical Science and Technology, University of Oulu, Oulu, Finland

Uninflamed inflammation seems to be a component in the development of atherosclerotic cardiovascular diseases. Highly sensitive (hs) C-Reactive Protein (hsCRP) is a good indicator of inflammatory processes. Our aim was to determine the role of hsCRP in the prediction of cardiovascular mortality.

The study group consisted of 1019 middle-aged Finnish subjects in our randomly recruited, population-based cohort (OPERa=Oulu Project Elucidating Risk factors), initiated in 1991. Mortality was followed for 18 years up to 2009 in the national death register. hsCRP was determined using commercial Elisa kit.
Are there ethnic differences in the association between family history of cardiovascular disease and prevalent cardiovascular disease in the UK?

J. Baker, R. Mitchell, J. Pell. University of Glasgow, Glasgow, United Kingdom

Purpose: Family history of cardiovascular disease is an established risk factor for developing cardiovascular disease and provides a potential tool for identifying individuals with high cardiovascular risk. There are ethnic inequalities in cardiovascular disease prevalence in the UK, with higher coronary heart disease prevalence in Indian and Pakistani groups and higher stroke incidence in Black ethnic groups compared to the White population. The purpose of this study was to investigate whether there are ethnic differences in the association between family history of cardiovascular disease and prevalent cardiovascular disease in the UK.

Methods: Cross-sectional analysis of the Health Survey for England 2003, 2004 and 2006 was performed. This large, annual survey collects self-reported health and lifestyle information, and in 2004 contained a boosted sample of the largest multiethnic sample. This may have implications for the use of family history as a tool for identifying individuals with high cardiovascular risk as its performance may vary between ethnic groups in the UK; these findings will be relevant to audiences from other countries where this approach could also be applied. Further research is being carried out to model ethnic differences in the use of family history in screening for high cardiovascular risk.

Results: Odds ratios (ORs) were calculated to investigate the association between family history of parental cardiovascular disease and prevalent cardiovascular disease were observed in this large, annual survey collects self-reported health and lifestyle information, and in 2004 contained a boosted sample of the largest multiethnic sample. This may have implications for the use of family history as a tool for identifying individuals with high cardiovascular risk as its performance may vary between ethnic groups in the UK; these findings will be relevant to audiences from other countries where this approach could also be applied. Further research is being carried out to model ethnic differences in the use of family history in screening for high cardiovascular risk.
gression analysis, the hazard of MI after adjustment for age and sex was 1.75 (95% CI: 1.29 to 2.37, p < 0.001) for the highest (>156 mmHg) versus the lowest systolic BP quartile (<111 mmHg), and 1.59 (1.71 to 2.16, p = 0.003) for the second highest (140-155 mmHg) versus the lowest quartile. In the subset of the subjects who deceased 81 years of age or older, the hazard of MI was 1.55 (p < 0.05) for the highest systolic BP quartile, and 1.63 (p < 0.05) for the second highest quartile.

**Conclusion:** Grade 1 hypertension was associated with autopsy-determined MI in octogenarians. There was no J-curve between systolic BP and MI determined by autopsy.

### 5-HTTLPR polymorphism and stroke. Findings from WOBASZ study

**J. Piwonski**, A. Piwonska, E. Sygnowska, R. Ploski. National Institute of Cardiology, Warsaw, Poland; Medical University of Warsaw, Warsaw, Poland

**Purpose:** The carriers of short allele of 5-HTTLPR gene are more susceptible to higher secretion of norepinephrine, so they could have the higher cardiovascular risk, higher risk of repeated cardiovascular events after myocardial infarction, and higher risk of hypertension which could be associated with stroke. We try to evaluate the association between polymorphism of 5-HTTLPR and self-reported history of stroke in person aged 20-74.

**Methods:** The genotyping of 5-HTTLPR gene was made in 1823 persons, examined in the frame of WOBASZ study, in 2003-2005. The stroke history was assessed based on answers to the questionnaire. Using logistic regression analysis we evaluated the association between genotypes: at least one s allele (ss and/or sl) vs LL, and as dummy variable (ss vs sl and vs LL).

**Results:** Out of 1823 persons, 1.7% of them had the history of stroke. Persons with stroke history had the ss genotype significantly more often than LL genotype (25.0% vs 12.6%, p < 0.001). Being a carrier of at least one s allele of 5HTTLPR gene (ss or sl) compared to LL genotype was associated with more than twice higher chance of having stroke (OR stroke = 2.35, 95% CI 1.01-5.63) after adjustment for gender and age. Further analyzes showed that the history of stroke was almost 3 times more prevalent (OR stroke = 2.82, 95% CI 1.02-7.79) among ss carriers compared to LL carriers after adjustment for gender and age.

**Conclusions:** The analyzed polymorphism of 5HTTLPR was associated with higher frequency of stroke in adult Polish WOBASZ population.

### Lifetime risk algorithm identifies more patients with carotid and femoral plaques than 10 year or 30 year framingham risk algorithms

**J. Postley**, Y. Luo, N.D. Dong, J.M. Gardin. Columbia University, College of Physicians and Surgeons, New York, United States of America; University of California, Heart Disease Prevention Program, Irvine, United States of America; Hackensack University Medical Center, Hackensack, United States of America

**Background:** Cardiovascular disease (CVD) is the leading cause of death in the United States. Current CVD prediction algorithms are successful in recognizing underlying risk factors in populations but have failed to identify those at highest risk due to underlying disease. We compared a newer algorithm, “Lifetime Risk” (LR), with 10 yr and 30 yr Framingham Risk Score (FRS) algorithms in the identification of subjects with carotid or femoral plaque.

**Methods:** We studied 809 adults between ages 20 and 60 with exclusions of previous CVD: myocardial infarction, angina, stroke or claudication. Both 10- and 30-yr Framingham risk algorithms obtained from the National Statistics Office of Korea. Subjects were followed for a median of 45.5 months. Mortality data were obtained from the National Statistics Office of Korea.

**Results:** There were 649 deaths (0.7%) during the follow up. The leading cause of death was cancer. The subjects who died were significantly older, had a male predominance, and had increased levels of inflammatory markers. A significant mortality difference was identified according to the CRP and HDL-cholesterol levels. Considering both parameters jointly, subjects with a CRP > 1.4 mg/L (highest quartile) and HDL-cholesterol < 45 mg/dL (lowest quartile) were at the highest risk for all-cause mortality, even after adjusting for covariates (hazard ratio: 2.29, 95% CI: 1.83 – 2.87). After matching on the propensity score, 630 subjects with a high CRP and low HDL-cholesterol were at risk of death (hazard ratio: 2.52, 95% CI: 1.59 – 4.01). Interestingly, the joint effect of CRP and HDL-cholesterol was observed for cardiovascular as well as cancer-related mortality prediction.

**Conclusions:** Elevated CRP and low HDL-cholesterol jointly contribute to the prediction of all-cause, cancer, and cardiovascular mortality in Koreans. The interactive relationship between them in mediating inflammatory processes might explain these results.

---

**Abstract P842 - Table 1. % plaques in each group by algorithm**

<table>
<thead>
<tr>
<th>Risk group</th>
<th>10 yr FRS</th>
<th>30 yr FRS</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>58</td>
<td>7</td>
<td>16</td>
</tr>
<tr>
<td>Intermediate</td>
<td>42</td>
<td>74</td>
<td>30</td>
</tr>
<tr>
<td>High</td>
<td>40</td>
<td>19</td>
<td>54</td>
</tr>
<tr>
<td>10 yr vs 30 FRS</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>10 yr vs LS FRS</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>30 yr vs LS FRS</td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.01</td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>
Cardiovascular risk profile in high risk primary care patients not treated with lipid-lowering treatment

J. Dalongeville1, E. Bruckert2, J. Ferrières3, P.H. Delage4, F. Thomas-Delecourt5, G. Bonnelye1, S. Kowastoff1, 1Inserm U1063, Pasteur Institute of Lille, Lille, France; 2AP-HP - Hospital Pitié-Salpêtrière, Division of Endocrinology and Metabolism, Paris, France; 3University Hospital of Toulouse - Rangueil Hospital, Department of Cardiology, B, Toulouse, France; 4University Hospital of Lille, Lille, France; 5AstAzeneca France, Rueil-Malmaison, France; 6Kantar Health, Montreoule, France; 7I allie Raymond Poincaré, Thiverval, France

Purpose: There is a paucity of data on the prevalence of high cardiovascular risk (HCVR) calculated with risk algorithms within a primary prevention population. The goal of the present study was to assess cardiovascular risk profile in high risk primary care patients not treated with lipid-lowering treatment.

Methods: This observational study was conducted among a sample of 1,147 general practitioners. All men and women aged 50 and 60 years and older, with at least one additional cardiovascular risk (CVR) factor among: smoking, high blood pressure (HBP), type 2 diabetes, low HDL-c (<0.40 g/l), in primary prevention, not treated for dyslipidemia, and attending a primary care clinic over a week, were included in the study. A questionnaire filled-in by the physician enabled calculation of the cardiovascular risk and age of arteries according to SCORE risk equation. Results: 9,049 patients were included (mean age: 68 years old; men: 57%; LDLc >1.3 g/L; 57%; HDLc <0.4 g/L; 16% and control BP:44%; type 2 diabetes: 21%; smoking: 21%). According to SCORE, the prevalence of HCVR reached 50% in men and women (49% vs. 51%, respectively). Age had the highest impact on CVR estimation, other risk factors may be screened to improve the management of HCVR. The adjustment by age and gender reduced regional disparities with a 52% and 21% increase of ACE circulation levels in the ACE I/D genotypes.

Objective: The main aim of this study was to fully understand as yet. Therefore, we assessed the long-term influence of serum hemoglobin on all-cause and cardiovascular mortality in patients with atherosclerotic disease.

Methods and Results: We prospectively studied 1065 of 1286 consecutive patients with asymptomatic carotid atherosclerosis. During a median follow-up of 6.2 years, corresponding to 5551 overall person-years, 275 (25.8%) patients died. Continuous measures of serum hemoglobin displayed a significant protective effect on all-cause mortality and cardiovascular mortality (adjusted HR [increase of 1-SD of hemoglobin] 0.73, 95%CI 0.64–0.83; p<0.001, respectively). The cumulative 6-year survival rates were 61%, 79%, 80% and 81% in the first, second, third and fourth quartile of serum hemoglobin (log rank p<0.001). Patients within the first quartile (<12.9 g/dL) had a significantly increased risk for all-cause mortality (adjusted HR 1.93, 95%CI 1.46–2.54, p<0.001) and cardiovascular mortality (adjusted HR 1.68, 95%CI 1.19–2.36, p=0.003) compared to patients with higher levels.

Conclusion: Our study demonstrates a significant association with hemoglobin levels and all-cause and cardiovascular mortality in patients with carotid atherosclerosis. Furthermore, further research, in terms of randomized controlled trials, is needed to warrant these findings and to evaluate potential therapeutic interventions.

Responsible factors for the increase of ACE circulation levels, independently of I/D genotype

R. Palma Dos Reis1, B. Silva2, A. Pereira2, S. Gomes2, A.C. Sousa3, S. Freitas1, G. Guerra1, I. Omeias1, J.J. Araújo1, M. Mendonça2, 1New University of Lisbon, Faculty of Medical Sciences, Lisbon, Portugal; 2Hospital Funchal, Funchal, Portugal

Introduction: Previous works have shown that high levels of ACE circulation levels may occur with all I/D genotypes. These levels increase from II to DD genotype, although it is also known that high ACE levels represent an increased risk for coronary artery disease. However, the factors leading to this increase remain unclear.

Objective: The present study aims to evaluate the factors responsible for the increase of ACE circulation levels in the ACE I/D genotypes.

Methods: Population with 955 individuals (mean age 53.7±7.7 years; 76.8% male) were evaluated in terms of ACE plasmatic levels and ACE I/D genotype. Participants were first divided by genotype (I/D) and, afterwards then, into two groups, according with the plasmatic ACE levels above or below the median for that genotype. We evaluated the main traditional risk factors and analyzed which ones modulate the ACE circulation levels, within the same genotype.

Results: The mean of plasmatic ACE levels were 29.62 U/mL. The median for II, I/D and DD genotype were 29.62, 32.53 and 33.52 U/mL, respectively. The risk factor which significantly increased the ACE levels was smoking, with OR=1.51; p=0.003. Arterial Hypertension (AHT) and age variables presented paradoxical values, OR=0.73; P=0.003 and age was higher in patients with low ACE circulation levels than in those with high circulation ACE (p<0.005), respectively. The first case may be due to the patient’s medication which may involve ACE inhibition. Concerning the age, the individuals with low circulation ACE were older than the ones with higher levels, because angiotensin-aldosterone system may be suppressed in the elderly.

Conclusions: Smoking factor leads to a significantly increase of ACE circulation levels, independently of the genotype. This result suggests that both patients with ACE DD genotype (with higher ACE levels) or the ones presenting higher ACE values, independently of their genotype, should be advised to quit smoking. This work supports the fact that enzymatic activity and plasmatic levels may be modulated by the control of the traditional risk factors.

Serum hemoglobin predicts long-term mortality in patients with carotid atherosclerosis

G. Gollasch, M. Schilling, F.J. Mayer, A. Wannrther, R. Koppensteiner, E. Minar, G. Maurer, M. Hoike. Medical University of Vienna, Vienna, Austria

Aims: Anemia is associated with cardiovascular outcome in healthy individuals but its impact on outcome in patients with cardiovascular disease has not been fully understood as yet. Therefore, we assessed the long-term influence of serum hemoglobin on all-cause and cardiovascular mortality in patients with atherosclerotic disease.

Methods and Results: We prospectively studied 1065 of 1286 consecutive patients with asymptomatic carotid atherosclerosis. During a median follow-up of 6.2 years, corresponding to 5551 overall person-years, 275 (25.8%) patients died. Continuous measures of serum hemoglobin displayed a significant protective effect on all-cause mortality and cardiovascular mortality (adjusted HR [increase of 1-SD of hemoglobin] 0.73, 95%CI 0.64–0.83; p<0.001, respectively). The cumulative 6-year survival rates were 61%, 79%, 80% and 81% in the first, second, third and fourth quartile of serum hemoglobin (log rank p<0.001). Patients within the first quartile (<12.9 g/dL) had a significantly increased risk for all-cause mortality (adjusted HR 1.93, 95%CI 1.46–2.54, p<0.001) and cardiovascular mortality (adjusted HR 1.68, 95%CI 1.19–2.36, p=0.003) compared to patients with higher levels.

Conclusion: Our study demonstrates a significant association with hemoglobin levels and all-cause and cardiovascular mortality in patients with carotid atherosclerosis. Nevertheless, further research, in terms of randomized controlled trials, is needed to warrant these findings and to evaluate potential therapeutic interventions.

Relationship between erectile dysfunction and chronicotropic response to exercise testing in middle-aged men with essential hypertension

A. Samentzas1, C. Vlahopoulos2, D. Terentes-Pingartzios2, A. Aggelis2, A. Synodinos2, N. Iakovimidou3, A. Tzikas2, C. Stefanidis2, 1Elpis General Hospital, Athens, Greece; 2Hippokration Hospital, University of Athens, Athens, Greece

Purpose: Hypertension is the most common comorbidity in men with erectile dysfunction (ED). ED may carry an incremental predictive value for future cardiovascular diseases. Chronicotropic incompetence, or an inability to increase heart rate during exercise, independently predicts death. The purpose of this study was to evaluate the association between ED and chronicotropic index (CI) during EST in middle-aged hypertensive men.

Methods: 97 non-diabetic, hypertensive (Grade II-III) ED patients (55±9 y/o) and 32 age-matched hypertensive men without ED underwent maximal EST under the standard Bruce protocol. CI was calculated as [(HRpeak – HRrest)/220 – age × HRrest]]. The CI was considered abnormal when ≤0.8 in patients not taking beta-blockers. All men with ED underwent penile color Doppler and peak systolic velocity (PSV) was measured as an index of penile vascular disease. Reduced PSV is associated with increased risk for cardiovascular events as well as the degree and distribution of atherosclerotic lesions.

Results: ED patients had a substantially reduced CI (left plot) and a higher prevalence of abnormal CI (42 vs 21%) than nonED subjects (all p<0.01). After adjusting for age and blood pressure, CI was decreased (0.78±0.20 vs 0.89±0.19) and prevalence of abnormal CI was increased (48 vs 17%) in patients with severe arterial insufficiency (PSV <25 cm/s) compared to subjects with higher Doppler velocities (p<0.001). The combination of severe penile arterial disease (PSV<25 cm/s) with an abnormal CI (≤0.8) showed a greater effect on 10-year risk of a CV event (right plot).

Conclusion: Our findings indicate that chronicotropic response to exercise testing is significantly associated with the presence and severity of ED among hypertensive patients.
**P849 Use of national intervention coronary registry data as cardiovascular surveillance system in developing countries**

G. Saade, A. Sarkis, G. Ghanem, J. Haddad, S. Arnaout, S. Dadah, M. Moussa on behalf of The Lebanese society of cardiology. Lebanese Society of Cardiology, Beirut, Lebanon

**Purpose:** The surveillance data are needed to help countries develop, implement and evaluate their prevention programs. In developing countries, with limited capacity to conduct surveillance, lack of resources, scarce utilization of information, compiling relevant data on CVD risk factors and their outcomes from the general population is almost impossible.

Since 2004, the “Lebanese Intervention Coronary angiography Registry (LICOR)” has established to collect and analyze data from centers that undertake catheterization procedures. The level of information obtained provides, on the one hand, knowledge of the situation of CVD incidence and outcome data and, on the other hand, guarantee sustainability and utility to allocate resource for planning of health programs and interventions

**Methods:** Software has been developed specially adapted to the needs of the proposed registry, and installed in 45 centers in the country. Data were collected monthly electronically by email or bysoft copy.

**Results:** Out of an estimated 75,915 procedures performed in Lebanon in 2004-2010, 40,678 invasive procedures (54%) were recorded and analyzed, of which 3,282 were angiographies and 8,054 PCI. Patients’ ages ranged between 18 and 95 years with a mean of 60.5 years and a standard deviation (SD) of 11.7 years. The majority of patients were men (67%) who are at a significantly younger age (59.0±11.9) than women (63.1±10.9). Hyper tension was the most common reported CVD risk factor reaching a prevalence of around 62%. Similarly, smoking was reported in around 42.5% of the patient sample. The other most commonly reported conditions and CVD risk factors included, in descending order of prevalence, diabetes (30.2%), dyslipidemia (28.8%), and CVD family history (26.5%).

**Conclusions:** The success of efforts to prevent and manage CVD is dependent on the availability of surveillance data at the national levels to assist health authority, and their partners in assessing prevention and treatment priorities and guiding program planning, implementation, and evaluation. Data from national intervention coronary registry are truly nationally representative however, has unique strengths and limitations could potential used as surveillance system for CVD prevention strategies and treatment especially in developing countries.

**CARDIOVASCULAR RISK ASSESSMENT: WHAT’S NEW?**

**P850 Head-to-head comparison of cardiac high-sensitive troponin I, high-sensitive troponin T and NT-proBNP for risk stratification in asymptomatic patients with end-stage renal disease**

Y. Matsue, M. Suzuki, W. Nagahori, M. Ohno, A. Matsumura, Y. Hashimoto, Kameda Medical Center, Kamogawa, Japan

**Purpose:** Cardiac troponin T (TnT) is recommended as mortality risk stratification tool in end-stage renal disease (ESRD) patients, since TnT is considered to be superior to troponin I (TnI) in ability to predict mortality. NT-proBNP is also shown to be a predictor of mortality in this population. However, there is no head-to-head comparison study for these three markers. Moreover, new high sensitivity assays are available for troponin I and troponin T, but little is known about the ability of these high sensitive assays in predicting prognosis in ESRD patients.

**Methods:** We enrolled 329 asymptomatic ambulatory hemodialysis patients. All patients had blood sampled for prospective assessment of the prognostic value and completed one-year follow-up. The biomarkers were obtained simultaneously just before dialysis. All patients were followed-up for combined cardiovascular endpoint (CCE) including acute coronary syndrome, stroke, amputation due to critical limb ischemia, and cardiovascular death. The predictive abilities of high-sensitive TnI (hsTnI), high-sensitive TnT (hsTnT), and NT-proBNP were compared by area under the curve (AUC).

**Results:** At baseline, the median hsTnI and hsTnT levels were 13 ng/L (IQR: 6-29) and 64 ng/L (IQR: 39-94), respectively. There were 50 CCEs during one year follow-up. In multivariate analyses, hsTnI (P = 0.001), hsTnT (P = 0.001) and NT-proBNP (P = 0.05) remained as independent predictors for CCE. The AUC of hsTnI for predicting CCE was superior to both hsTnT (0.83 vs 0.75, P = 0.04) and NT-proBNP (0.83 vs 0.70, P = 0.04).

**Conclusions:** In head-to-head comparison, hsTnI was superior to hsTnT and NT-proBNP for providing prognostic information in asymptomatic ESRD patients.

**P851 Reduction of adverse cardiovascular events in patients with severe psoriasis treated with biologic agents or methotrexate: a Danish real-world cohort study**

O. Ahlehoff1, L. Skov1, G. Gislason1, L. Iversen2, S. Lashen3, M. Gniadecka4, R. Gniadecki4, T. N. Dam5, C. Torp-Pedersen1, P.R. Hansen1, 1Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup, Denmark; 2Aarhus University Hospital, Aarhus, Denmark; 3Odense University Hospital, Odense, Denmark; 4Bispapi治病院 of the Copenhagen University Hospital, Copenhagen, Denmark; 5Roskilde Hospital, Roskilde, Denmark

**Purpose:** Psoriasis is a chronic inflammatory disorder associated with cardiovascular morbidity and mortality. Systemic anti-inflammatory drugs, including biologic agents, are widely used in the treatment of patients with moderate to severe psoriasis and may attenuate the risk of cardiovascular events in the general population.

**Methods:** Individual-level-linkage of nationwide administrative databases was used to assess the risk of a primary composite endpoint of death, myocardial infarction, and stroke in patients with severe psoriasis treated with biologic agents, methotrexate, or other therapies, e.g., retinoids, cyclosporine, and phototherapy in Denmark from 2007 to 2009.

**Results:** A total of 2,400 patients with severe psoriasis, including 693 patients treated with biologic agents were identified. Patients treated with biologic agents were younger at baseline (46.6±12.9 vs. 53.7±15.2 years) and were more often men (66.7% vs. 47.5%) compared to patients not treated with biologic agents. Incidence rates per 1000 observation years and 95% confidence intervals (CIs) for the composite endpoint were 6.0 (CI 2.7-13.4), 17.3 (CI 12.3-24.3), and 44.5 (CI 34.6-57.0) for patients treated with biologic agents, methotrexate, and other therapies, respectively. Hazard ratios adjusted for confounding variables were 0.28 (CI 0.12-0.64) and 0.65 (CI 0.42-1.00) for patients treated with biologic agents and methotrexate, respectively. Corresponding HRs for a composite cardiovascular endpoint, i.e., cardiovascular death, myocardial infarction, and stroke, were 0.48 (CI 0.17-1.38) and 0.50 (CI 0.26-0.97). The results were confirmed in sensitivity analyses excluding patients with a history of hospitalizations or those receiving cardiovascular pharmacotherapy at baseline.

**Conclusions:** In a nationwide study of patients with severe psoriasis, systemic anti-inflammatory treatment with biologic agents or methotrexate was associated with lower risk of a composite endpoint of death, myocardial infarction, and stroke compared to patients treated with other therapies.

**P852 Late cardiac damages after chest radiotherapy: a long-term follow-up and screening project**

C. Lestuzzi1, L. Tartufi1, M. Berretta1, E. Viel1, M. Cassin2, F. Macor2, R. Piazza3, F. Baldessin4, E. Franceschini1, N. Meneguzza1, 1CRD, National Cancer Institute, Department of Cardiology, Aviano, Italy; 2CRO, National Cancer Institute, Department of Oncology, Aviano, Italy; 3Santa Maria degli Angeli Hospital, Department of Cardiology, Pordenone, Italy; 4Ca Fornoello Hospital, Department of Cardiology, Treviso, Italy

**Introduction:** Medialastial (MED) and left chest wall (LCW) radiotherapy (RT) may cause several late damages to the heart: constrictive pericarditis (CP), valvular (VHD) or coronary artery (CAD) disease, left ventricular dysfunction (LVD). RT cardiotoxicity is usually incidentally detected when the patients (pts) become symptomatic. Few prospective screening studies on asymptomatic pts have been carried on so far.

**Methods:** We prospectively studied by echocardiography (ECHO) and stress test 98 asymptomatic pts (33 males, 65 females; screening group) undergone MED (n=81; 80 lymphomas, 1 thymoma) or LCW (n=17, all breast cancer) RT from 1974 to 2004, and followed up for up to 37 years after RT. Age at treatment ranged from 8 to 64 (median 33); 84 pts also received radiochemical chemotherapy (CT). Radiation burden ranged from 16 to 50 Gy, median 40. The follow-up (FU) lasted 6–37 years, mean 17, median 16. A total of 449 ECHO and 167 stress tests were done.

**Results:** Significant cardiac abnormalities were detected in 23/98 (23%) pts undergoing screening: 10 males, 13 females, aged 40-76 (mean 56). At ECHO we observed LVD in 9 pts (one of them had also CAD) and VHD in 3 (requiring surgery in one). Stress test revealed ischemia in 9 pts (7 silent, 2 with angina; 6 needed cardiac revascularization). We observed 7 more patients (not on screening) who presented because of cardiac symptoms: 3 males, 4 females, 3 with
severe LVD, 2 with acute myocardial infarction (AMI), 2 with symptomatic VHD. Overall, cardiotoxicity was evident to 35 years after RT (mean 17). Age at treatment was 14 to 64 (mean 37), at toxicity detection 36 to 76 (mean 54). As regards LVD (n=12), all the pts had received also cardiotoxic chemotherapy and 3 of them had associated CAD; the interval from RT was 1-27 years (mean and median 12). Seven of 12 pts with CAD had also dyslipidemia; the time from RT was 2-26 years (mean 16, median 19). For VHD (n=6) the interval was 16-36 (mean 26, median 27) years. Among the screening group, in 22/23 pts symptomatic events were prevented by timely treatments; only one had AMI 2 years after a negative stress test.

Conclusions: At long-term follow-up a significant percentage of pts treated with RT are at risk of clinically relevant heart disease at a rather young age. LVD is usually detected in pts treated with both RT and CT, and is clinically evident earlier; CAO and VHD occur later. CAD is clinically silent in most cases. In pts treated with MED or LCW radiotherapy we suggest a long-term follow-up with ECHO and stress test, mostly for those treated >20 years ago, to prevent life-threatening events.

Clinical outcomes at 12-month follow up

Focal type (n=27, 26.7%) Segmental type (n=32, 31.7%) Diffuse type (n=42, 41.6%) p value
Rehospitalization 7 (25.9%) 8 (25.0%) 3 (7.1%) 0.381
Acute Myocardial infarction 2 (7.4%) 4 (12.5%) 1 (2.4%) NA
Sudden cardiac death 1 (3.7%) 0 (0%) 0 (0%) NA
AMI or SCD 3 (11.1%) 4 (12.5%) 1 (2.4%) 0.216
Combined MACES 10 (37.5%) 12 (37.5%) 5 (11.9%) 0.014

Conclusion: Focal and segmental type of coronary spasms in provocation test was significantly associated with adverse cardiac events at 12-month follow-up in patient with vasospastic angina. These results suggest that focal and segmental type of coronary spasms may need more intensive treatment for variant angina.

Clinical impact of the morphologic classification of coronary spasm in ergonovine provocation test

H.Y. Jin1, K.N. Choi1, J.S. So1, J.S. Jang1, T.H. Yang1, D.K. Kim1, D.K. Kim2, K.H. Kim3, D.I. Kim4, D.S. Kim5. 1Inje university college of medicine, Haeundae Paik hospital, Busan, Korea, Republic of; 2Inje university college of medicine, Haenundae Paik hospital, Busan, Korea, Republic of

Background: Coronary vasospasm plays an key role in provoking myocardial ischema, acute myocardial infarction (AMI) and sudden set of risk factors (SCD) in variant angina. But there are little data about the adverse cardiac events according to morphologic type of provoked spasms.

Method: A consecutive 164 patients with clinically suspected variant angina were performed ergonovine provocation test without significant stenosis (>50% diameter stenosis) and total 105 patients with a positive provocation test were enrolled. Coronary vasospasm was defined as a transient vessel narrowing (>90%) which was associated with angina and/or ST-depressive or elevated changes. These patients were divided to three groups according to the extent of coronary spasms: Focal type, segmental type and diffuse type. We compared the occurrence rates of 12 adverse cardiac events (MACES) during follow-up period, inculding use of calcium channel blockers and/or nitrates.

Results: There were no significant differences in baseline characteristics between three groups, including use of calcium channel blockers and/or nitrates. During follow up period, one arrhythmic death occurred in focal type. There are no differences in SCD or AMI between three groups. But, when we compared the two groups (non-diffuse type vs diffuse type), focal and segmental type (non-diffuse type) had significantly higher rate of adverse cardiac events compared to diffuse type (37% vs 44.4% vs 18.5%, p=0.018).

Conclusions: This risk score for stable CAD comprising a comprehensive and routinely available set of risk factors, measures of cardiac function and comorbidities outperforms established risk prediction algorithms and might improve the selection of high-risk patients for a more intensive treatment.

A variant in the epithelial sodium channel affects the arterial stiffness in a Portuguese population

M. Mendonca1, A. Pereira1, S. Gomes1, B. Silva1, A.C. Sousa1, S. Freitas1, C. Freitas1, A.I. Freitas1, J.J. Araujo1, R. Palma Dore Reis2, 1Hospital Funchal, Funchal, Portugal; 2New University of Lisbon, Faculty of Medical Sciences, Lisbon, Portugal

Pulse Wave Velocity (PWV) is a simple, non-invasive and sensitive method, widely used as an index of arterial stiffness. This parameter has been shown as an important risk marker for cardiovascular mortality and morbidity. The sodium channel gene (SCNN1G), located on human chromosome 16p12, encodes the gamma subunit of the epithelial sodium channel. Minor polymorphic changes in its promoter region may result in an increased sodium channel activity and have been associated to arterial hypertension and consequently higher PWV values.

Objective: The aim of this study is to evaluate whether this variant in the epithelial sodium channel affects the PWV values and, consequently, the arterial stiffness in a Portuguese population.

Methods: An epidemiological study with 863 individuals (51.3% male, mean age 49.8±7.6 years) was performed and all the PWV measurements were distributed in quartiles according to the increasing values of this parameter. The first quartile consisted of 250 individuals with a mean age 47.5±7.2 years and a PWV=8.8 m/s; the fourth quartile included 187 individuals with a mean age 52.3±7.1 years and a PWV=10.9 m/s. As PWV is strongly reliant on age, some individuals were excluded from each group (after fixing this variable) and two groups with 177 individuals and similar mean age were established. These were compared in terms of SCNN1G A-173G variant frequency. Categorical variables were presented by the respective frequency and analyzed by χ2 test or Fisher's exact test. Continuous variables were expressed as mean±standard deviation and compared by using Student's t-test or Mann Whitney. In order to investigate which variables significantly influence the increase of PWV, a multivariate analysis was performed with all the confounding variables. P-values<0.05 were considered significant.

Results: The GG SCNN1G A-173G variant was significant and independently associated with the increase of PWV values (OR=1.95, P=0.048) together with male sex (OR=2.88, P<0.0001), arterial hypertension (OR=4.06, P<0.0001) and heart rate (OR=1.03, P<0.005).

Conclusions: According to our results, this variant increases the PWV values and, consequently, reduces the arterial distensibility in our population, independently of arterial hypertension. The individuals carrying this polymorphism, which is associated with a lower capacity to manage the sodium and water, may present, in the future, a higher risk of cardiovascular complications benefiting from a more careful prevention.

Routinely available biomarkers improve prediction of long-term mortality in stable coronary artery disease

G. Gollasch1, B. Richter1, M. Pischcke1, A. Haschemi1, R. Marculescu1, G. Endler2, O. Wagner1, K. Huber2, C. Mannhalter1, A. Niessner1. 1Medical University of Vienna, Vienna, Austria; 2Wilhelmulinum Hospital, Vienna, Austria

Aims: Previous risk assessment scores for CAD patients have predominantly focused on primary prevention and patients presenting with acute coronary syndrome. However, especially in patients with stable CAD improved long-term risk prediction is needed to efficiently apply measures of secondary prevention. Our aim was to create a clinically applicable mortality prediction score for patients with stable CAD based on routinely determined laboratory biomarkers and clinical determinants of secondary prevention.

Methods and Results: We prospectively included 547 patients with stable CAD in our study. Thirty-nine percent (n=211) of patients died during a median follow-up of 11.3 years. Independent risk factors for patients with stable CAD were selected using bootstrapping based on Cox regression analysis. Age, left ventricular function, serum cholesterol, creatinine, heart rate, HbA1c, albumin and platelet count were selected as significant mortality predictors for the final multivariable model. Receiver Operating Characteristic (ROC) analysis demonstrated an excellent discriminatory power for 10-year survival of a multi-marker score using the aforementioned variables with an area under the curve (AUC) of 0.83 (P<0.001), significantly better than an established risk score based on conventional cardiovascular risk factors (AUC=0.64, P<0.001). Net reclassification confirmed a significant improvement of individual risk prediction by 38.9% (95%CI:25.7-52.1%) compared to the conventional risk score (P<0.001).

P853

P854

P855
Characterization of cocaine cardiotoxicity with cardiovascular magnetic resonance at 3T
A.M. Macieira Gonzalez1, C. Ripoll2, J. Cosin Sales3, B. Igual1, J. Salazar4, V. Bellido1. 1Cardiac Imaging Unit – ERSEA, Valencia, Spain; 2Hospital Arnau de Vilanova, Department of Cardiology, Valencia, Spain; 3Hospital Arnau de Vilanova, Department of Psychiatry, Valencia, Spain; 4Hospital Arnau de Vilanova, Department of Anaesthetics, Area Valencia-La Fe, Valencia, Spain; 5Hospital Arnau de Vilanova, Department of Cardiology, Valencia, Spain; 6Hospital Arnau de Vilanova, Department of Psychology, Valencia, Spain. Cocaine is a highly addictive drug with potentially cardiovascular lethal effects. The real prevalence and features of cocaine cardiotoxicity are unknown as they have been evaluated only in selected groups. We aimed to assess this using a comprehensive 3T cardiovascular magnetic resonance (3TCMR) protocol in consecutive cocaine addicts.

Methods: Consecutive, non-selected, cocaine abusers first attending a rehabilitation clinic were recruited. Medical history and examination, ECG, blood test and 3TCMR were done. CMR protocol included TrueFISP views for measurement of left and right ventricular (LV, RV) volumes and ejection fraction (EF), STIR sequences, dipiridamole (0.84mg/kg) myocardial perfusion study with gadolinium-DTPA (0.1mmol/kg), myocardial late gadolinium enhancement (LGE) and T2WSTSE study of the aorta. Images were analyzed by 2 independent, blinded observers and compared to those of 90 age and gender-matched healthy controls previously reported.

Results: 94 cocaine abusers were initially included. One subject had a sudden cardiac death 2 days before 3TMC MR and another individual was excluded because he was diagnosed of previously unknown hypertrophic cardiomyopathy. Finally, 92 consecutive cocaine abusers were included (13 females, 37.5 ± 10.6 years, age range 22-53 yrs, 7.7 ± 0.8yrs of addiction). Only 4 patients referred mild cardiotoxic symptoms (palpitations during abuse). In a per-group analysis, end-systolic volumes were slightly enlarged (LV: 31.8 ± 24.2 mL/m², RV: 38.8 ± 28.3 ± 3 mL/m², all P < 0.001) and so was the LV mass index (80 ± 13 vs 69.4 ± 49.4 g/m², P = 0.001), while EF was significantly decreased (LV: 59.6 ± 8% vs 68.4 ± 14%, RV: 55.5 ± 6% vs 61%, all P < 0.001). Unidad de Conductas patient analysis, 32 subjects (35%) had LVEF below the lower norm of normal and 18 (20%) had decreased RVFE. 27 patients (9%) showed LV hypertrophy (14 concentric, 13 eccentric) while 11 (12%) showed concentric remodelling. There were no perfusion defects or necrotic patterns but 25 patients (26%) showed LGE (1 subendocardial, 2 subepicardial, 13 intramyocardial, 9 inferior ventricular junction). Finally, 7 subjects showed abnormalities of the major thoracic arteries.

Conclusion: 3TCMR detected cardiovascular disease of variable degree in 69% of this cohort of consecutive, non-selected, cocaine abusers. The main findings were decrease in LV and RV EF, increase in LV mass index and presence of myocardial LGE, which in the majority of cases was suggestive of previous myocardial infarction.

Preoperative serum levels of mid-regional proadrenomedullin and NTproBNP predict postoperative major adverse cardiovascular events and organ failures
A. Meinders1, H.J. Gillmann1, J. Larmann1, B. Sahmlann1, R. Lichtinghagen1, S. Rustum1, T. Aper1, O. Teebken1, A. Grosser1, H. Theimer1. 1Hannover Medical School, Department of Anesthesiology and Intensive Care Medicine, Hannover, Germany; 2Hannover Medical School, Institute for Clinical Chemistry, Hannover, Germany; 3Hannover Medical School, Department of Cardiothoracic, Transplantation and Vascular Surgery, Hannover, Germany; 4Hannover Medical School, Institute for Biometry, Hannover, Germany.

Purpose: Preoperative risk stratification to predict cardiovascular and critical care complications to date relies on clinical indices. Biomarkers could improve the detection of patients at risk. We examined the performance of NTproBNP and mid-regional adrenomedullin (ADM), a marker of neurohumoral activation, for major adverse cardiovascular events (MACE) and sepsis, SIRS or organ failure (ICU-Comp). Methods: With IRB approval and informed consent, we prospectively enrolled 402 patients undergoing vascular surgery. The protocol conformed to the principles of Helsinki. We determined the revised cardiac risk index (RCRI, ≥2) and measured preoperative levels of ADM and NTproBNP. The primary endpoint was 30d MACE (MI, TnT, CV-death). Secondary endpoint was 30d ICU-Comp. Cutoffs for both endpoints were calculated for NTproBNP (> 188 pg/ml or > 153.1 pg/ml) and ADM (> 1,062 nmol/l or > 0.8127 nmol/l) using the DeLong method. We performed uni- and bi-variable logistic regression; data are presented as odds ratios (OR) or RR vs. all criteria; 95% CI and area under the receiver operating curve (AUC).

Results: 40 patients experienced MACE; 103 patients reached the secondary endpoint. NTproBNP levels (OR 2.82; 95% CI 1.37-5.81) and ADM levels (OR 3.27; CI 1.64-6.51) above the cutoff were independently associated with MACE. RCRI was also associated with ICU-Comp (OR 2.47; CI 1.54-3.94). NTproBNP (OR 1.73; CI 1.08-2.76) and ADM (OR 2.89; CI 1.82-4.58) were also associated with ICU-Comp. Bivariate analysis showed an independent association of ADM with the RCRI (ADM: OR 2.39; CI 1.48-3.88; RCRI: OR 1.90; CI 1.16-3.23, but not to NTproBNP for ICU-Comp. The individual AUCs were 0.61 for RCRI, 0.57 for NTproBNP and 0.63 for ADM. Using combined cutoffs for the RCRI and ADM, AUC was 0.66 (1 vs 0; OR 1.41; CI 0.77-2.56; 2 vs 0: OR 4.36; CI 2.45-7.75) compared to the comparable score derived from RCRI, ADM and NTproBNP (0.65).

Conclusions: Preoperative levels of ADM and NTproBNP are better predictors of perioperative risk in vascular surgical patients than the RCRI alone. A combined cutoff score using both RCRI and ADM also predicted ICU-Comp. A diagnostic algorithm based on biomarkers could improve therapeutic management. Based on these data further trials investigating the use of preoperative biomarkers to direct therapy can be designed.

Aim: To reveal the relationship between psychological stress and the aortic hardening using CAVI.

Objective: 43 healthy volunteers and 32 patients with cardiovascular risk factors. Methods: In 43 healthy volunteers, CAVI was measured on the 1st day, 7th to 10th day, and 30th day after the earthquake. And in 32 patients with cardiov...
Ankle blood pressure and dementia - a prospective follow-up study

**H. Hietanen**1, L. Pietila2, V. Salomaa2, 1Deaconess Institute in Helsinki, Helsinki, Finland; 2National Institute for Health and Welfare (THL), Helsinki, Finland.

**Background and objective:** To investigate the relationship between ankle blood pressure and clinically incident dementia. The ankle blood pressure may be a useful indicator of arterial stiffness but very few studies have considered the independent value of the ankle blood pressure without indexing it to the brachial blood pressure (ABI-index).

**Methods:** This prospective follow-up study is based on individuals (mean age 50 years, 66% male) referred to a symptom-limited exercise test between the August 1989 and December 1995. The cohort of 3,859 subjects free of dementia and vascular disease at baseline was followed for 18 years. The significance of ankle blood pressure as a predictor of incident dementia was analyzed using Cox proportional hazard models, controlling for several confounders including brachial systolic blood pressure.

**Results:** Clinically incident dementia was observed in 123 (3%) of the 3,859 participants during the mean follow-up period of 18 years. Altogether, 592 participants had a vascular event (15%). Participants with incident dementia were older than those without dementia and the majority of them were women. Significant associations were found between the elevated ankle blood pressure at baseline and clinically incident dementia during the follow-up. In persons with normal resting and exercise brachial blood pressure but elevated ankle blood pressure the hazard ratio was 1.58 (95% CI 1.04 – 2.40, p<0.03, adjusted for age and sex) and 1.59-fold (95% CI 1.00 – 2.56, p=0.05) in the wider model (adjusted for age, sex, resting systolic blood pressure, smoking and early parental cardiovascular diseases). On the other hand, good physical exercise capacity at baseline, measured as METs, was significantly protective (p<0.01) from dementia.

**Conclusion:** These results suggest that the ankle blood pressure has an independent value as a marker of arterial stiffness or subclinical atherosclerosis. Elevated ankle blood pressure in persons with otherwise normal blood pressure may indicate increased risk of cardiovascular complications and dementia.

Increased cardiovascular morbidity and mortality in apparently healthy middle-aged men and women with frequent episodes of leg cramps

**M.R. Moursund, O.W. Nielsen, A. Saadieh, Bispebjerg Hospital, Copenhagen, Denmark**

**Purpose:** Leg cramps are a common and bothering symptom, especially in the elderly. The prognostic significance of this phenomenon is unknown. We aimed to investigate the prognostic value of leg cramps and a thorough examination of the lower extremity arteries in a prospective epidemiological study.

**Method:** A total of 678 healthy men and women between the age of 55 and 75, included in the Copenhagen Holter Study, reported either to have 1, 2, 3, 4 or more leg cramps. The absence/presence of palpable pulse in the legs was determined. The follow-up time was 76 months and an adverse outcome was defined as all-cause mortality and the combined endpoint of cardiovascular death, MI, revascularization, and stroke.

**Results:** 47 (6.9%) subjects had often/daily episodes of leg cramps. Cramps were more frequent among women than men, 9.6% vs 5% (p=0.03) and were associated with an increased risk of reaching the combined cardiovascular endpoint, HR=2.57 (1.26-5.22), p=0.009. This association remained significant after correcting for traditional risk factors, and intermittent claudication, HR=2.54 (1.23-5.25), p=0.01. Leg cramps were not associated with all-cause mortality, HR=1.38 (0.67-2.85), p=0.38. In 243 (36.4%) subjects palpable pulse was absent in 1 or more regions and was not associated with the 1st cardiovascular endpoints (HR=1.47 [0.87-2.46], p=0.15) or all-cause mortality (HR=1.32 [0.86-2.03], p=0.21). In 49 (7.3%) subjects pulse was absent in 4 or more regions and neither was this finding associated with endpoints.

**Conclusion:** In apparently healthy subjects frequent leg cramps are associated with increased cardiovascular risk. The absence of palpable pulse did not have prognostic value. These findings give reason to reconsider leg cramps as a pure benign phenomenon.

### Table 1

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Quartile values (mg/L)</th>
<th>HR (95% CI) for CHD events after 1 year</th>
<th>P</th>
<th>HR (95% CI) for CHD events after 1 year</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline hsCRP, adjusted for conventional risk factors</td>
<td>1.22</td>
<td>1</td>
<td>0.31</td>
<td>1</td>
<td>0.07</td>
</tr>
<tr>
<td>Change in hsCRP, adjusted for conventional risk factors</td>
<td>-0.99</td>
<td>-0.99</td>
<td>0.87</td>
<td>0.99</td>
<td>0.99</td>
</tr>
</tbody>
</table>

**Abstract P863**

High-sensitivity CRP does not independently predict subsequent events in stable CHD patients in the Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) study


**1Monash University, Department of Epidemiology & Preventive Medicine, Melbourne, Australia; 2University of Sydney, NHMRC Clinical Trials Centre, Sydney, Australia; 3Baker IDI Heart and Diabetes Institute, Melbourne, Australia; 4Royal Prince Alfred Hospital Department of Clinical Biochemistry, Sydney, Australia; 5Sir Charles Gairdner Hospital, Perth, Australia; 6University of Queensland, Department of Medicine, Brisbane, Australia; 7Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; 8University Heart Center Hamburg, Hamburg, Germany.

Is high sensitivity C-reactive protein (hsCRP) an independent risk factor for atherothrombotic events? We examined hsCRP levels to 1 year of a trial of pravastatin in 9014 patients (17% F) with a history of MI or unstable angina, median age 62 years, and total cholesterol 4.0-7.0 mmol/L.

**Methods:** Plasma hsCRP measurements (Abbott CRP Vario, CV 3.9%) were available from 7863 patients at baseline and 6775 at 1 year. Outcomes were CHD events (CHD death, nonfatal MI and major CVD events (CVD death, nonfatal MI, nonhernorrhagic stroke). Proportional hazards models were fitted by baseline quartile of hsCRP and adjusted for statin treatment and 23 biomedical risk factors, including age, sex, lipids, diabetes, smoking, hypertension, WBC, eGFR, and BMI. Further models also adjusted for quartiles of novel biomarkers (BNP, sensTNI, Lp(a), LP-PLA2, Dimer, Mr-proADM and cystatin C). The prognostic value of change in hsCRP between baseline and 1 year for subsequent events was similarly assessed.

**Results:** hsCRP predicted events in univariate models and after adjustment for conventional risk factors (Q4vQ1 HR = 1.28 (1.07-1.54) for CHD events, and 1.36 (1.16-1.60) for CVD events), it was not significant when models also included the other novel biomarkers. WBC remained significant. Change in hsCRP did not predict outcomes after 1 year in models adjusted for conventional risk factors (table). Baseline hsCRP and hsCRP change were weakly correlated with continuous risk factors and other novel biomarkers.

**Conclusions:** In stable CHD patients, baseline hsCRP predicts events in univariate models but not in models adjusted for other novel biomarkers. Change in hsCRP levels to 1 year did not predict events independently of conventional risk factors.
**P864**

**Relationship between plasma choline and betaine levels and risk of acute myocardial infarction in patients with stable coronary heart disease**

H. Schartum-Hansen1, E.R. Pedersen1, G.F.T. Svingen1, P.M. Ueland2, R. Seltler1, J.E. Nordehaug1, M. Ebbing2, D.W. Nilsen3, N.O. Nygaard4,1, University of Bergen, Institute of Medicine, Bergen, Norway; 2University of Bergen, Institute of Internal Medicine, Section for Pharmacology Bergen, Norway; 3Haukeland University Hospital, Department of Heart Disease, Bergen, Norway; 4Stavanger University Hospital, Department of Medicine, Stavanger, Norway

**Purpose:** High plasma choline and its derivative betaine have been associated with cardiovascular disease, and circulating choline levels predict adverse events in patients with acute coronary syndrome. We studied relations of plasma choline and betaine to long-term risk of acute myocardial infarction (AMI) in patients with stable angina pectoris (SAP).

**Methods:** Samples were obtained from 2566 participants in the Western Norway B-Vitamin Intervention Trial (WENBIT). Hazard ratios (HR) (95% confidence interval) were calculated per quartile increment, using Cox regression analyses adjusted for age, sex, fasting status, smoking, body mass index, diabetes mellitus, left ventricular ejection fraction, estimated glomerular filtration rate, LDL-cholesterol and medication and stratified by study site.

**Results:** During a mean (SD) follow-up of 4.8 (1.4) years, 8.3% suffered from AMI. Plasma choline was not associated with AMI (HR 0.99 (0.87, 1.14), p=0.91) in the total population. However, the relationship of plasma choline with risk of AMI was significantly modified by smoking (p=0.001), showing increased risk in non-smokers (HR 1.24 (1.02, 1.51), p=0.033) and decreased risk in smokers (HR 0.77 (0.62, 0.94), p=0.010). Plasma betaine was not associated with AMI (HR 0.99 (0.87, 1.13), p=0.74), and did not interact with smoking.

**Conclusion:** In SAP patients, high plasma choline is associated with increased risk of AMI in non-smokers, but with decreased risk in smokers. These results motivate further research into the relation between atherosclerosis, smoking and choline metabolism.

---

**P865**

**Pulse wave velocity as a predictor of cardiovascular events in coronary artery disease**

O.V. Ilyushin1, M.V. Ilyushina1, E.L. Kalganova1, T.H. Temirsultanova2, Y.M. Lopatin3,1, State Medical University, Volgograd, Russian Federation; 2Volgograd State Medical University, Volgograd Regional Cardiology Centre, Volgograd, Russian Federation

Pulse wave velocity (PWV) is a well known marker of end organ damage in patients (pts) with arterial hypertension. As for pts with coronary artery disease (CAD), there are limited data and it remains unclear whether the change in PWV has prognostic value and negative influence on survival.

**Objective:** To evaluate the prognostic value of carotid-femoral PWV as predictor of major cardiovascular events (cardiovascular mortality, nonfatal myocardial infarction, acute stroke, the need for coronary revascularization) in pts with proven CAD.

**Material and methods:** 160 pts (68% male) with proven CAD (mean age 54±11.3 years), normal blood pressure and left ventricular ejection fraction were included into the study. PWV was calculated using an automated computerized system according to the widely accepted method of Coleson. Cumulative incidence of major cardiovascular events during 5 years of follow up was determined by Kaplan-Meier method.

**Results:** Average of the value of was 11.5±0.5 m/s in pts with normal value for healthy age-matched subjects is 9.3±0.2 m/s, p=0.001. Pts with CAD were divided into 3 groups, depending on the PWV (Figure). The first group included 94 patients, the second – 35 pts and the third group – 31 pts with PWV of 10-12 m/s and the third 19 (12%) pts with an index of more than 12 m/s. It was found that the probability of major cardiovascular events in group 2 compared with group 1 increased by 25.3% (p=0.012), RR 1.9; 95% CI 1.3-2.9 (p<0.05). The difference between the 2 nd and 3 rd groups was 25.6% (p=0.043), RR 1.5; 95% CI 1.02-2.16 (p=0.05), 1-st and 3-rd groups – 50.9% (p=0.0007), RR 3.1; 95% CI 1.91-4.39 (p<0.05).

**Conclusion:** Elevation of carotid-femoral PWV in pts with CAD may be considered as a strong predictor of major cardiovascular events.

---

**P866**

**Combination of serum albumin, C-reactive protein and body mass index improves the predicting of cardiovascular mortality in end-stage renal disease patients who started hemodialysis therapy**

Y. Kumada1, H. Ishii2, H. Takahashi1, T. Ayama1, D. Kami1, M. Tanaka1, T. Murohara1, Nagaoy Kyoritsu Hospital, Nagaoy, Japan; 2Nagoya University Graduate School of Medicine, Dept. of Cardiology, Nagaoy, Japan

**Purpose:** Main nutrition and chronic inflammation statuses are highly prevalent in patients with end-stage renal disease (ESRD). We investigated the interaction among serum albumin, C-reactive protein (CRP) and body mass index (BMI) at initiation of hemodialysis (HD) therapy as a predictor of cardiovascular (CV) mortality in ESRD patients.

**Methods:** 1,228 consecutive ESRD patients who were stably induced into HD therapy were enrolled. To clarify the joint role of these valuables, serum albumin (<3.5g/dl, serum CRP >4.0mg/l and BMI >19.6kg/m2 were defined as risk factors using ROC analysis, thereafter, the patients were divided into groups according to the number of risk factors; patients without any factors (group 0, n=314), with one factor (group 1, n=409), with two factors (group 2, n=385) and with all factors (group 3, n=120). They were followed up for 10 years.

**Results:** Serum albumin, CRP and BMI were individually independent predictors for CV mortality (HR 0.64, 95%CI 0.41-0.98, p=0.042; HR 1.01, 95%CI 1.00-1.02, p=0.0033 and HR 0.89, 95%CI 0.82-0.97, p=0.0088 respectively). Regarding the joint role of these factors, 10-year survival rates for CV mortality were 91.2%, 83.4%, 72.5% and 52.2% among group 0, 1, 2 and 3 respectively (p<0.0001). Adjusted HRs were 2.28 (95%CI 1.92-5.09) for group 1 vs. 0, 3.92 (95%CI 1.76-8.25 for group 2 vs. 0) and 6.75 (95%CI 2.91-15.6 for group 3 vs. 0), respectively. In addition, C-index for CV mortality significantly increased in a model including the number of risk factors compared to other models (Table). Similar results were also seen for all-cause mortality.

C-index of various models for mortality

<table>
<thead>
<tr>
<th>Model</th>
<th>Cardiovascular death</th>
<th>All-cause death</th>
</tr>
</thead>
<tbody>
<tr>
<td>C-index (95%CI)</td>
<td>p value</td>
<td>C-index (95%CI)</td>
</tr>
<tr>
<td>Basic model</td>
<td>0.614 (0.565-0.671)</td>
<td>reference</td>
</tr>
<tr>
<td>Basic model+number of risks</td>
<td>0.754 (0.710-0.798)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Basic model+albumin</td>
<td>0.669 (0.609-0.731)</td>
<td>0.018</td>
</tr>
<tr>
<td>Basic model+CRP</td>
<td>0.693 (0.640-0.745)</td>
<td>0.0010</td>
</tr>
<tr>
<td>Basic model+BMI</td>
<td>0.692 (0.640-0.745)</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

**Conclusion:** Serum albumin, CRP and BMI at starting HD therapy were independent predictors for CV mortality in ESRD patients, individually. Furthermore, combination of these valuables could more accurately predict the mortality than these valuables alone.
Conclusions: Preoperative BNP levels may predict not only perioperative cardiovascular events and mortality but also noncardiovascular complications in patients undergoing noncardiac, nonvascular surgery.

P868
Incremental value of endogenous sex hormones as determinants of subclinical atherosclerosis in apparently healthy postmenopausal women
G. Georgiopoulou, I. Lambrinoudaki, M. Kazani, E. Armeri, A. Mareti, D. Rizos, A. Avgoulea, N. Zakopoulos, C. Papamichael, K. Stamatiopoulos. Regional General Hospital Alexandra of Athens, Athens, Greece

Introduction: Although controversial, accumulating evidence suggest that endogenous sex hormones may play a pivotal role in mechanisms mediating accelerated atherosclerosis in postmenopausal women. We aimed to assess the incremental value of endogenous sex hormones over traditional risk factors to detect the presence of subclinical atherosclerosis in a sample of apparently healthy postmenopausal women.

Methods: In this cross-sectional study, serum follicle-stimulating hormone, luteinizing hormone, estradiol, testosterone, sex hormone-binding globulin, dehydroepiandrosterone sulfate (DHEAS), and Δ4-androstenedione were measured in 424 healthy postmenopausal women consecutively recruited from the Menopause Clinic of an academic hospital. Pulse wave velocity (PWV), flow mediated dilatation (FMD), augmentation index (AI), stiffness index (SI) and intima media thickness (IMT) in the carotid and common femoral arteries were measured in all women. The presence of subclinical atherosclerosis was defined by the presence of one or more of the following: IMT >0.9mm and/or the presence of an atherosclerotic plaque at any site and PWV above the reference values for age matched European population with risk factors.

Results: The free androgen index (FAI) was an independent determinant of PWV (β= 0.935, p=0.008) and inversely (β= -0.081, p=0.05) correlated with FMD. Total testosterone was independently associated with common carotid IMT (β= 0.215, p=0.001) and the presence of subclinical atherosclerosis (β= 1.7, p=0.001). In contrast, estradiol was inversely associated with stiffness index (β= -0.187, p=0.03) and IMT in the femoral arteries (β= -0.233, p<0.001). Total testosterone incrementally determined elevated common carotid IMT (β=0.02) and the presence of subclinical atherosclerosis (β=0.045) and FAI predicted abnormal PWV (β=0.034) over the core model of traditional risk factors. Finally, net reclassification improvement (NRI) was significant for the presence of subclinical atherosclerosis (NRI=2.44, p=0.015) and increased common carotid IMT (NRI=0.22, p=0.003) when adding testosterone over a core model including traditional risk factors.

Discussion: Estrogens were associated with favorable while androgens with adverse cardiovascular effects in postmenopausal women. However, among the sex hormones assessed in this study, total testosterone provided the highest incremental value and more accurate reclassification over traditional risk factors as a determinant of the presence of subclinical atherosclerosis.

P870
Plasma Lp(a) concentration shows modest predictive power for coronary heart disease events: results from the Long-term Intervention with Pravastatin in Ischaemic Disease (LIPID) trial
P. Nestel1, D.R. Sullivan2, M. Fournier3, A.M. Tonkin4, S. Blankenberg5, D.M. Colquhoun6, R.J. Simes2 on behalf of LIPID study investigators. Baker IDI Heart and Diabetes Institute, Melbourne, Australia; 2Royal Prince Alfred Hospital, Department of Clinical Biochemistry, Sydney, Australia; 3University of Sydney, NHMRC Clinical Trials Centre, Sydney, Australia; 4Monash University, Department of Epidemiology & Preventative Medicine, Melbourne, Australia; 5University Heart Center Hamburg, Hamburg, Germany; 6University of Queensland, Department of Medicine, Brisbane, Australia

Background: Lp(a) has been an elusive risk factor for CHD. Population studies and meta-analyses show association between Lp(a) and first ever CHD events among people with high global risk, but there is a paucity of evidence from population studies with overt CHD. We tested the potential association of CHD events (death or nonfatal MI) with Lp(a) concentration and interactions with treatment and conventional risk factors in patients with prior clinical CHD (myocardial infarction (MI) or hospitalization for unstable angina) randomly allocated to pravastatin or placebo.

Methods: Plasma samples were available from 7863 patients (6530 men and 1333 women, mean age 62 years) at baseline. The prognostic value of Lp(a) on each outcome was assessed by fitting proportional hazards models by baseline biomarker quartile. Hazard ratios (HR) by quartile of Lp(a) levels were first adjusted for treatment and sex (Model 1) and then additionally adjusted for diabetes, smoking, hypertension, major lipid classes including apoB and apoA-I, age, WBC, eGFR, BMI, and other CVD at baseline (Model 2).

Results: Lp(a) was not associated with the primary outcome, coronary events (P=0.15, Model 1; P=0.09, Model 2). Total CHD events (CHD death, nonfatal MI, unstable angina, revascularization) showed a significant trend with biomarker concentration (P=0.02, Model 1; P=0.03, Model 2) owing to subjects with the highest levels (Table). There was no association with stroke or total mortality.

Conclusion: In contrast to the relatively consistent predictive strength of Lp(a) for future CHD events in subjects without prior clinical disease, our findings suggest a much weaker influence of Lp(a) among patients with pre-existing stable CHD.

P871
Hs-CRP, PC-PLC and MCP-1 as independent predictors of cardiac events in patients with acute coronary syndrome
M. Zhang, X. Hu. The Key Laboratory of Cardiovascular Remodeling and Function Research, Qilu Hospital, Jinan, China, People’s Republic of China

Background: The purpose of this study is to investigate the predictive value of high-sensitive C-reactive protein (hs-CRP), secretory phospholipase A2 (sPLA2), phosphatidylcholine-specific phospholipase C (PC-PLC), soluble CD40 ligand (sCD40L), intercellin-6 (IL-6), myeloperoxidase (MPO) and monocyte chemoattractant protein-1 (MCP-1) to cardiac events in patients with acute coronary syndrome (ACS).

Methods: We enrolled 337 patients with ACS in this study. The peripheral concentrations of hs-CRP, sPLA2, PC-PLC, sCD40L, IL-6, MPO and MCP-1 were measured...
assayed. Each patient underwent a continuous follow-up of one time every 6 months. The main end point included relapsed unstable angina pectoris, myocardial infarction, sudden cardiac death and coronary revascularization. COX proportion risk model was used to evaluate the prediciton power of conventional cardiac risk factors and inflammation biomarkers to cardiac events.

Results: The average follow-up period was 26 months. There were 36 censored patients. Among these patients, age, smoking history, hypertension and diabetes possessed predictive power to cardiac events (hazard ratio: 1.04, 2.75, 2.44, 2.09, respectively, all p < 0.05). HS-CRP, PC-PLC and MCP-1 could independently predict cardiac events beyond conventional cardiac risk factors in patients with ACS (hazard ratio: 1.21, 1.02 and 2.04, respectively). HS-CRP above 3 pg/ml, PC-PLC above 84.9 mU/ml and MCP-1 above 101.2 pg/ml could significantly increase the cumulative hazard for cardiac events (p < 0.05).

Conclusion: HS-CRP, PC-PLC and MCP-1 possess independent predictive value to cardiac events beyond conventional cardiac risk factors in patients with acute coronary syndrome.

Predictive value of neutrophil to lymphocyte ratio in clinical outcomes of non-ST elevation myocardial infarction and unstable angina pectoris: 3-years follow-up

M. Gul1, H. Uyar2, M. Engelen3, M. Ugru3, C. Turkyilmaz4, E. Ayhan5, T. Icli6, C. Akbulut6, H. Uzun Aksoy1, N. Uslu7,1.*, Istanbul Mehmet Ali Ersoy Thoracic-Cardiovascular Surgery center, Department of Cardiology, Istanbul, Turkey; 2Beyazitam University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey; 3Siyami Ersek Thoracic and Cardiovascular Surgery Center, Department of Cardiology, Istanbul, Turkey; 4Balikesir University, Medical Faculty, Department of Cardiology, Balikesir, Turkey

Background: Neutrophil to lymphocyte (NLR) is the strongest white blood cell predictor of adverse outcomes for stable coronary artery disease and mortality in patients presenting with ST-segment elevation myocardial infarction. We sought to determine the prognostic value of NLR in non-ST elevation myocardial infarction (NSTEMI) and unstable angina pectoris (UAP).

Methods: A total of 308 (mean age 59.2±11.93; 234 males, 74 females) patients with NSTEMI and UAP were prospectively evaluated. Admission NLR was measured as part of the automated complete blood count. The study population was divided into tertiles based on admission NLR values. A high NLR (n=102) was defined as a value in the third tertile (>3.04), and a low NLR (n=206) was defined as a value in the lower two tertiles (<3.04). Patients were followed for clinical outcomes for up to 3-years after discharge.

Results: Kaplan-Meier survival analysis showed 3-years mortality rate of 21.6% in patients with high NLR versus 3% in low NLR group (p<0.001). In a receiver operating characteristic curve analysis, a NLR value of 3.04 identified an effective cut-point in NSTEMI and UAP of 3-years cardiovascular mortality (area under curve=0.86, 95% confidence interval 0.8 to 0.92). A NLR value of >3.04 yielded a sensitivity of 79%, a specificity of 71%. We used Cox proportional hazard models to examine the association between NLR and adverse clinical outcomes. A significant association was noted between high admission NLR level and the adjusted risk of cardiovascular mortality (hazard ratio: 6.3, 95% confidence interval 1.6-24.3, p=0.008). There was a good correlation between NLR and the adjusted risk of cardiovascular mortality (hazard ratio: 6.3, 95% confidence interval 1.6-24.3, p=0.008).

Conclusion: High admission NLR is a strong, and independent predictor of 3-years cardiovascular mortality (area under curve=0.86, 95% confidence interval 0.8 to 0.92). A high NLR (n=102) had an AUC=0.73, in 17% of patients we found significant carotid stenosis (>50%) and the finding of a higher LAD velocity >70 mm/sec at any of the 3 sampled tracts had an AUC=0.89 (the added value is summarized in the graph).

Do changes in HDL-C after increasing the dose of atorvastatin have prognostic significance?

1San Francisco General Hospital, and the University of California at San Francisco, San Francisco, United States of America; 2Massachusetts General Hospital, Division of Cardiology, Boston, United States of America; 3Northwestern University, Feinberg School of Medicine, Division of Cardiology, Chicago, United States of America; 4Fizer Inc, New York, United States of America

Purpose: High-density lipoprotein cholesterol (HDL-C) levels are predictive of major cardiovascular events (MCEs). Whether on-treatment changes in HDL-C are related to outcomes has not been well defined.

Methods: In the Treating to New Targets (TNT) trial, 10,001 patients with stable coronary disease were randomized to 10 or 80 mg/day of atorvastatin and followed for a mean of 4.9 years. Mean low-density lipoprotein cholesterol (LDL-C) during follow-up was 101 mg/dL (2.6 mmol/L) in the 10-mg arm and 77 mg/dL (2.0 mmol/L) in the 80-mg arm. This difference was associated with a 22% relative risk reduction in MCEs, which were significantly different from those in homoyzogotes for the wild-type allele (62.4±7.1% vs. -55.1±10.1% vs. -51.0±12.5%, p<0.008), Subjects with one or the other alleles of the TaqI variant allele (n=683) had 4.4% (95% CI: 1.2, 7.5%, P=0.008) and 2.6% (95% CI: 0.3, 5.0%, P<0.05) greater reductions in LDL-C and total cholesterol, respectively, when compared with those with homozygous wild-type allele (n=314). The associations remained significant after adjusting for potential confounding factors including age, gender, body mass index, having FH and variants in ABCG2 and SLC101.

Conclusions: These study showed that the variant allele of the FXR -1G>T polymorphism defined cardiac events. A lipid response to rosuvastatin in Chinese patients with hypercholesterolemia. This association is probably through the influence of the FXR -1G>T polymorphism on the expression of the efflux transporters.

Integrated ultrasound study as a gatekeeper for coronary and carotid atherosclerosis

F. Rigo1, E. Grolla2, G. Osseen2, F. Ronco2, M. Barbiere2,1.*
1 della Angelo Hospital Department of Cardiology, Mestre-Venice,Italy; 2Hospital "della Angelo", Department of Cardiology, Mestre-Venice, Italy

Background: A correct diagnosis of coronary atherosclerosis can only be done in the presence of clinical signs and/or by applying invasive techniques. A non-invasive diagnosis of systemic atherosclerosis could provide effective prevention.

Aim: To compare the diagnostic value of an integrated study based on conventional risk factors, echoangiography parameters, and ultrasound carotid investigation performed at the same time in patients suspected of having a coronary artery disease (CAD).

Methods: Since 2009, we have prospectively enrolled 266 consecutive patients undergoing coronary angiography (186 males, mean age 69±16 years) at first diagnosis using cardiac and carotid ultrasound. Apart from the standard echocardiographic data, rest left anterior descending coronary artery (LAD) velocities were sampled at the proximal-mid and/or distal tract Carotid ultrasound was performed at the same time using a vascular probe and c-IMT and plaques were evaluated by using a dedicated software (Esaote) based on semi-automated radiofrequency backscatter analysis. Each patient underwent coronary angiography within 15 days and a stenosis ≥ 50% was considered significant.

Results: An increased c-IMT (>800 mc) had an AUC=0.83, the presence of plaque had an AUC=0.73, in 17% of patients we found significant carotid stenosis (≥50%) and the finding of a higher LAD velocity >70 mm/sec at any of the 3 sampled tracts had an AUC=0.89 (the added value is summarized in the graph).
and subsequent MCEs using Cox proportional hazards regression. For this analysis, we excluded 236 patients with either incomplete data or an event before the 3-month visit.

Results: From baseline (after an 8-week run-in on 10 mg of atorvastatin) to the next visit at 3 months, HDL-C levels increased from 47.16±10.8 mg/dL (1.22±0.28 mmol/L; mean ±SD) to 47.49±11.0 mg/dL (1.23±0.28 mmol/L) in the 10-mg arm. Both treatment groups, decreased from 47.47±11.1 mg/dL (1.23±0.29 mmol/L) to 47.01±11.3 mg/dL (1.22±0.29 mmol/L) in the group that had been increased to 80 mg atorvastatin at baseline (P<0.001 for the change difference between groups). Patients were divided into quintiles of HDL-C change, ranging in the 80 mg arm from -7.75±3.8 mg/dL (-0.20±0.11 mmol/L) to Q1 = < -7.75 to Q5 = ≥ 4.1 mg/dL, (0.20±0.11 mmol/L) in Q5. Change in HDL-C was not predictive of subsequent MCEs in the entire group; the adjusted hazard ratio per 1-mg/dL (0.03- mmol/L) increase in HDL-C was 0.997 (95% confidence interval: 0.984–1.010, P=0.65). The rate of MCEs was 9.6% in Q1 and 9.6% in Q5. Changes in HDL-C were similarly not predictive in the 10-mg and 80-mg groups when examined separately. At visits after 3 months, approximately 70% of patients did not remain in the same quintile of HDL-C change as at 3 months. In comparing categories from 3 months to later visits, both the weighted kappa statistic and Kendall’s Tau b coefficient were <0.30, indicating marginal concordance.

Conclusions: Although on-treatment HDL-C levels are strong predictors of MCEs in change in the 80-mg arm from -7.75 mg/dL, HDL-C levels increased from 47.16 mg/dL to 47.49 mg/dL at the 3-month visit. We found that the Duke Treadmill Score may be useful for predicting severe coronary stenosis (AUC= 0.666, p < 0.0009) but not of ischemia (AUC=0.551, p = 0.1211).

Conclusions: We demonstrated that the Duke Risk Model, calculated from a physician’s initial assessment of patient history, physical examination and ECG, may be useful as a pretest selection tool to predict ischemia as determined by MPI and severe coronary stenosis (≥70%) as determined by CCTA. In contrast, we found that the Duke Treadmill Score may be useful for predicting severe coronary stenosis, but not presence of ischemia. In our population, Duke Risk Model cutoffs of 0.20 and 0.12 achieved predictive values of 100% and 90% in detecting severe stenosis and ischemia, respectively. Our findings need to be assessed prospectively.

**ARTERIAL STIFFNESS AND PULSE WAVE VELOCITY**

**P876 Relationship between arterial stiffness, cardiac baroreflex sensitivity and blood pressure variability in normotensive healthy adults**

J.E. Ochoa1, J.K. Balparda2, M.M. Correa2, A.M. Valencia2, M. Alvarez2, J.G. Mowchen2, G. Bilò3, P. Salvi2, D. Aristizabal2, G. Parati4,5,6, University of Milan-Bicocca, Ospedale San Luca, Istituto Auxologico Italiano, Milan, Italy; Centro Clínico y de Investigacion, SICOR, Medellin, Colombia; Dept. Cardiology, Ospedale San Luca, Istituto Auxologico Italiano, Milan, Italy

Purpose: An increased arterial stiffness has been proposed as a likely mechanism responsible for a reduced cardiac baroreflex sensitivity (BRS) and the associated increases in 24-h blood pressure (BP) variability. Aim of the present study was to explore this issue in a group of 90 normotensives (Systolic BP 101.7±9.3; diastolic BP 66.6±7.7 mmHg), non-obese, healthy adults (mean age 48±10 yrs, 50% F) from the city of Medellin, Colombia.

Methods: BRS was assessed by computer analysis of 10 min beat-to-beat BP and ECG recordings obtained while in resting supine. The linear regression slope of spontaneous concomitant increases or decreases in systolic (S)BP and RR interval (SBBP+RR+ and SBBP−RR−) respectively were calculated, averaged and expressed as total slope of BRS (ms/mmHg). Simultaneous recordings of pulse waveforms were obtained by means of a previously validated oscillometric device for ambulatory BP monitoring with inbuilt transfer-function like method, and pulse wave velocity (PWV, m/s) and other indices of arterial stiffness were calculated. Subjects were divided into quintiles of PWV (≥7.0 vs < 7.0 m/s), according to presence of the cutpoints based on the study of Emre et al.

Results: In both groups, there was a significant inverse relationship between BRS and PWV, with a higher PWV being associated with a lower BRS (p<0.05).

Conclusions: We demonstrated that arterial stiffness, as assessed by PWV, has a strong negative effect on BRS variability (beta=−0.49, p < 0.001), followed by HR and male sex. No significant effect was observed for age or MAP on BRS in this selected cohort (See table). A similar independent analysis showed a significant inverse relationship between BRS and daytime SBP SD (beta=−0.23, p<0.039).

**P877 The value of pretest risk stratification before coronary computed tomographic angiography and myocardial perfusion imaging**

H. Koh1, L. Chia2, J.C. Allen1, T. Chua2, R. Ng1, F.K. Cheah2, S.Y. Tan2. 1Duke-NUS Graduate Medical School Singapore, Singapore; 2University of Sheffield, Department of Cardiovascular Sciences, Uppsala, Sweden; 7University of Sheffield, Centre of Excellence - Inflammation, Department of Medical Sciences, Uppsala, Sweden; 2Uppsala University, Center of Excellence - Inflammation, Department of Medical Sciences, Uppsala, Sweden; 4Clinical Research Institute, Durham, United States of America; 8Postgraduate Medical School, Grochowski Hospital, Warsaw, Poland; 9University Hospital of Heredia, Medical Clinic, Hedenberg, Germany; 10University of Antwerp, Department of Cardiology (Edegem), Antwerp, Belgium; 11University of Sheffield, Department of Cardiovascular Sciences, Sheffield, United Kingdom; 12Uppsala University, Uppsala Clinical Research Center, Uppsala, Sweden.

Purpose: During treatment of acute coronary syndrome (ACS) with ticagrelor there is a transient slight increase in arterial markers as compared to clopidogrel. We investigated if the increase in arterial markers corresponded to changes in outcome with an improved risk prediction in discharge samples.

Methods: In the Platelet inhibition and patient Outcomes trial (PLATO) plasma cystatin C concentration were determined from samples taken within 24 hours of symptom onset (baseline) and at discharge. The cystatin C concentrations were log-transformed and evaluated in a multivariable Cox regression analysis including: background characteristics, previous cardiovascular disease, coronary interventions and established risk factors as well as log-transformed biomarkers NT-proBNP and troponin I. The primary endpoint was the occurrence of cardiac death or myocardial infarction. C-statistics and Integrated Discrimination Improvement (IDI) were obtained to evaluate the incremental predictive ability of cystatin C.

Results: Cystatin C concentrations were available in 2133 ticagrelor- and 2162 clopidogrel-treated patients with mean concentrations at baseline (0.86 mg/L and 0.86 mg/L) and discharge (1.01 mg/L and 0.97 mg/L; p<0.0005) respectively. Median change and interquartile intervals for ticagrelor and clopidogrel were 0.12 (0.02 — — 0.27) mg/L and 0.10 (0.04 — 0.25) mg/L respectively. Multivariable c-statistics and the relative IDI of the primary outcome after hospitalization for the cystatin C concentration were 0.08 and 5.2% at baseline and 0.684 and 4.5% at discharge respectively (P=0.043).

Conclusions: Cystatin C concentrations increase in the majority of patients with ACS during hospitalization. The discharge Cystatin C concentration does not improve risk prediction. The initial transient increase in cystatin C concentrations in ticagrelor-compared to clopidogrel-treated patients is not associated with any difference in long-term outcome.
Relationship between arterial stiffness and circadian pattern of blood pressure

J-S. Park1, J.H. Shin1, J.B. Park2, D.J. Choi3, H.J. Youn1, C.G. Park4, J. Kwan5, Y.K. Ahn6, D.W. Kim7, S.J. Rim8 on behalf of the Chicago Heart Health Study. 1Aju University School of Medicine, Suseong, Korea, Republic of; 2Kwandong University, Cheil General Hospital, Seoul, Korea, Republic of; 3Seoul National University Bundang Hospital, Division of Cardiology, Seongnam, Korea, Republic of; 4Catholic University of Korea, Seoul, Korea, Republic of; 5Korea University Guro Hospital, Cardiovascular Center, Seoul, Korea, Republic of; 6Inha University Hospital, Incheon, Korea, Republic of; 7Chonnam National University Hospital, The Heart Center, Gwangju, Korea, Republic of; 8Chungbuk National University Hospital, Cheongju, Korea, Republic of; 9Yonsei University College of Medicine, Cardiology Division, Seoul, Korea, Republic of

Background: Arterial stiffness is a risk factor for cardiovascular morbidity and mortality. The relationship between the arterial stiffness and the circadian pattern of blood pressure (BP) has been controversial. The objective of the present study was to investigate the relationship between arterial stiffness by pulse wave analysis (PWA) and variables of 24-hour ambulatory BP monitoring (ABPM) in patients with pre-hypertension (pre-HTN) and hypertension (HTN).

Methods: 773 patients (442 males, 48±12 year-old) with pre-HTN and HTN were enrolled in this study. BP was measured at the outpatient clinic and 24-hour ABPM was performed. Using radial application tonometry, PWA was performed for evaluation of systemic arterial stiffness expressed as augmentation index. "Nocturnal dipping" was defined as a decrease in systolic BP by >10% in the SBP as isolated diastolic non-dipping and reduction of >10% in both SBP and DBP as both systolic and diastolic non-dipping. For adjustment of age, population was divided to 2 groups: old group (≥55 year-old (n=213, 107 males), young group (55 year-old (n=560, 234 males).

Results: Patients with SBP and DBP, daytime BP mean of 24-hour ABPM, gender and body mass index were not statistically different. Augmentation pressure (AP), augmentation index (AI) and heart rate (75bpm) adjusted AI (AI@HR75) showed statistically significant difference (p=0.009, 0.018 and 0.011, respectively). Multivariate analysis showed that isolated diastolic non-dipping was correlated with arterial stiffness expressed as AI and AI@HR 75, only in young group (β=0.069 and β=0.503, p=0.029, respectively). No statistical difference among circadian BP patterns was demonstrated in old group.

Conclusion: In present study, the isolated diastolic non-dipper was closely related with arterial stiffness in patients with HTN and pre-HTN under 55 years old. Arterial stiffness might be closely related with the pattern of non-dipping in young patients with HTN and pre-HTN.

Wave reflection intensity but not arterial stiffness is a major determinant of postural hypotension

Z.Y. Chen, S.H. Sung, H.M. Cheng, C.H. Chen. Taipei Veterans General Hospital, Division of Cardiology, Taipei, Taiwan

Purpose: Orthostatic hypotension (OH) represents an important cause of hospitalization and functional impairment. Vascular aging is considered a major predisposing factor for OH. Our aim was to investigate the relative importance of arterial stiffness and wave reflection in the determination of orthostatic hypotension.

Methods: A total of 419 patients (66.8±16.4 years, 80.4% men) were enrolled in this study. All participants received measurements of supine brachial and carotid systolic (SBP) and diastolic (DBP) pressures, carotid-femoral pulse wave velocity (cf-PWV), carotid augmentation index (cAI), carotid arterial stiffness (cAP), and reflected wave amplitude (Pb) from a decomposed carotid pressure wave. Orthostatic blood pressures were measured after a 3-minute standing. Orthostatic hypotension was defined as a 20-mmHg fall in SBP or a 10-mmHg drop in DBP. In addition, they also had a heart rate (HR) ≥85% of the age-predicted heart rate (apHR), men required significantly greater workload (p=0.05) and showed higher systolic blood pressure (BP, p=0.03) than women. Imaging at 60% apHR, sustained by hand-grip exercise, revealed an increase in stroke volume and cardiac index in men (p<0.05), whereas women showed no significant differences in both SBP and DBP at rest and during exercise.

Results: cAI showed no difference from rest (p=0.45). Men showed a strong increase in PWV (p=0.02), whereas women showed only a trend towards a difference (p=0.09).

Conclusion: In present study, isolated diastolic non-dipper was closely related with arterial stiffness in patients with HTN and pre-HTN under 55 years old. Arterial stiffness might be closely related with the pattern of non-dipping in young patients with HTN and pre-HTN.

Gender differences in pulse wave velocity in young healthy adults at rest and exercise - the wellheart study

V. Punthtann1, K.N. Assress1, A. Pastor1, S. Redwood2, S. Plein3, M. Marber4, E. Nagel1. 1King’s College London, Cardiovascular Division, St. Thomas’ Hospital, London, United Kingdom; 2King’s College London, Cardiovascular Division, London, United Kingdom

Background: Elderly women have increased aortic stiffness, measured by pulse wave velocity (PWV), and show little increase in PWV with pharmacological inotropic stress. The aim of this study was to examine gender-related differences in aortic stiffness at rest and during physiological exercise stress in young non-athletic subjects.

Methods and results: Eighteen healthy subjects without known cardiovascular disease (mean age 28 years; male=10, all non-smokers) underwent cardiovascular magnetic resonance (CMR) imaging at rest and supine bicycle exercise for cine and in-plane flow with high temporal resolution (Figure 1). At rest both genders demonstrated similar haemodynamic parameters and PWV. To achieve 85% of the age-predicted heart rate (apHR), men required significantly greater workload (p=0.02) and showed higher systolic blood pressure (BP, p=0.03) than women. Imaging at 60% apHR, sustained by hand-grip exercise, revealed an increase in stroke volume and cardiac index in men (p<0.05), whereas women showed no significant differences in both SBP and DBP at rest and during exercise.

Results: cAI showed no difference from rest (p=0.45). Men showed a strong increase in PWV (p=0.02), whereas women showed only a trend towards a difference (p=0.09).

Conclusion: In present study, isolated diastolic non-dipper was closely related with arterial stiffness in patients with HTN and pre-HTN under 55 years old. Arterial stiffness might be closely related with the pattern of non-dipping in young patients with HTN and pre-HTN.

Factors influencing the increase of pulse wave velocity in a Portuguese population

R. Palma Dos Reis1, B. Silva2, A. Pereira2, H. Cafe2, S. Gomes2, A.C. Sousa2, S. Freitas3, I. Ornelas4, J.J. Araujo5, M. Mendonca5. 1New University of Lisbon, Faculty of Medical Sciences, Lisbon, Portugal; Hospital Funchal, Funchal, Portugal

Pulse wave velocity (PWV) has emerged as a new marker of cardiovascular risk and is currently used as an index of arterial distensibility. Several factors have been associated with contradictory results with increasing PWV.

Objective: In this study, we intend to evaluate whether there is any association between genetic, demographic, metabolic, nutritional and inflammatory markers with increase of PWV.

Methods: This study included 1195 participants with a mean age 50.6±7.5 years and 50% of them were male. We analyzed in the participants genetic polymorphisms: ACE I/D, AT1R A1166C, CYP11B2 C344T, ACE A2350G 8, ADD1 250A/G, and currently is used as an index of arterial distensibility. Several factors have been associated with contradictory results with increasing PWV.

Results: After logistic regression, variables that remained in the equation and influence the increase of PWV were age OR = 1.15 (1.11 to 1.18) p = 0.0001; gender OR = 2.99 (1.92 to 4.64) p = 0.0001; systolic blood pressure OR = 1.03 (1.01 to 1.04) p = 0.005; diastolic blood pressure OR = 1.06 (1.03 to 1.10) p < 0.0001; Heart Rate OR = 1.02 (1.00 - 1.04) p=0.019; Homocysteine OR = 0.87
Arterial stiffness and pulse wave velocity / Aorta and carotid arteries

137

(0.94 to 1.01) p = 0.096; Obesity OR = 0.47 (0.29 to 1.77) p = 0.003 and Diabetes OR = 2.41 (1.15 - 5.05) p = 0.020.

Conclusions: According to the results obtained, genetic polymorphisms vary in the multivariate analysis equation to determine the increase of the PWV, which can be explained either by being included in the selected variables such as hypertension, or on the other hand, they may not have enough strength to remain in the equation. So, according to this study, PWV has much more to do with behaviors and traditional risk factors than the genetic heritage.

P883

Endothelial dysfunction, pulse wave velocity and augmentation index are correlated in subjects with systemic arterial hypertension?


Direct evidence of a relationship between endothelial function and more definitive measures of arterial stiffness is studied in patients with cardiovascular disease and risk factors, but the relationship between endothelial function and Pulse Wave Velocity (PWV), the gold standard measure of stiffness, has been described partially. Aim of our study was to evaluate a positive correlation between results of two non-invasive methodologies: endogenous nitric oxide-dependent vasodilation (FMD) by right brachial scanning validated procedure and PWV and Augmentation Index (AIx) by using a simple upper arm cuff and an analysis of the oscillometric pressure waveform (SphygmoCor), in subjects with recent diagnosis of systemic arterial hypertension compared with healthy young people.

Methods: We have studied 100 subjects, 50 healthy and 50 with a new diagnosis of systemic arterial hypertension without medications. All of the subjects were free of dyslipidemia, diabetes, previous cardiovascular event, arrhythmias, heart failure.

Clinical and hemodynamic data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normotensives (n=50)</th>
<th>Hypertensives (n=50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>36.7±4.8</td>
<td>40.7±7.0</td>
</tr>
<tr>
<td>Gender, m/f</td>
<td>27/23</td>
<td>30/20</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>24.1</td>
<td>25.5</td>
</tr>
<tr>
<td>Total cholesterol, mg/dl</td>
<td>185.6</td>
<td>194.8</td>
</tr>
<tr>
<td>Triglyceride, mg/dl</td>
<td>130</td>
<td>117.1</td>
</tr>
<tr>
<td>Glucose, mg/dl</td>
<td>92</td>
<td>81.1</td>
</tr>
<tr>
<td>Peripheral SBP, mmHg</td>
<td>113.7</td>
<td>150.0</td>
</tr>
<tr>
<td>Peripheral DBP, mmHg</td>
<td>75.8</td>
<td>95.5</td>
</tr>
<tr>
<td>Central SBP, mmHg</td>
<td>103.1</td>
<td>146.7</td>
</tr>
<tr>
<td>Central DBP, mmHg</td>
<td>71.6</td>
<td>94.8</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>87.2</td>
<td>117.8</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>72</td>
<td>66.3</td>
</tr>
<tr>
<td>Augmentation Index, %</td>
<td>22.2%</td>
<td>27.7%</td>
</tr>
<tr>
<td>PWV, m/s</td>
<td>8.7</td>
<td>8.5</td>
</tr>
<tr>
<td>MDF</td>
<td>21.8%</td>
<td>9.4%</td>
</tr>
</tbody>
</table>

Results in the table: Robust statistical correlation was found among different early preclinical parameters, FMD differentiates the better the two population.

P884

Stage 1 hypertensive subjects may improve small artery compliance practising regular physical activity

C. Druinški, L. Mosis, O. Vrlić, F. Saladin, P. Palatin, E. Benetti, 1Hospital of San Daniele del Friuli, Department of Cardiology, ASSA Udine, Italy; 2University of Padova, Padova, Italy

Purpose: The aim of this study was to investigate the effect of regular physical activity on small artery compliance (C) in stage 1 hypertensive subjects.

Methods: We studied 365 never treated stage 1 hypertensive subjects (mean age=38±ys, blood pressure=145±92 mmHg, % of women=28%). Subjects were divided into 2 groups: sedentary (n=261) and physically active (n=104). We measured C with a tonometer sensor array (HDI CR2000 device) by obtaining radial arterial pulse waves. We repeated C measurements in 152 subjects (sedentary n=110, physically active n=42) after 6 years of follow-up.

Results: Resting heart rate (HR) was lower in physically active subjects (70±11, p<0.001; DM, p=0.020) compared to the lower was the heart rate, the higher was the compliance (p<0.0008). In an ANCOVA analysis, C (adjusted for age, gender, BMI, lifestyle factors, parental hypertension and blood pressure) was greater in the physically active group compared to the sedentary group (7.0±2.2 vs 6.4±1.1 mmHg/m² x 10^-5, p<0.004). When total cholesterol, triglycerides and glucose were included in the analysis, the association remained highly significant (p<0.001). After 6 years, we repeated C measurements and C remained unchanged in sedentary subjects (n=110) but slightly increased in physically active subjects (n=42). In a 2-2 way repeated-measure ANCOVA, taking into account also antihypertensive therapy (n=62), physical activity had a significant effect on C (p<0.001) especially in women (p=0.024).

Conclusions: Young-to-middle-age stage 1 hypertensive subjects performing regular physical activity have a more elevated small artery compliance compared to their sedentary peers. The relationship is independent from the effects of exercise on HR, BMI, blood pressure and metabolic parameters, persist over time and is stronger in women than in men.

P885

The influence of change of autonomic balance by reactive hyperemia maneuver on conduit arterial and resistant arterial endothelial function tests

M. Yoshida, H. Tomiyama, K. Shima, M. Odate, A. Yamashina. Tokyo Medical University, Tokyo, Japan

Background: While the maneuver of reactive hyperemia in the assessment of endothelial function is thought to affect sympathetic/pasypathetic nerve activities, the details of the effects of such change of autonomic activities on endothelial function have not been clarified. This study was conducted to examine the influence of the changes of sympathetic/pasypathetic nerve activities during the maneuver of reactive hyperemia on conduit arterial and resistant arterial endothelial function.

Methods: In 36 subjects with hypertension (age 62±9 years old), flow-mediated vasodilatation of brachial artery assessed by ultrasound examination (FMD) ( conduit arterial function; n=26) and peripheral arterial (reactive hyperemia) assessed by laser Doppler (LasDOP) (resistant arterial endothelial function) were conducted. Reactive hyperemia was induced by the 5 minutes’ clamp of forearm blood flow. Heart rate was continuously monitored throughout this reactive hyperemia, and high frequency domain (HF), low frequency domain (LF) and their ratio (LF/HF) were obtained in every 5 minutes’ interval. Then, percent change of HF (perHF) (HF value after the hyperemia – HF value before the hyperemia)/ HF value before the hyperemia, percent change of LF (perLF), and percent change of LF/HF (perLF/HF) were calculated.

Results: FMD had a significant correlation with neither perHF (r=-0.09, p=0.59), nor perLF (r=-0.07, p=0.69). On the other hand, LasDOP had significant correlations with perHF (r=0.36, p<0.05) and perLF (r=0.35, p=0.05), but not with perLF/HF (r=0.07, p=0.69).

Conclusion: The change of sympathetic/pasypathetic nerve activities caused by the maneuver of reactive hyperemia affect resistant arterial endothelial function, but not conduit arterial endothelial function. This influence should be taken into account for the interpretation of data of resistant arterial endothelial function.

AORTA AND CAROTID ARTERIES

P886

Advanced oxidation protein products’ level in serum is positively correlated with intima-media thickness in carotid arteries

L. Klima1, K. Kawaec-Jaszcz1, K. Stolarz-Skrzypek1, J. Menne2, A. Olszanecka1, W. Weczerewiecki1, G. Bilò1, D. Czarnecka1. 1First Department of Cardiology and Hypertension, Jagiellonian University Medical College, Cracow, Poland; 2Klinik für Nieren- und Hochdruckerkranke, Hannover, Germany; 1Department of Cardiology, Istituto Auxologico Italiano, Milan, Italy

Objectives: Oxidative stress plays considerable role in pathophysiology of cardiovascular disease. The objective of the study was to evaluate oxidative stress markers (dimethylated L-arginine (ADMA), symmetric dimethyl-L-arginine (SDMA), oxidized low density lipoproteins (ox-LDL)) and advanced oxidation protein products (AOPPs) in essential hypertension and search for possible relations between oxidative stress markers and arterial remodeling assessed by intima-media thickness (IMT).

Design and Methods: We recruited 50 families at the Outpatient Hypertension Clinic (hypertensive index person with at least 3 first-degree relatives, at least one relative of hypertensive) altogether 217 subjects; male 114 and 103 female. Blood pressure was measured with validated oscilometric device, on two separate occasions (2 x 3 consecutive measurements). Hypertension was defined as use of antihypertensive drugs and/or blood pressure >140/90 mmHg. In every subject carotid intima-media thickness (IMT) was measured with Vivid Q7 device. For the measurement of oxidative stress markers we collected fasting blood samples in the morning.

Results: The study group included 155 hypertensive subjects. Hypertensive and normotensive subjects differed in terms of age, blood pressure and carotid IMT (respectively 49±15.2 vs 37±14.7 years, p<0.001; 144±22.1 vs 165±8.1 mmHg, p<0.001; 127±6.1 vs 117±9.8 mmHg, p<0.001 for both; 0.63±0.16 vs 0.53±0.13 mm, p<0.001). We found a significant positive correlation between AOPP and IMT (r=0.16, p=0.024) in our study group. In multivariate analysis in hypertensives carotid IMT was related with AOPP (r=0.09, p=0.037) after adjustment for, BMI, uric acid, eGFR, smoking status and pulse pressure.

Conclusion: The observed significant relation between advanced oxidation protein products and intima-media thickness in carotid arteries in hypertensive subjects might suggest role of the oxidative stress in the pathogenesis of arterial wall remodeling in the natural history of hypertension.
Conclusions: Incremental value of poor penile arterial inflow for the prediction of significant coronary artery stenosis in hypertensive men with increased carotid wall thickness: a prospective angiographic study.

Methods: 181 consecutive asymptomatic ED patients with hypertension were prospectively evaluated for CAD. All patients underwent dynamic (after postaglandin E1 stimulation) penile Doppler ultrasonography, carotid-femoral pulse wave velocity (PWV) and carotid IMT evaluation. Mean PPSS values below 25 cm/sec are considered to indicate severe arterial insufficiency (SAI).

Results: Coronary angiography revealed significant stenosis in 43 (24%) patients with a positive stress test. SAI was found in 23 of 43 (53.5%) CAD patients and in 30 of 138 (22%) non CAD subjects (P<0.001). The prevalence of high PWV (≥10.7 m/s) was 65% in CAD patients, 46% in non CAD subjects and 94.8 mmHg/s/mmHg and PWV were significantly higher among CAD patients than among non CAD controls (39.5% ± 19.4% vs. P<0.001 and 55.2% ± 26.7% vs. P<0.001, respectively). By conditional logistic regression analysis, SAI conveyed no additional predictive information beyond high PWV values. On the contrary, SAI confers an incremental value over high IMT values in predicting CAD (OR: 4.62 CI: 2.34-9.57, P<0.001).

Conclusions: Adjunctive assessment of PPSS with carotid wall thickness enhances the detection of silent CAD among hypertensive ED patients.
Aorta and carotid arteries / Heart, eye, kidney and blood vessels

individuals with or without cardiovascular risk factors and body posture played a role in this relationship. These findings suggest that leg BP evaluation might be an alternative approach in order to predict AoRD.

**Ascending aortic dilatation: a new landmark for pulse wave velocity versus left ventricular mass**


Aortic root dilatation is a common clinical phenotype in hypertensive patients (10%). Sinus of Valsalva (SoV) enlargement, routinely evaluated during a transthoracic echocardiography, has been shown to be related to hypertensive cardiomyopathy. The second tract of the aorta, the proximal Ascending Aorta (pAA) can be easily evaluated through echocardiography.

**Purpose:** Aim of the study was to assess: a) prevalence of pAA dilatation in essential hypertensive patients (EH) and in healthy controls (HC), b) the clinical and echocardiographic features associated to AA enlargement.

**Methods:** 472 essential hypertensive patients (age 53±12 years, mean ± standard deviation) had their cardiac structure and function evaluated through echocardiography. Exclusion criteria were aortic bicuspidia, diabetes, any valvular pathology more than mild, atrial fibrillation or associated clinical conditions.

**Results:** Patients with pAA dilatation were 115 (24% of the global population): 40 (8%) had isolated dilatation of the SoV, 44 (9%) asymptomatic enlargement of pAA, and 31 (6.5%) a combined dilatation of SoV and pAA. Patients with pAA dilatation were significantly older (85.5±12 vs 72.1±11.3; p<0.001), but the two groups were similar in BI and blood pressure levels. Patients with dilatation involving SoV and pAA showed a significant increase of left ventricular mass indexed to body surface area (LVMI) compared to patients with normal aorta or selective SoV dilatation.

**Conclusion:** Ascending aorta dilatation is a frequent finding in essential hypertensive and is associated to a greater degree of left ventricular hypertrophy compared to dilatation of SoV alone.

**Role of the proximal aorta in the pathogenesis of orthostatic hypotension**

M.M. Lin. Taipei Veterans General Hospital, Taipei, Taiwan.

**Objective:** Characteristic impedance (Zc) defines the stiffness of the proximal aorta and the resistance to left ventricular ejection during early systole. The present study investigated the role of Zc in the determination of orthostatic hypotension (OH), in comparison to other mechanical indices along the arterial tree.

**Methods:** A total of 243 patients (mean age: 65.7±17.6 years; 74.9% men) were enrolled. Measures of the vascular properties from the proximal aorta to terminal arteries including Zc, carotid-femoral pulse wave velocity (cf-PWV), carotid augmentation index (cAI), augmentation pressure (AP), decomposed forward (Pf) and backward wave amplitude (Pb), and systemic vascular resistance index (SVRI) were obtained during supine position, using arterial tonometry, echocardiography, and impedance cardiography. Orthostatic blood pressures were measured after a 3-minute standing. Orthostatic hypotension was defined as a 20-mmHg fall in brachial systolic blood pressure (SBP) or a 10-mmHg drop in diastolic blood pressure (DBP).

**Results:** Thirty patients (mean age: 73.6±13.5 years; 80% men) with OH were identified. Comparing to the patients without OH, they were older, had significantly higher SBP, Zc, cf-PWV, AP, Pb, and SVRI. cAI and Pf were not different between groups. After accounting for age and supine SBP and DBP, only Zc (1.56 [1.02-2.38], P=0.004) was significantly independently associated with the presence of OH. Using receiver operating characteristic curves analysis in predicting OH, Zc had the largest area under curve (0.691) among all indices of mechanical property along the arterial tree.

**Conclusion:** Mechanical properties of the arterial tree are associated with the presence of OH. Increased proximal aortic stiffness may impair the maintenance of BP during postural changes and may play a central role in the pathogenesis of OH.

**Pulse wave velocity versus left ventricular mass as determinants of Coronary Artery Disease in patients with essential hypertension: data from a Greek 6-year-follow-up study**


**Purpose:** Although arterial stiffening is related to atherosclerosis progression, its prognostic role in hypertension is not fully elucidated, while augmented left ventricular mass index (LVMI) is linked to adverse outcome. The aim of the present study was to compare the predictive role of arterial stiffness and LVMI for the incidence of coronary artery disease (CAD) in a cohort of essential hypertensive patients.

**Methods:** We followed up 1128 essential hypertensives (mean age 56.1 years, 587 males, office blood pressure (BP) ≥144/91 mmHg) free of cardiovascular disease, for a mean period of 6 years. All subjects had at least one annual visit and a baseline assessment. Complete echocardiographic study for estimation of LVMI and blood sampling for assessment of metabolic profile. Arterial stiffness was evaluated through the ratio of carotid to femoral pulse wave velocity (PWV), by means of a computerized method (Complior SP) and the distribution of PWV was split by the median (8.1 m/sec) and accordingly subjects were classified into those with high (n=566) and low values (n=562). Moreover, LV hypertrophy (LVH) was defined as LVMI ≥125 g/m2 in males and LVMI ≥110 g/m2 in females, while CAD was defined as the history of myocardial infarction or significant coronary artery stenosis revealed by angiography or coronary revascularization procedure.

**Results:** The incidence of CAD over the follow-up period was 2.83%. Hypertensives who developed CAD (n=32) compared to those without CAD at follow-up (n=1096) had at baseline higher waist circumference (101.6±11.1 vs 97.2±11.9 cm, p=0.033), LVMI (123.7±22.9 vs 107.2±24.2 g/m2, p=0.014), prevalence of LVH (46% vs 25%, p=0.027) and prevalence of high PWV levels (69% vs 48%, p=0.019). No difference was observed between hypertensives with CAD and those without CAD with respect to the use of office BP serum creatinine and lipid levels (p=NS for all). By univariate Cox regression analysis it was revealed that high baseline PWV levels predicted CAD (hazard ratio=2.657, p=0.008). However, in multivariate Cox regression model, waist circumference (hazard ratio=1.016, p=0.04) and LVMI (hazard ratio=1.023, p=0.018) but not high baseline PWV turned out to be independent predictors of CAD.

**Conclusion:** In essential hypertensive patients, LVMI predicts future development of CAD, whereas high baseline PWV exhibits no independent prognostic value. These findings support that LVMI constitutes a superior prognosticator of events than PWV and its estimation is essential in order to improve overall risk stratification in hypertension.

**Leg blood pressure measured in orthostatic posture is a predictor of left ventricular mass in normotensive subjects**

T. Gemignani, J. Matos-Souza, K. G. Franchini, W. Nadruz Junior. UNICAMP - State University of Campinas, Department of Cardiology, Campinas, Brazil.

**Purposes:** Changing from supine to orthostatic posture is associated with substantial increments in BP levels in the lower limbs, which could ultimately influence the hemodynamic burden imposed to the heart. This study investigated the relationship between brachial and leg BP and left cardiac chambers structure and further assessed the role of body posture changes in this regard.

**Methods:** One hundred thirty normotensive, nondiabetic, nonsmoker, normolipemic subjects (59% women) were evaluated by clinical history, anthropometric and anthropometric analysis, analysis of metabolic parameters, echocardiography, and had their BP measured in the arm and calf in supine and orthostatic positions.

**Results:** Changing from supine to standing substantially increased BP levels in the legs (p<0.001). Leg orthostatic pulse pressure (PP) was the measurement showing the strongest correlation with left ventricular (LV) wall thickness (r=0.38; p<0.001) and LV mass (r=0.38; p<0.001), while leg orthostatic systolic BP (SBP) exhibited the highest correlation with left atrial size (r=0.34; p<0.001). Stepwise regression analysis adjusted for brachial BP, anthropometric and metabolic variables confirmed that leg orthostatic PP was independently related to LV wall thickness (p=0.02) and LV mass (p=0.03). Moreover, leg orthostatic SBP was associated with left atrial size even after adding LV mass to the statistical model (p=0.02). At last, triglycerides levels were the variable showing the most significant relationship with leg orthostatic PP and SBP. Conversely, brachial orthostatic PP and SBP only associated with age and anthropometric variables.

**Conclusion:** Orthostatic leg BP might be an alternative approach in order to predict cardiac structure in normotensive subjects.

**Pulse pressure and effects of losartan/hydrochlorothiazide in patients with hypertension and left ventricular diastolic dysfunction**

H. Oe1, H. Ito2, N. Toh3, K. Ikawara4, K. Inishi5, H. Watanabe6, K. Shimada7, J. Yoshikawa1. 1Okayama University,Okayama, Japan; 2Okayama University, Department of Cardiovascular Medicine, Okayama, Japan; 3Sakurashi-Watanabe Hospital, Osaka, Japan; 4Kansai Electric Power Hospital, Osaka, Japan; 5Sakakibara Heart Institute, Fuchu, Japan; 6Osaka City University Graduate School of Medicine, Osaka, Japan; 7Nishinomiya Watanabe, Cardiovascular Center, Nishinomiya, Japan.

**Background:** Pulse pressure (PP), measured as the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP) rises due to arterial stiffening with age. PP is known as an independent predictor of heart failure and inversely related to left ventricular (LV) diastolic function. We aimed to investigate the association of PP and effects of Losartan/hydrochlorothiazide (HCTZ) in patients with hypertension and LV diastolic dysfunction.
Retinal vascular deterioration is accompanied by hypertensive patients with diabetes mellitus and posterior wall endiastolic thickness (p=0.232). Regarding left atrial volume (p=0.287), left atrial volume index (p=0.319) and posterior remodeling, as well as respective global impairment of left ventricular systolic function, as venous blood samples were collected at determination of Scheie scale and all participants underwent ambulatory blood pressure monitoring (ABPM). All subjects underwent fundoscopy examination and were distributed to five groups according to Scheie’s grading system. Groups A, B, C, D and E, for Scheie’s scale 0, I, II, III, and IV, respectively. Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (c-f PWV) by means of a computerized method (Complior SP).

Conclusions: In hypertensive subjects there is a progressive stiffening of the aorta in parallel to the evolution of the fundus lesions according to Scheie’s scale. A possible explanation derives from the fact that same pathophysiological processes, like wall remodeling or endothelium impairment occur in small and in large vessels in the setting of essential hypertension.

Association between eye vasculature alterations and renal damage in essential hypertensives with metabolic syndrome

V. Katsi, G. Souretis, I. Vlasseros, D. Vrachatis, D. Tousoulis, C. Stefanadis, I. Kalikazaros. Hippokration General Hospital, Athens, Greece

Purpose: In the ongoing debate about metabolic syndrome (MS), it is still unresolved whether it is a marker or a mechanism. We sought to unravel the mystery of the interrelationships of the hypertensive fundus, a time honored target organ damage (TOD), especially in the setting of MS. We hypothesized that there might be an association between retinal alterations and the other parameters of target organ damage, such as renal dysfunction and inflammatory activation.

Methods: Our population consisted of 202 consecutive subjects with newly diagnosed untreated stage I-II essential hypertension (aged 60±11 years, 122 female), without overt cardiovascular disease. All participants underwent fundoscopy examination and were classified according to Scheie’s grading system into 5 categories (Scheie’s scale 0, I, II, III, IV: normal, arteriolar narrowing, arteriovenous nicking, hemorrhages-exudates and papilloedema respectively). Anthropometric parameters, as well as lipid profile, plasma glucose, high sensitivity C-reactive protein (hs-CRP) and serum creatinine levels were assessed. Renal function was classified according to the estimated glomerular filtration rate (eGFR) calculated by the Cockroft-Gault formula. MS was identified according to the Third Report of the National Cholesterol Education Program Adult Treatment Panel. The subjects were divided in two groups regarding the absence (group A), or the presence of MS (Group B).

Results: Group B compared to group A had increased levels of uric acid and hs-CRP (5.5±0.33 vs 4.5±0.27 mg/dl and 2.9±0.16 vs 1.6±0.11 mg/dl respectively, all p<0.05). The two groups did not differ regarding age, sex and office blood pressure. In each of the five Scheie’s categories there was a significant divergence, within the categories, in the constellation of MS components, presenting a prevalence of 6%, 14%, 47%, 71% and 62%, respectively (p<0.05).

Conclusions: The metabolic syndrome, although not an established pathogenetic entity, is associated with accelerated acceleration of the hypertensive retinal damage, kidney dysfunction and inflammatory activation.
patients with hypertension and DM reflect tubulo-interstitial damage or increased arterial stiffness.

Methods: We studied hypertensive patients between 28 and 75 years, in chronic and intensive care therapy, with or without DM, with normal renal function (creatinine clearance > 60 mL/min), RRI (peak systolic velocity – end-diastolic velocity)/peak systolic velocity) was calculated by the analysis of the Doppler flow wave obtained at renal interlobar arteries and considered pathologic when > 0.70.

Results: We evaluated 34 patients (57 ± 10 years, 22 M/12 F). Patients with DM (n=18) were older (63 ± 9 vs 59 ± 9 years, p = 0.001) and had significantly higher RRI values (0.70 ± 0.0 vs 0.65 ± 0.06, p = 0.001) and prevalence of pathologic RRI (61% vs 13%, p = 0.05) compared with patients without DM. There was no significant difference in PWV values between hypertensive patients with or without DM (7.8 ± 1.7 vs 7.8 ± 1.3 m/sec, p > 0.95). DM resulted a significant independent predictor for pathologic RRI even after adjustment for age (O.R. 8.06; IC 95% 1.03–62.78; p = 0.046) and PWV (O.R. 11.09; IC 95% 1.90–64.86; p = 0.008).

Conclusions: In our hypertensive patients with DM, increased RRI values may reflect a reduction in intra-renal compliance due tubulo-interstitial damage, rather than an increase in systemic arterial stiffness.

Incidence of renal artery stenosis and its related factors of cardiac ultrasonographic findings in hypertensive patients

Yao Municipal Hospital, Yao, Japan

Purpose: The incidence of systemic atherosclerotic diseases has increased in patients with hypertension. Renal artery stenosis (RAS) could be a cause of an effect of hypertension. The aim of this study was to define the incidence of RAS and its related factors of cardiac ultrasonographic findings in hypertensive patients.

Methods: When cardiac ultrasonographic examination was performed in consecutive 974 hypertensive patients (male/female 578/396, mean age 68 years) from December 2009 to June 2011, peak systolic velocity (PSV) of renal artery was examined at the same time. The criteria for RAS was > 180 m/sec in PSV. We compared the presence or absence of RAS with indices obtained by cardiac ultrasonographic examination.

Results: Compared with the patients without RAS (n=929, male/female 545/384), the patients with RAS (n=45, male/female 33/12, 4.6%) were significantly old (p = 0.017) and the ratio of male to female was significantly high (p = 0.036). In patients with RAS, left ventricular mass (LVM) was significantly large both in males (p = 0.047) and females (p = 0.032) compared with those without RAS. In hypertensive patients with > 65 years, the incidence of RAS was low (2.4%), but LVM was significantly large compared with those with < 75 years (p = 0.019), although the ratio of male to female did not differ in these groups. There was no difference in LVM between < 75-year patients with and without RAS.

Conclusions: In younger hypertensive patients, RAS was associated with larger LVM, indicating the relation with RAS and the severity of hypertension. In contrast, in older hypertensive patients, no association was observed between RAS and LVM, possibly indicating the gradual progression of RAS without relating to the severity of hypertension.

STEMI: EPIDEMIOLOGY CONSIDERATIONS AND ELECTROCARDIOGRAM FINDINGS

C. Dong, S. Junejo, M. Farrer. City Hospitals Sunderland NHS Foundation Trust, Sunderland, United Kingdom

Purpose: Patients presenting to Rapid Access Chest Pain clinic (RACPC) patients in the UK: a single centre experience

Methods: Retrospective audit demonstrating that national guidelines should be applied with confidence in the diagnosis of rapid access chest pain clinic (RACPC) patients in the UK: a single centre experience

Results: 694 of 848 (81.8%) patients presented to RACPC had investigations performed, of which n=137 (19.7%) had first-line investigations in accordance with NICE guidelines. Of these, n=98, n=40, and n=5 were performed for CA, myocardial perfusion scan, and CT CS respectively. 249 (35.9%) coronary angiographies (CA) were performed in total, n=86 were NICE-recommended of which n=57 (65.1%) was subsequently reported to have had CAD, confirming NICE statistics. Disparities were found in n=17 in low-risk cohort where invasive angiography was required in n=12 were found with no CAD. Overall performance improved compared to previous figures: 2.5% increase of CS from 0, and consistent improvements in the rest of the categories.

Conclusion: Majority of patients presented had investigations but only a minority required tests according to NICE recommendations. Clinical judgments are less reliable compared to Duke score on indicating first-line investigations. CT calcium scoring is a valuable diagnostic tool in excluding significant CAD in low-risk patients. Within appropriately performed coronary angiographies, disease rate matched that stated in NICE guidelines.

Effect of smoking on angiographic results and long term clinical outcomes in patients treated with primary angioplasty

V. Oduncu1, A. Erkci1, I.H. Tamboga1, T. Akgun1, M. Kurt2, C.Y. Karabay3, C. Korna3, 1Medical Park Hospital, Istanbul, Turkey; 2Derince Education and Research Hospital, Kocaeli, Turkey; 3Mustafa Kemal University, Hatay, Turkey

Purpose: We sought to investigate the effect of active smoking on procedural success, short and long term clinical outcomes in patients with ST elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (p-PCI).

Methods: In a retrospective design, we evaluated 2007 patients treated with p-PCI for STEMI (between January 2006 – January 2008). The patients were divided into two groups as active smokers (n=1025) and nonsmokers (n=972).

Results: Smokers were younger and comorbidities such as diabetes mellitus, hypertension, anemia were less frequent in this group. Postprocedural final TIMI grade 3 flow (91.2% vs 86.9%, p < 0.002) and myocardial blush grade 3 (68.9% vs 39.5%, p < 0.001) were more common in the active smokers. While in-hospital mortality rate (1.6% vs 6.7%, p < 0.001) was significantly lower in the smokers, there was no difference between the groups with respect to the incidences of reinfarction and stent thrombosis at short-term follow-up. At long-term follow-up (median 40 months), stent thrombosis (3.4% vs 1.7%, p=0.022) and reinfarction (9.3% vs 6.7%, p=0.047) were significantly more common in the smokers. However, there was no difference between the groups with respect to the long-term mortality rates (7.6% vs 7.4%, p=0.88).

Conclusion: Smoking is associated with better myocardial perfusion after p-PCI and lower mortality during early in-hospital period. However, stent thrombosis and reinfarction at long-term follow-up were more common in the smokers.

Age related mortality of primary PCI patients at a high volume UK cardiac centre

N. Malik1, G.G. Babu2, J.R. Davies3, N.M. Robinson3, 1University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom; 2King George Hospital, Ilford, United Kingdom; 3Basildon and Thurrock University Hospitals NHS Foundation Trust, Essex Cardio-thoracic Centre, Basildon, United Kingdom

Purpose: Despite being the fastest growing population group, the elderly have usually been excluded from reperfusion clinical trials. We studied the difference in mortality in different age groups after primary percutaneous coronary intervention (PCI) for ST elevation myocardial infarction (STEMI) at our high volume 24/7 cardiac centre.

Methods: From the start of our PCI service, there has been no age criteria to access the service. We collected data from our prospective cardiac database for the 24 months period between September 2009 and September 2011, with mortality provided by the summary care records.

Results: There were 1322 PCI procedures with an age range of 14 to 98 years (mean 65.3). 656 patients (50%) were under 65 years, 326 (25%) were 65-74, 275 (21%) were 75-84, and 65 (5%) were 85 years or above.
Does a regional system of care impact on reperfusion strategies in ST-segment elevation myocardial infarction?

1. Hospital, Angers, France; 2. University hospital, Grenoble, France; 3. Hospital, Douai, France; 4. University hospital, Paris, France

Purpose: Regionalization of care for ST-segment elevation myocardial infarction (STEMI) has been advocated, although its effect on processes of care - compared to a non-regional model - remains unclear. The aim of this study was to evaluate the impact of a regional system of care on reperfusion strategies for STEMI patients relative to control hospitals.

Methods: We analyzed the original data from two nationwide, prospective cohort studies, with the same methods. The first was conducted in November 2000 (FAST MI 2010) and the second in November 2005 (FAST MI 2005). A total of 166 hospitals participated in both studies. Seven hospitals (2 with percutaneous coronary intervention facilities and 5 without) were involved in a regional system of care implemented in the Northern Alps in 2002 (RESURCOR); 153 control hospitals located in other French regions with no corresponding regional system of care. From 2002 to 2005, RESURCOR promoted prehospital fibrinolysis followed by routine/rescue coronary angiography. We compared change in rate of prehospital fibrinolysis and routine/rescue coronary angiography after fibrinolysis between 2000 and 2005 in the RESURCOR region versus the control hospitals.

Results: A total of 102 STEMI patients were enrolled in the Northern Alps hospitals and 2077 in the control hospitals. In the RESURCOR area we observed a larger absolute increase in the use of prehospital fibrinolysis (18% vs 63%, p < 0.01, respectively, in 2000 and 2005) compared with the control hospitals (14% vs 31%, p < 0.01, respectively, in 2000 and 2005). In the RESURCOR area we observed a larger absolute increase in the use of routine/rescue coronary angiography after fibrinolysis (9% vs 44%, p < 0.01, respectively, in 2000 and 2005) when compared with control hospitals (7% vs 22%, p < 0.01, respectively, in 2000 and 2005).

Conclusions: Regionalization of care for STEMI patients may impact on reperfusion strategy in STEMI.

New insight into mental stress induced myocardial ischemia: prevalence and demographic/clinical characteristics

W. Jiang, Z. Samad, S. Boyle, R. Williams, R. Becker, T. Ortel, C. Kuhn, C. O’Connor, E. Velazquez
Duke University Medical Center, Durham, United States of America

Background: Mental stress induced myocardial ischemia (MSIMI) is a risk for poor prognosis of patients with coronary artery disease (CAD). Past studies examining MSIMI were primarily included patients with exercise induced myocardial ischemia (ESIMI), thus the true prevalence of MSIMI remains unknown. We prospectively addressed the limitations employing data collected during the recruitment phase of a clinical trial designed to assess if a selective serotonin reuptake inhibitor reduces MSIMI.

Method: Both male and female adult patients with documented CAD, regardless of status of exercise or pharmacological tests, were recruited for screening stress test for the following 24-48 hour beta-blocker withdrawal, consented patients underwent a battery of mental stress tests (three tasks) followed by a treadmill test. Stress induced ischemia was defined as 1) any development or worsening regional wall motion; 2) reduction of left ventricular ejection fraction (LVEF) ≥ 8% from pre-test to post-test; and/or 3) horizontal or downsloping ST segment depression ≥ 1mm in 2 or more leads lasting for ≥ 3 consecutive beats, relative to rest. MSIMI was considered present when ischemia occurred in at least one mental test.

Results: A total of 310 CAD patients (17.2% women, and mean age of 63.0 years) underwent the screening. MSIMI occurred in 43.45% while ESIMI occurred in 33.79% of the study population; 23.79% had both MSIMI and ESIMI, 19.66% had MSIMI only, and 10.0% had ESIMI only. Relative to exercise stress, mental stress induced greater reduction of LVEF. Univariate analysis demonstrated that women (OR = 1.88, 95% CI 1.04 – 3.42), patients who were not married (OR = 1.59, 95% CI 1.19 – 3.38) and patients who lived alone (OR = 2.24, 95% CI 1.19 – 4.20) were more likely to have MSIMI. Multivariate analysis showed that compared to married men, unmarried men (OR = 2.57, 95% CI 1.33-4.97) and married women (OR = 3.72, 95% CI 1.21-11.16) were more likely to have MSIMI. Further, compared to men living with someone, men and women living alone had higher risk for MSIMI (OR = 2.25 [95% CI 1.02 – 4.93] and CR = 2.72 [95% CI 1.17-6.42], respectively). None of those factors, however, were associated with ESIMI.

Conclusion: MSIMI is more common than ESIMI in clinically stable CAD patients. Women, unmarried, married men, and ones living alone are at higher risk for MSIMI. Further, these factors are needed to understand the underlying mechanisms of MSIMI, sex differences, and of the interactions with marital and living statuses. Appreciation of and effective management to reduce MSIMI are greatly needed in this highly prevalent population.

Intracoronary administration of darbepoetin-alpha at onset of reperfusion in acute myocardial infarction

1. University Hospital of Montpellier, Montpellier, France; 2. University Hospital of Nimes, Department of Cardiology, Nimes, France; 3. AP-HM - Hospital Nord, Marseille, France; 4. IBN SINA University Hospital, annaba, Algeria; 5. Functional Genomics Institute (IGF), CNRS UMR5203-Inserm U661, University of Montpellier, Montpellier, France; 6. University Hospital of Clermont-Ferrand - Hospital Gabriel Montped, Clermont-Ferrand, France

Background: Experimental data suggest that erythropoietin may be a good candidate as an adjunct to reperfusion therapy in myocardial infarction (MI). Recent reports in patients with acute MI indicate that previous published clinical trials have been rather disappointing. In these trials, the timing of the cardio protective strategy could have missed crucial events that occur in the first few minutes of myocardial reperfusion. The objective of the present study was to determine whether the intracoronary administration of darbepoetin-alpha (DA) at the onset of reperfusion reduces the infarct size (IS) in patients with acute MI.

Methods: We randomly assigned 56 patients who had acute ST-elevation MI to confirming that increasingly less women than men had been investigated at 30 days for each passing year. Among those examined with CAG within 30 days, 28,219 (74%) received reperfusion therapy. The fraction of patients receiving reperfusion therapy was similar over time (range 69-76%). Women were less invasively treated than men (66% vs. 74% in 2000–02, 66% vs. 78% in 2003–05 and 65% vs. 80% in 2006–09; all p < 0.0001) with an adjusted OR 0.56 (0.53-0.59). The interaction-term between sex and year of admission was OR 0.94 (0.92-0.96; p < 0.0001). Hence, women were increasingly less likely to undergo invasive reperfusion therapy for each passing year compared to men.

Conclusions: During 2000–2009 women with a first AMI were less likely to receive both invasive examination and subsequently reperfusion therapy than men and the gender-associated bias strengthened for each passing year. The findings are surprising as women with high risk AMI benefit similarly from invasive treatment as men and the guideline-recommended therapy is the same for both genders.
receive either an intracoronary bolus of 150 µg of DA (DA group) or normal saline (control group) at the onset of reflow obtained by primary percutaneous coronary intervention (PCI). IS was assessed both by measuring serum creatine kinase (CK) release and by performing cardiac magnetic resonance (CMR).

Results: There was no difference between the two groups with regard to the duration of ischemia, the TIMI flow grade at admission and after PCI, the size of the area at risk, and the extent of the collateral circulation that are the main determinants of IS. The release of CK after reperfusion was not significantly different in the DA group as compared with the control group even when the data were adjusted to the size of the area at risk. Between 3 and 7 days and at 3 months, the area of hyperenhancement on CMR expressed as percentage of the left ventricular myocardium was not significantly reduced in the DA group as compared with the control group even when the data were adjusted to the size of the area at risk.

Conclusions: The intracoronary administration of DA in patients with acute MI at the time of reperfusion does not significantly reduce IS.

Trial Registration clinicaltrials.gov Identifier: NCT01043991

Incidence and prognostic value of infections during an acute coronary syndrome
B. Alvarez-Alvarez, S. Rassopoulos, R. Beu Assi, C. Cambeiro-Gonzalez, N. Bouzas, A. Granda, M. Castineira, P. Cabanas-Grandio, P.C. Gil, J.R. Gonzalez-Juanatey, University Clinical Hospital of Santiago de Compostela, Santiago de Compostela, Spain

Introduction: A growing amount of clinical and experimental evidence suggests a link between infection and atherosclerotic diseases. On the one hand it is known that during the acute phase of myocardial infarction there is a proinflammatory state. On the other hand several studies have demonstrated that infection causes a hypercoagulable state which increases the risk of thrombosis. The aim of our research is to evaluate the incidence of infections during the admission by acute coronary syndromes (ACS) and its influence in the risk of in-hospital mortality.

Methods: Using data from 4,497 consecutive patients with ACS (32.1% STEMI, 19.2% unstable angina) from our hospital (2003-2010), we analyzed the incidence of bacterial and viral acute infections and associated it with in-hospital mortality. Further a multivariate analysis was performed to show the prognostic value of infections during ACS regardless of the GRACE risk score.

Results: There were 534 infections during ACS hospitalization (11.9%) and 265 in-hospital deaths (5.9%). The mortality in the group with infections was 17.6%, increasing in-hospital mortality 3.8-fold in comparison with not-infection group (mortality 4.6%, p < 0.001). A predictor of in-hospital death independently of GRACE risk score (OR: 1.584, 95% CI: 1.141-2.198, p=0.006 for acute infections; OR: 1.035, 95% CI: 1.032-1.039, p=0.001 for GRACE R))

Conclusions: Infections are a frequent complication during the ACS hospitalization increasing the risk of in-hospital mortality independently of GRACE risk score.

Impact of smoking on six-month angiographic and clinical outcomes in patients undergoing elective percutaneous coronary intervention with drug eluting stents
B.G. Choi, S.W. Rha, A. Elnagar, S.I. Im, S.W. Kim, C.U. Choi, J.W. Kim, C.G. Park, H.S. Lee, D.J. Oh. Korea University Guro Hospital, Seoul, Korea, Republic of

Background: “Smoker’s Paradox” in patients undergoing percutaneous coronary intervention (PCI) in the drug-eluting stent (DES) era has been controversial. In a recent study, enhanced clopidogrel response in smokers with cytochrome P450 CYP 1A2<163C→A allele carriers was reported. This study was to evaluate whether smokers paradox is exists in real world clinical practice in a series of Asian population.

Methods: The study population consisted of 1093 consecutive patients (pts) who had received clopidogrel and underwent elective PCI with DESs between January 2004 and April 2009. Non-Smoker (NS) was defined as inexperience in smoking (n=498pts) and smoking (S) as (n=595)

The proportion of individuals with CHF did not differ significantly between the two groups (NS vs. S: 11.3% vs. 12.9%, p=0.40). However, the proportion of patients with diabetes was significantly higher in the smoking group than in the non-smoking group (NS vs. S: 15.3% vs. 30.4%, p<0.001). In terms of smoking, patients with diabetes had significantly higher rates of smoking (24.7% in NS vs. 52.2% in S, p<0.001).

Conclusion: The results of the present study suggest that smoking may be an independent predictor of MACE, particularly in patients with diabetes.
smoking before admission (n= 625 pts. 57.2%), Current Smoker (CS) as smoking within 1 month before admission (n= 293 pts. 26.8%) and Ex-Smoker (ES) as quit smoking more than one-year before admission (n=175 pts). Six-month angiographic and 5-years cumulative clinical outcomes were compared among three groups.

Results: A total 974 pts (89.1%) were finished 2-year clinical follow up. The baseline clinical and procedural characteristics were similar among the three groups except more male gender in the CS group with hypertension in the NS group. At six months, the incidence of angiographic binary restenosis was lower in the CS group. At ten years, cumulative major clinical outcomes were also similar between NS with CS group except that the incidence of repeat revascularization (target lesion revascularization, TLR and target vessel revascularization, TVR) and major adverse cardiac events were lower in the CS group (table).

Conclusion: In our data, “smoker’s paradox” still seems to be exists in Asian patients undergoing PCI with DESs in real-world clinical practice.

### Relationship with clinical outcomes and circadian pattern in patients with AMI at primary PCI era

**W. Kim**, J.S. Woo**, M.H. Jeong**, Kyung Hee University Hospital, Yongin, South Korea, Republic of Korea; Chonnam National University Hospital, The Heart Center, Gwangju, Korea, Republic of Korea

**Background:** Many epidemiologic studies have reported the morning peak incidences of acute myocardial infarction (AMI). However, short and long-term clinical outcomes of circadian pattern have not been fully investigated in patients with AMI.

**Methods:** From Korea Acute Myocardial Infarction Registry (KAMIR) database, we analyzed data from 2793 eligible patients (2793 STEMI, 1961 NSTEMI; age≥62±12.1 years) who had primary percutaneous coronary intervention (PCI) and early invasive PCI. The clinical impact of circadian variation was evaluated among four 6-hour intervals (12:00 midnight-6:00 AM, 6:00 AM-12:00 noon, 12:00 noon-6:00 PM, 6:00 PM-12:00 midnight). Various major adverse cardiac events (MACEs) at 12 months were evaluated.

**Results:** There was a marked circadian variation with increased incidences of AMI during the second quarter of day (6:00 AM to 12:00 noon), in concordance of previous studies, hypertension was more prevalent during the second quarter of day (STEMI: 45% vs. 51% vs. 46% vs. 46%, respectively; NSTEMI: 53% vs. 55% vs. 51% vs. 48%, respectively p<0.001). Among four 6-hour-intervals, symptom-to-door time, door-to-balloon time, procedural complexity, and success rates of PCI were not significantly different. As shown in table, in-hospital mortality, MACEs were not significantly different for 12-month follow up. Instead, old age, diabetes, and Killip class higher than II were independent factors for 12-month MACEs.

**Conclusion:** Older age and additional comorbidities, but not the onset time of AMI, are likely to explain the deteriorating short-and-long term outcomes in patients with primary PCI and early invasive PCI.

### Systematic data feed of primary PCI network: impact on delay of reperfusion

F. Badalzzi, A. Santarelli, S. Marzaloni, V. Masini, N. Franco, M. Ruffini, D. Santoro, D. Grossotto, A. Corsa, G. Piovaccari, 1Infermi Hospital, Cardiology Department, Rimini, Italy; 2Infermi Hospital, Emergency Department, Rimini, Italy

**Purpose:** Treatment delay is an important predictor of survival in STEMI patients undergoing primary PCI. Guidelines recommend that the PCI-related delay time (PCI-RDT) must be shorter than 90 minutes. This study sought to identify the effect of formalized data assessment and systematic feedback on the PCI-STEMI network.

**Methods:** We analyzed PCI-related delay time (first medical contact to first balloon inflation) of 386 patients who refer to the hub hospital between January 1st 2009 and December 31st 2010. The AMI network, serving a population of about 300,000, consists of three predefined referral routes: pre-hospital diagnosis and direct transportation (125 pts), emergency department of PCI hub center (107 pts) and emergency department of spoke hospitals (154 pts). The first medical contact and the rivascolarization time were assessed, analyzed and presented in an interactive session to hospital and emergency staff members. Data, from patients of 2010, were analyzed in four different quarters and were presented in the same manner.

**Results:** The median of PCI-RDT for direct transportation was 63 min and 66 min, for emergency department of PCI hub center was 93 min and 78 min, and for emergency department of spoke hospitals was 103 min and 91 min in 2009 and 2010, respectively. We observed that in 2009 50% and in 2010 64% of patients had a PCI-related delay time less than 90 minutes (p<0.008).

**Conclusion:** Formalized data feedback leads to significant reduction in rivascolarization time in patients with STEMI.
Prognosis over a 20 year-period in elderly patients with first STEMI (1988-2008)

A. Viana Tejedor, H. Bueno, M. Juarez, R. Rubio, F. Fernandez-Avilés, University General Hospital Gregorio Maranon, Department of Cardiology, Madrid, Spain

Purpose: The general population is gradually aging in the Western world, so that patients over 75 years and older comprise a substantial proportion of all acute myocardial infarction patients. However, this population has been traditionally less likely to receive evidence-based medications and to undergo primary Percutaneous Coronary Intervention (PCI) for ST-Elevation Myocardial Infarction (STEMI). We aim to provide insight in demographic and clinical characteristics of the STEMI patients ≥75 years and the prognosis over a twenty-year observational period.

Methods: This is a single-centre observational study. Between 1988 and 2008, we collected data from all the patients ≥75 years who presented with a first STEMI and were admitted in our Coronary Care Unit. Patients admitted to the cardiology ward, in the Intensive Care Unit and in the geriatric ward were excluded from the present study. We analyzed their baseline characteristics, the inhospital mortality and five-year mortality.

Results: From 1988 to 2008 a total of 1393 patients ≥75 years were included in the present study. Mean age was 80.7±4.7 years and 51% were women, 59.4% had hypertension, 31.4% diabetes, 28.1% dyslipidemia, 21.2% were smokers and 33.9% had previous history of cardiovascular disease. 25.9% had three-vessel coronary disease, 21.8% presented severely depressed left ventricular ejection fraction and 74.4% developed any complication during the hospitalization: tachycardia, ventricular arrhythmias, complete AV block, mechanical complications, renal impairment and others. 92.7% received aspirin, 62% ACE inhibitors, 47.6% β-blockers, 30.9 statins and 21.8 clopidogrel. 52.7% of the patients underwent reperfusion therapy (PCI in 47.4% patients and fibrinolysis in 26.1%). In the total cohort of 1393 patients, in-hospital mortality was 24.8%, one year mortality was 41.7% and five-year mortality was 63.6%.

Conclusion: Mortality among STEMI patients ≥75 years was acceptable in our cohort, in spite of their high risk profile and comorbidities. Adherence to evidence-based therapies was limited. Unfortunately, little is known about the optimal treatment of this elderly as they are underrepresented in many randomized clinical trials. Further studies into the optimal STEMI management strategy for the elderly are warranted.

Available of cath lab facilities and contemporary inter-hospital transfer patterns for the management of ACS patients: findings from the EPICOR study


Purpose: We aimed to evaluate the significance of fragmented QRS (fQRS) in predicting mortality in acute myocardial damage in patients with STEMI elevation myocardial infarction (STEMI).

Methods: The level of cardiac enzymes (Troponin I, MB fraction of creatine kinase (CKMB)) and transthoracic echocardiographic findings were prospectively examined in 184 patients with STEMI who have undergone primary percutaneous coronary intervention (PCI). Fragmented QRS on 12-lead electrocardiography was defined by the presence of single or multiple notches in the R or S wave, without a typical bundle branch block, in > or =2 contiguous leads in 1 of the major coronary artery territories at the 48th hour after primary PCI. Patients were classified into two groups according to the fragmentation; with fragmentation-Group 1 and without fragmentation-Group 2.

Results: Three hundred thirty five patients were included in the study and evaluated during the index hospitalization. Of these, 211 patients (63%) were in Group 1 and 124 patients (37%) in Group 2. The troponin I and CKMB levels were significantly higher in Group 1 (p<0.001). The left ventricular ejection fraction was 41.66±11.45 in Group 1 versus 50.21±10.47 in Group 2 (p<0.001). Also left ventricular systolic dimension (LVSD), diastolic dimension and the grade of mitral regurgitation were significantly higher in Group 1 (p<0.001). The left ventricular ejection fraction was 41.66±11.45 in Group 1 versus 50.21±10.47 in Group 2 (p<0.001). Also left ventricular systolic dimension (LVSD), diastolic dimension and the grade of mitral regurgitation were significantly higher in Group 1 (p<0.001).

Conclusion: The presence of fQRS at the 48th hour is a significant predictor of myocardial damage in patients with STE elevation myocardial infarction (STEMI).
patients met the inclusion criteria. In the same period of time, 40 consecutive STEMI patients without SCD were selected as an age- and gender-matched control group. Clinical characteristics of both groups were similar (Table 1). No differences were found on the culprit coronary artery, but a significant association was found in the localization of the artery occlusion. Proximal segment occlusion was more frequently seen in patients with SCD (75% vs. 28%, p < 0.001). After logistic regression analysis, angiographic culprit lesion in proximal coronary artery segment was associated significantly with SCD in patients with STEMI (p = 0.003; OR 7.02, 95% CI 1.14-43).

### Table 1

<table>
<thead>
<tr>
<th>SCRD (n=32)</th>
<th>No SCRD (n=13)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>61±13.4</td>
<td>60±13.1</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>91</td>
<td>88</td>
</tr>
<tr>
<td>Hypertension %</td>
<td>58</td>
<td>40</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>25</td>
<td>23</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>44±15</td>
<td>44±18±8</td>
</tr>
</tbody>
</table>

Conclusions: Culprit lesions in STEMI cluster in the proximal coronary arteries in patients with SCD compared those without SCD. This finding could suggest a relationship between SCD and the amount of myocardium at risk in patients with STEMI.

### Clinical and electrocardiographic characterization of reciprocal ST segment changes in patients with acute coronary artery occlusion


**Purpose**: Acute coronary artery occlusion can induce reciprocal ST segment depression in leads non-related to the ischemic area. It can be caused either by concurrent subendocardial ischemia or simply result from a passive electrical phenomenon, but this is not well known. The purpose of the study was to characterize reciprocal ST segment changes in patients with acute coronary occlusion and single coronary vessel disease.

**Methods**: We reviewed the clinical records of 545 patients with acute myocardial infarction treated with primary coronary angioplasty and we selected the 124 patients with single vessel disease in whom the culprit artery was the only affected vessel. We measured ST segment deviation in the 12-lead ECG and coronary angiographic data.

**Results**: Occlusion of proximal and mid-distal left anterior descending coronary artery (LAD) induced significant ST segment elevation (p < 0.001) in precordial leads (1.12±0.75 mV and 1.14±0.89 mV, respectively). Concurrent ST segment depression were observed in inferior leads after proximal (0.52±0.42 mV) but not after mid-distal (-0.13±0.22 mV) LAD occlusion (p = 0.01 for the difference). Occlusion of proximal and mid-distal right coronary artery (RC) induced significant ST segment elevation (p < 0.001) in inferior leads (0.75±0.39 mV and 0.62±0.44 mV, respectively) associated with ST segment depression (p < 0.001) in precordial leads (-0.57±0.49 mV and -0.58±0.47 mV, respectively) with no difference between both groups.

**Conclusion**: Reciprocal ST segment depression occurs after acute coronary occlusion in patients with single vessel disease thus suggesting that concurrent subendocardial ischemia is not the likely mechanism. Reciprocal ST segment changes appear after proximal and mid-distal RC occlusion and after proximal but not mid-distal LAD occlusion.

### The number of fragmented QRS predicts the low percent of ST segment resolution in patients with STEMI

**M. Ceîn, S.A. Kocaman, T. Kirs, T. Endogan, A. Canga, M.E. Durakoglugil, Y. Cicik, S. Dogan, O. Satoğlu, F. Education and Research Hospital, Department of Cardiology, Rize, Turkey; 2 Ondu State Hospital, Ondu, Turkey; 3 Rize University Medical Faculty, Department of Cardiology, Rize, Turkey**

**Background**: The QRS complex fragmentations (iQRS) are associated with increased morbidity and mortality. The causative relationship between iQRS and cardiac fibrosis has been shown, but whether presence and number of iQRS on admission ECG predicts the ST segment resolution in patients undergoing primary percutaneous coronary intervention (p-PCI) was not studied until now.

**Methods**: The study included one hundred and eighty-four consecutive patients with ST elevation myocardial infarction (STEMI) who underwent p-PCI. Presence or absence of iQRS on pre and post-PCI ECGs and their relation with myocardial infarction and perfusion parameters were investigated.

**Results**: Patients with iQRS on admission ECG had increased inflammatory markers, higher cardiac enzyme levels, increased pain to balloon time, prolonged QRS time, more extended coronary involvement and more frequent Q waves on ECG in comparison to patients with non-fragmented QRS. Presence and higher number of iQRS on admission or post-PCI ECGs were significantly related with low percent of ST resolution and myocardial perfusion parameters.

### Conclusions

The present study suggests, that additional training in ECG interpretation may be a critical component of the education of physicians who care for patients presenting with acute coronary syndrome. Prehospital evaluation and treatment decisions of a presumed acute coronary syndrome: what are the problems?

**M.-A.G. Ohlow, M. Schreiber, B. Lauer. Central Hospital Bad Berka, Department of Cardiology, Bad Berka, Germany**

**Purpose**: Interpretation of prehospital 12-lead ECG in acute ST-elevation myocardial infarction (STEMI) remains a diagnostic challenge in many cases. The aim of this study was to determine whether board-certified emergency-physicians (BCEP) are able to differentiate STEMI from non-STEMI in a high percentage of cases, thus to assure more precise prehospital treatment and triage.

**Methods**: Eight electrocardiograms (ECG) of patients with acute non-traumatic chest pain (6 STEMI-ECG, one pericarditis, and one pulmonary embolism) were analyzed by the BCEP in a blinded fashion. Decisions had to be made regarding the diagnosis (STEMI or not) and regarding the treatment (immediate reperfusion or transfer to the next hospital without percutaneous coronary intervention facility).

**Results**: 73 BCEP (19 (26%) female, mean age 37±5.3 years) participated in our study. In case of STEMI 83% (60/73) of BCEP were able to establish the correct diagnosis. The results in interpreting non-STEMI were better in older (p < 0.05) patients. The BCEP were 73% (55/73) of BCEP established the correct diagnosis. In case of non-STEMI-ECG only 30% (22/73) of BCEP established the correct diagnosis. The therapeutic decisions in case of non-STEMI again were better in older (p < 0.05) and in BCEP with a background in internal medicine (p < 0.05).

**Conclusion**: In case of acute non-traumatic chest pain the evaluation of the electrocardiogram in prehospital emergency medicine leads to unsatisfactory results. The present study suggests, that additional training in ECG interpretation may be a critical component of the education of physicians who care for patients presenting with acute coronary syndrome.

### Impact of logistic network organization in reduction of STEMI mortality in an unselected population from central Romania

**I.S. Benedek, B. Jako, T. Benedek. University Emergency Hospital, Targu Mures, Romania**

**Aims**: To investigate evolution of ST-Elevation Myocardial Infarction (STEMI) treatment and STEMI-related mortality in an unselected population from a region of 1 million people in central Romania in the period of 2004-2011, and to show the role of organizational and educational factors in increasing rates of primary PCI and reducing STEMI mortality in this region.

**Methods and results**: In 2004 a STEMI network for organization of logistics related to STEMI treatment was initiated in a territory of 1 million people, encompassing a primary PCI centre and 13 administrative territorial hospitals. Data related to all unselected patients presenting with STEMI in these hospitals were collected and introduced in a Regional Registry of STEMI, the first registry of such kind in Romania. In order to increase the number of patients...
Impact of the site of first medical contact, pre-hospital

Background: Early medical contact in a pre-hospital setting in patients with ST-elevation myocardial infarction (STEMI) remains the standard of care. The impact of pre-hospital versus in-hospital first medical contact on outcomes in patients presenting with ST-elevation myocardial infarction is not clearly understood.

Methods: A total of 910 patients were enrolled in ATOLL; 643 (70%) had first medical contact in the ambulance with a physician on board. We compared the outcomes in Pre-Hosp pts with those whose first contact was In-Hosp. Composite endpoints of clinical benefit, ischemic outcomes, and safety consisting of death, complication of MI, procedure complications, and blood transfusions were also similar in both groups.

Conclusions: Reduction of STEMI-related mortality was possible via implementation of pre-hospital PCI even in a region with the lowest budget dedicated to healthcare from Europe. It took at least 5 years of intensive work to implement a new therapeutic strategy in the community. A national strategy for pre-hospital PCI could have a significant impact especially in those regions where the territory has been prepared with appropriate organizational efforts, including education and logistic measures.

Table 1

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Pre-Hosp (n=463)</th>
<th>In-Hosp (n=267)</th>
<th>RRT (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death, complication of MI, failure, or major bleeding</td>
<td>185 (38.6%)</td>
<td>96 (36%)</td>
<td>1.17 (0.95-1.44)</td>
<td>0.14</td>
</tr>
<tr>
<td>Death, recurrent MI or ACS, or urgent revascularization</td>
<td>51 (11.5%)</td>
<td>31 (11.8%)</td>
<td>1.67 (0.66-4.73)</td>
<td>0.78</td>
</tr>
<tr>
<td>Major bleeding</td>
<td>31 (4.9%)</td>
<td>11 (4.2%)</td>
<td>0.54 (0.25-1.19)</td>
<td>0.11</td>
</tr>
<tr>
<td>Minor bleeding</td>
<td>47 (10.4%)</td>
<td>24 (9.3%)</td>
<td>1.21 (0.74-1.98)</td>
<td>0.44</td>
</tr>
<tr>
<td>Blood transfusion</td>
<td>15 (2.4%)</td>
<td>3 (1.2%)</td>
<td>0.34 (0.08-1.42)</td>
<td>0.11</td>
</tr>
</tbody>
</table>

1 Adjusted by the propensity score.

Conclusions: Early medical contact in a pre-hospital setting in patients with STEMI is a safe and effective strategy. Randomized prospective studies are required to further analyze any superiority of this approach. Our study is limited by being a retrospective non-randomized analysis.

ST-segment elevation myocardial infarction and distortion of the QRS: long-term mortality

Background: The distortion of the terminal portion of the QRS has been widely related with increased mortality and worse prognosis after an ST-segment elevation myocardial infarction (STEMI). Our objective was to assess whether this adverse association was maintained after long-term follow up.

Methods: We analyzed 635 consecutive patients admitted with a STEMI diagnosis to coronary care unit. We defined two ECG groups according to the presence of ST segment elevation with onset distortion of the terminal portion of the QRS in two or more adjacent leads (QRS+) or the absence of this pattern (QRS-). Clinical, angiographic, treatment features, and all cause mortality, together with other cardiovascular outcomes were retrospectively recorded.

Results: QRS+ was present in 141 patients (22.2%). Median overall follow up was 470 days (interquartile range: 190-799). Gender distribution, Arterial hypertension, dyslipemia, diabetes mellitus, smoking habit, and previous infarctions did not display differences between groups.

Medium age was slightly higher in the QRS+ cohort (64.6 Vs 62.03 years, p<0.04), with bigger infarction size, assessed by CK and Troponin I levels (142.0 Vs 82.2; p<0.001). Regarding adverse events including mortality, acute pulmonary oedema, cardiogenic shock, ventricular fibrillation and asystole; were all significantly more frequent in the QRS+ group. However, after long term follow up, these mortality differences disappeared (figure). Multivariate Cox analysis displayed similar results (HR QRS+ =0.56; 95% CI 0.2-1.6; p=0.30).

Conclusion: The distortion of the terminal portion of the QRS in STEMI is significantly related to adverse prognosis during admission. However, after long term follow up, mortality differences seem to disappear.

Exclusive involvement of interventional cardiologist in the decision making process improves door-to-balloon time by significant shortening of decision-to-balloon time in STEMI

Background: We have had a “one call activation system” for primary PCI at our regional academic center since 1999. The ED physician initiated the system with the decision for primary PCI made by cardiologist (interventional or non-interventional) on call. But since July 1, 2009, only interventional cardiologists are involved in the decision making process. Otherwise, the comprehensive strategy remained the same. As we have reported previously, this new strategy resulted in a shortened door-to-balloon (D2B) time. In the present study, we analyzed the D2B timeline intervals to determine were the major gains were achieved.

Methods: We conducted a retrospective analysis of 665 consecutive patients presenting to our institution with suspicion of acute STEMI during a 30-month period. Group 1 consisted of patients in the 12 months (July 1 2008-June 30 2009) before and Group 2 consisted of patients in the 18 months (July 1 2009-Dec. 31 2010) after the system change was instituted. Mann-Whitney U test and chi-square test were used for statistical analysis.

Results: 218 patients in group 1 were taken to the cath lab of which 180 received primary PCI. 349 patients in group 2 were taken to the cath lab of which 275 received primary PCI. The results were presented in the table.

D2B time intervals (median, unit: mins) before (group 1) and after (group 2) new system in STEMI patients undergoing PCI

<table>
<thead>
<tr>
<th>Group 1 (n=180)</th>
<th>Group 2 (n=275)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D2B</td>
<td>76</td>
</tr>
<tr>
<td>Arrival-to-EKG</td>
<td>9</td>
</tr>
<tr>
<td>EKG-to-decision</td>
<td>12</td>
</tr>
<tr>
<td>Decision-to-balloon</td>
<td>54</td>
</tr>
</tbody>
</table>

Conclusions: Comprehensive strategy with exclusive involvement of interventional cardiologist in the decision making process resulted in a significant decrease in decision-to-balloon time. The EKG-to-decision time did not decrease, contrary to our expectation.
Smoking impacts symptom onset time and outcome in primary percutaneous coronary intervention: further insights into the smoker’s paradox

K.D. Mahmoud1, M.W. Nijsten2, V. Fidler3, B.J. De Smet4, 1University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; 2University Medical Center Groningen, Department of Critical Care, Groningen, Netherlands; 3University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands.

Purpose: Circadian variation in the onset of acute myocardial infarction has been well characterized, but the significance of modifying factors is underexplored. We studied smoking and other factors potentially associated with time of onset of STElevation myocardial infarction (STEMI) and their clinical impact.

Methods: From a prospectively collected registry, baseline parameters as well as outcome were studied in 1954 consecutive patients with STEMI undergoing primary percutaneous coronary intervention (PCI) between January 2006 and April 2010. In 656 patients, symptom onset to first medical contact time (patient delay) and first medical contact to treatment time (system delay) were available.

Results: Among 13 baseline factors in our study population, only smoking was associated with time of symptom onset (P=0.014). Circadian variation in symptom onset was attenuated in smokers with higher occurrences of STEMI during the night and fewer occurrences during the morning compared with non-smokers. Significant diurnal variations (longer than 32% vs. 69 years: P<0.001) and a lower rate of multivessel disease (56% vs. 67%; P<0.001). Smoking was independently associated with longer ischemic time (estimate +7.2%, 95% confidence interval [CI]: +13% to +15%; P<0.001). However, this association lost its statistical significance after adjustment for symptom onset time between 12:00 AM and 06:00 AM (estimate +23%; 95%CI: +14% to +33%; P=0.001). Irrespective of smoking status, patient delay was longest for patients with symptom onset between 12:00 AM and 06:00 AM (P<0.001), while system delay did not vary by symptom onset time. Post-PCI, smokers had better myocardial blush grades (odds ratio for grade 0/1: 0.73; 95%CI: 0.57-0.93; P<0.001). One-year mortality was 5.9% in smokers and 7.4% in non-smokers (P=0.03). However, both smoking (hazard ratio 1.81; 95%CI: 1.18-2.78; P=0.006) and any doubling of ischemic time (hazard ratio 1.21; 95%CI: 1.01-1.45; P=0.038) were independently associated with mortality at 1-year follow-up.

Conclusions: Smoking underpins primary PCI have a favorable baseline profile, irrespective of time of day. Smoking is a risk factor for poor outcomes in STEMI, even after adjustment for confounders. This well-known “smoker’s paradox” may be partially explained by the differential pattern in symptom onset time seen in smokers with higher occurrences during the night resulting in longer ischemic time due to patient delay. Continuing efforts to reduce patient delay, especially among smokers, are warranted.


Purpose: To analyze the secular trends in management and short- and long-term outcomes of elderly STEMI patients.

Methods: The PRIMMIS/Registry is a single-center observational study, which enrolled all first AMI in patients≥70 years admitted to our Coronary Care Unit since 1988. Patients with first STEMI admitted between 1988 and 2008 were included in the cohort. Patients with confirmed diagnosis of STEMI, treated by a prehospital emergency service, were included. The final cohort consisted in 1147 patients. During the study period, from 1988-2008, there was a significant increase in median age (from 79 years in 1988-92 to 80 years in 2005-08), time delay <6 hours at admission (from 59.7% to 68.9%) and in the use of aspirin, β-blockers and ACE inhibitors. A significant reduction in the incidence of cardiogenic shock (from 16.3% to 4.4%) and mechanical complications (from 11.9% to 3.2%) was seen. The use of reperfusion therapy increased significantly, due to a wider use of primary percutaneous coronary intervention (PCI) while 30-day, 1-year and 5-year mortality decreased throughout the 20-year study period (P<0.001 for all analyses) (Table). After adjusting for age, gender, diabetes, time delay to admission, Killip class, and MI location, patients treated with PCI showed a significantly lower 30-day (OR 0.47; 95% CI 0.32-0.70) and 1-year mortality (OR 0.62; 95% CI 0.43-0.88) while fibrinolysis (FL) showed a non-significant improvement in 30-day (OR 0.90; 95% CI 0.59-1.39) and 1-year mortality (0.86, 0.58-1.29).

Conclusions: Mortality in STEMI during pre-hospital care is high. It’s associated with: female sex, call reason due to atypical symptoms, large infarctions with 5 or more leads involved, anterior location AMI, initial hypotension and ventilricular fibrillation episodes.

Use and impact of the pre-hospital electrocardiogram in acute coronary syndrome

T. Quinn1, S. Johnson1, S. McLean2, M. Woollard1, H. Snooks1, C. Gale2, C. Weston2 on behalf of MINAP Steering Group. 1University of Surrey, Guildford, United Kingdom; 2Barts and The London NHS Trust, London, United Kingdom; 3Coventry University, Coventry, United Kingdom; 4Swansea University, Swansea, United Kingdom; 5University of Leeds, Leeds, United Kingdom.

Background: Guidelines recommend use of pre-hospital ECG (PHECG) in suspected ACS. PHECG use is suboptimal, leading to delayed or denied reperfusion in STEMI. PHECG is associated with faster reperfusion, but little is known of the impact in NSTEMI. Mortality benefit of PHECG has not been demonstrated.

Table 1. Variables associated pre-hospital mortality in STEMI

<table>
<thead>
<tr>
<th>Variable</th>
<th>Odds Ratio</th>
<th>CI 95%</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female sex</td>
<td>2.737</td>
<td>1.259-5.951</td>
<td>0.01</td>
</tr>
<tr>
<td>Call reason, atypical chest pain</td>
<td>3.560</td>
<td>1.559-8.125</td>
<td>0.003</td>
</tr>
<tr>
<td>Systolic Blood pressure -90 mm Hg</td>
<td>3.725</td>
<td>1.655-8.402</td>
<td>0.002</td>
</tr>
<tr>
<td>Anterior AMI location</td>
<td>2.460</td>
<td>1.126-5.732</td>
<td>0.02</td>
</tr>
<tr>
<td>Ventricular Fibrillation</td>
<td>2.757</td>
<td>1.172-7.488</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Total of leads involved ≤5 (ST elevation) 2.709 1.206-6.211 0.01

STEMI: epidemiology considerations and electrocardiogram findings
Temporal trends in pre-hospital management of ST segment elevation myocardial infarction from 2002 to 2010: Data from the RICO Survey

E. Milovetch1, L. Lorgis2, N. Falvo3, P. Buffet4, G. Dentan4, A. Wagner5, P. Amouyel4, V. Bongard6, A. Bingham5, E. Cottin5, M. Freyza1,1
1Prehospital Care Department, Hospital General, Dijon, France; 2University Hospital, Department of Cardiology, Dijon, France; 3University Hospital Department of Internal Medicine and Clinical Immunology, Dijon, France; 4Department of Cardiology, Fontaine les Dijon, France

Background: Myocardial infarction with ST segment elevation (STEMI) is a medical emergency requiring specific management aiming to achieve reperfusion as early as possible.

Aims: We aimed to evaluate the temporal trends between 2002 and 2010 in STEMI management and time delays in an eastern region of France (Cote d’Or).

Methods: All consecutive patients admitted for a first STEMI in the RICO survey (Observatoire des Infarctus de Côte d’Or) from 1st January 2002 to 31st December 2010 have been included. We analysed trends in pre-hospital and hospital management times and reperfusion.

Results: 1045 STEMI patients were included over the study period. Mean age and GRACE risk score increased from 2002 to 2010 (64 to 67 y, p = 0.001 and 152 to 155 p = 0.049). At symptom onset, there was an increase in the rate of patients who called the emergency number (dial 15) and a decrease in the rate of call to GP as first medical contact (from 24.8 to 39.4% and from 57.1 to 34.2%, respectively). However, prehospital times including patient time (from onset of symptoms to call for medical seeking) remained stable over time. There was a significant decrease in time to first medical contact according to age, with patients aged under 50 years getting help on average 40 to 100 minutes earlier than patients aged over 50 years (p = 0.019). The average time from first medical contact to reperfusion decreased significantly from 339 minutes in 2002 to 259 minutes in 2010 (p = 0.009). Over the study period, there was an inversion in the distribution of reperfusion strategies, with a decrease in fibrinolysis and an increase in primary PCI from 25% to 32% and from 21% to 36.7%, respectively. The rate of patients without acute reperfusion dropped from 41.3 to 36.3% (p < 0.001).

We found a marked improvement in time to reperfusion including fibrinolysis and door to balloon time (from 150 to 120 min and from 70 to 45 min, respectively).

Conclusion: Between 2002 and 2010, despite marked improvements in management including reperfusion strategies, there is still a room for improvement in order to achieve earlier reperfusion in STEMI patients.

Importance of out-of-hospital case fatality and early-life-threatening complications in 28-day mortality of acute coronary syndrome

P.L. Vervuuren1, D. Arveiler1, J. Dalongeville1, J.B. Ruidavets1, A. Wagner2, P. Amouyel4, V. Bongard6, A. Bingham5, M. Elbaz1, J. Ferrieres1,2, S. Acher1,2, M. Swahn1,2, C. Avena1, J.C. Beer2, M. Zeller2, Y. Cottin2, M. Freyza1,1
1SAMU Lifour Nord, University Hospital of Lille, Lille, France; 2Inserm U744 Inserm, University of Lille Nord, France; 3University Hospital of Lille, Lille, France; 4University Hospital of Toulouse, Hourguell Hospital, Department of Cardiology A, Toulouse, France; 5University of Strasbourg, Medical Faculty, EA 3430, Department of Epidemiology and Public Health, Strasbourg, France; 6Pasteur Institute of Lille, U0744 Inserm - University of Lille Nord, France, UDSL, Lille, France; 7University Hospital of Toulouse, Department of Epidemiology, Inserm UMR1027, Toulouse, France; 8Inserm U970, Paris Cardiovascular Research Center (PARCC), Paris, France; 9University Hospital of Toulouse - Rangueil Hospital, Department of Cardiology B, Toulouse, France

Purpose: The death rate of acute coronary syndromes (ACS) has decreased for 40 to 50 years. Out-of-hospital mortality remains high despite the improvement of ACS care and in-hospital mortality has decreased a lot but reaches currently a plateau. The aim of our study was to evaluate the importance of out-of-hospital mortality and the main determinants of in-hospital mortality in France with recent data.

Methods: Our study was based on 2006 data from the French MONICA population-based registry which collects all cases of ACS occurring in people aged 35-74 in 3 French areas located in North, North-Eastern and South-Western France. The study assessed the rate of out-of-hospital deaths and the 28-day case fatality (out-of and in-hospital deaths) in 2547 patients. Then we analysed the 28-day case fatality in 2003 out-of-hospital phase survivors using logistic regression analysis. The early-life-threatening complications, composed of resuscitated cardiac arrests, shocks and use of vaso-active drugs, were considered as the main explanatory variables. The results were adjusted for age, gender, living area, patients’ background (previous treatments), type of ACS and out-of-hospital management delay (acute care and treatment).

Results: The 28-day global case fatality was 27% (95% confidence interval (CI): 0.25 to 0.29). Among all deceased patients, the proportion who died before reaching hospital was 77% (95% CI: 0.75 to 0.79). The 28-day case fatality of people reaching the hospital was 7.8% and the rate of early-life-threatening complications was 9.6% (6.1% of cardiac arrest, 4.5% of shocks and 3.4% of vaso-active drugs). Such complications were associated with 63.7% of in-hospital deaths and the mortality of patients presenting such complications was 51.3%. The adjusted odds ratio for early-life-threatening complications was 27.0% (95% CI: 16.1 to 45.2, p < 0.0001) and remained comparable after exclusion of deaths occurring before the first 24 hours of hospitalisation.

Conclusion: For ACS, a large proportion of deaths occurs in the out-of-hospital phase. Moreover, a large proportion of the in-hospital mortality was associated with early-life-threatening complications with a poor prognosis and probably non-reversible damage before reaching the hospital. Most of the 28-day deaths could not benefit of classical ACS treatments because of the severity of the initial presentation. It underlines the importance of cardiovascular prevention, population education and better out-of-hospital emergency management.

CRUSADE bleeding score validation for ST-segment-elevation myocardial infarction

G. Sanchez Elvira, A. Ariza, J.C. Sanchez-Salado, V. Lorente, R. Romaguera, J.L. Ferreiro, M. Nato, P. Moliner, J.A. Gomez-Hospital, A. Ceguer, Bellvitge University Hospital, Barcelona, Spain

Introduction: CRUSADE (Can Rapid Risk Stratification of Unstable Angina Patients Suppress Adverse Outcomes With Early Implementation of the ACC/AHA Guidelines) bleeding score predicts accurately the risk of bleeding in non-ST-segment-elevation myocardial infarction. No study has validated its use in ST-segment-elevation myocardial infarction. We aimed to evaluate the CRUSADE score accuracy to predict bleeding complications in ST-segment-elevation myocardial infarction treated with primary angioplasty.

Methods: We prospectively included all comers with ST-segment-elevation myocardial infarction treated with primary angioplasty. CRUSADE bleeding score was calculated for each patient. All patients were treated according to ACC/AHA and ESC guidelines for ST-segment-elevation myocardial infarction. All bleeding complications (according to CRUSADE bleeding classification) were recorded. We assessed the power of the score to discriminate major bleedings by c statistics.

Results: We included 1091 patients (79% males). The average CRUSADE score was 24.8. There were 35 (3.2%) cases of major bleeding. Most of them (26 2.5%) with a drop of hematocrit<12. Patients with major bleeding had a mean score of 27.9±13.9 compared with 28.3±12.8 in patients without major bleeding 24.3. The rate of major bleeding increased by bleeding risk score quintiles: 0.4% for those at very low risk (score<ors=20); 2.8% for those at low risk (score 21-30); 4.2% for those at moderate risk (score 31-40); 6.7% for those at high risk (score 41-50); and 13.8% for those at high risk.

Conclusion: The CRUSADE score does not validate in ST-segment-elevation myocardial infarction.
Determinants of myocardial salvage in patients with acute ST-segment elevation myocardial infarction: the critical role of prodromal angina

P.G. Masci1, S. Mustag2, L. De Luca3, J. Boggeri4, E. Bertella2, M. Franccone2, S. Bertì1, M. Mariani5, L. Agati1, L. Lombardi1
1Gabrielle Monasterio Foundation-CNR Region Toscana, Pisa, Italy; 2Cardiology Center Monzino (IRCCS), Milan, Italy; 3La Sapienza University, Rome, Italy; 4University Hospitals (UZ) Leuven, Campus Gasthuisberg, Leuven, Belgium; 5Gabrielle Monasterio Foundation-CNR Region Toscana, Heart Hospital, Massa, Italy

Background: Determinants of myocardial salvage (MS) in acute myocardial infarction (MI) patients are yet poorly known. Although in humans the time-to-reperfusion has been regarded as the main factor influencing MS, animal models suggest that other parameters may modulate the ischemic jeopardize myocardium. A better understanding of these pathophysiological mechanisms could be crucial for planning more beneficial reperfusion strategies.

Methods: Ninety-seven ST-segment elevation MI patients treated by primary percutaneous coronary intervention (PCI) were prospectively studied by cardiovascular magnetic resonance (CMR) at 7±2 days after MI in 4 tertiary referral hospitals. The following clinical and angiographic data were considered: mean rate-pressure product (RPP) before PCI, new-onset prodromal angina (PA), medications administered before PCI, Rentrop grade and TIMI flow pre/post PCI. T2-weighted STIR fast-spin-echo and post-contrast segmented T1-weighted gradient-echo imaging short-axis images were used to quantify area-at-risk (AAR) and infarct size (IS), respectively. MS-index was calculated as (AAR-IS)/AAR.

Results: Patients with (n=33,[34%]) and without (n=64,[67%]) PA showed similar baseline clinical characteristics, albeit hypertension and hypercholesterolemia were less common in the former (41% vs 65% and 41% vs 59%, both P<0.05). Peak of troponin I was lower in PA-patients than non-PA patients (24±13 vs 59±33 pg/ml, P=0.05). Mean RPP time-to-reperfusion, door-to-balloon time, medications before PCI, TIMI flow pre/post PCI and Rentrop grade were similar in the two groups. Patients with and without PA showed comparable AAR (28±18 vs 26±20 g, P=0.99) though IS was lower in PA-patients than non-PA patients (15±13 vs 19±16 g, P=0.004) yielding greater MS-index (0.51±0.25 vs 0.31±0.25, P<0.001), better left ventricular regional and global systolic function. The inverse relationship between MS-index and time-to-reperfusion was observed only in patients without PA (r=−0.291, P=0.020) but not in those with PA (P=0.49). At multivariable linear regression analysis MS-index was independently associated with PA (β-coefficient: 0.300, P=0.004) after correction for TIMI flow pre/post PCI, Rentrop grade and infarct size. Conclusion: In patients with reperfused MI, new-onset PA is a strong and independent predictor of MS-index. Considering that pattern of anterograde or collateral blood flow to AAR is not influenced by PA, it is conceivable that PA protects myocardium at-risk through preconditioning. Notably, in PA-patients the MS-index is not any longer related to time-to-reperfusion.

Purpose: Patients with myocardial infarction often suffer from complicating anxiety and depression disorders leading to poorer prognosis and symptoms are particularly common in women. Little is known about long-term anxiety and depression in patients with angina and how this relates to chest pain, severity of coronary artery disease (CAD) and gender. We investigated the prevalence of anxiety and depression in relation to persistent chest pain.

Methods and results: We invited 360 patients (193 men and 167 women) who had a first time coronary angiography in 2008–2009 due to suspected stable angina subsequently treated with angioplasty or medical treatment (according to guidelines and physician preference) to participate in a questionnaire survey in 2011 with the Hospital Anxiety and Depression Scale as a key element. A cut-off point of 8 was used to identify anxiety and/or depression. Response rate was 84% and median time since angiography was 2.8 years. 24% of patients with obstructive CAD and 38% of patients without obstructive CAD reported persistent chest pain defined as symptoms once a week or more. In both men and women, anxiety and depression was more common in patients with persistent chest pain: 30% vs. 9% reported anxiety and 47% vs. 24% reported depression. Symptoms were equally common in patients with and without obstructive CAD and are shown in the table. In a multivariate logistic regression persistent chest pain predicted persistent depression (OR 2.68 [95% CI 1.57 – 4.59]) whereas this was not the case for gender or CAD. Similarly, persistent chest pain predicted anxiety (OR 4.56 [95% CI 2.31 – 9.02]) whereas gender and CAD did not.

Long-term anxiety and depression

<table>
<thead>
<tr>
<th>Obscutive CAD</th>
<th>No obstructive CAD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Angina</td>
</tr>
<tr>
<td>Anxiety</td>
<td>33</td>
</tr>
<tr>
<td>Depressiol</td>
<td>40</td>
</tr>
</tbody>
</table>

Conclusion: Persistent chest pain was common in both patients with and without obstructive CAD. In this study, persistent chest pain was associated with higher prevalence of anxiety and depression independently of gender and degree of CAD. Future studies should evaluate whether patients with no obstructive CAD would benefit from improved symptom control and identification of anxiety and depression disorders to the same extent as patients with obstructive CAD.

BIOMARKERS IN ACUTE CORONARY SYNDROMES

Combination of anemia and high B-type natriuretic peptide levels is indicative of in-hospital mortality of patients with acute myocardial infarction

Sendai City Medical Center, Sendai Open Hospital, Sendai, Japan

Background: Anemia is an important factor negatively affecting the prognosis of patients with ischemic heart disease. B-type natriuretic peptide (BNP), a marker of heart failure, is also closely associated with mortality in patients with acute myocardial infarction (AMI). However, only a few studies have assessed the relationship between hemoglobin (Hb) concentrations and BNP levels in such patients with regard to in-hospital prognosis. Methods and Results: This study included 508 patients with AMI; their Hb concentrations were determined on admission, and their BNP levels, approximately 2 days after MI in 4 tertiary referral hospitals. The combined effect of these values on in-hospital mortality was evaluated. Patients were classified into 4 groups according to the presence of anemia and their median BNP values. Anemia was defined according to the World Health Organization criteria (hemoglobin levels of <13 g/dl for men and <12 g/dl for women were indicative of anemia), and the cutoff value for BNP was 178.5 pg/ml for all patients. The incidence of in-hospital mortality for nonanemic patients with low BNP levels was 0.5%; for nonanemic patients with high BNP levels,12.8%; for anemic patients with low BNP levels, 10.8%; and for anemic patients with high BNP levels, 20.5%. In-hospital mortality was higher in anemic patients with high BNP levels than in nonanemic patients with low BNP levels (odds ratio, 55.6; 95% confidence interval [CI], 11.4–1001.1; p<0.0001).

Conclusion: Combination of anemia and high BNP levels is an independent predictor of in-hospital mortality of patients with AMI.
Lower serum free tri-iodothyronine levels are associated with presence and severity of coronary artery disease in the euthyroid patients

F. Ertas, H. Kaya, H. O. Akk, Z.A. Aliyan, I. Islamoglu, M. Oylumlu, E. Tekbas, M.S. Soydylic, M.S. Ulgem. Dicle University, Faculty of Medicine, Diyarbakir, Turkey

Objectives: Thyroid hormones have many effects on the heart and cardiovascular system. The aim of this study was to investigate the relationship between serum thyroid hormone levels, with the normal range, and the presence and severity of CAD in patients referred for coronary angiography.

Methods: We have studied a total of 119 consecutive patients (77 men, mean age (67.3±13.8 years) who underwent coronary angiography. Blood samples were tested for serum thyroid stimulating hormone (TSH) concentrations and for free tri-iodothyronine (FT3) and free thyroxine (FT4) concentrations. Additionally, conventional risk factors, clinical characteristics and angiographic results of coronary artery assessment were obtained. The Gensini scores were calculated for determination of the severity of CAD.

Results: FT3 levels were significantly lower in subjects with CAD (4.6±0.6 vs 4.0±0.7, P=0.0001). Moreover, severe CAD was significantly associated with lower FT3 levels (3.9±0.7 vs 4.5±0.6, P=0.0001). Multivariate logistic regression analysis demonstrated that the lower serum FT3 levels was associated with presence (OR: 0.266, 95% CI: 0.007-0.731, P=0.001) and severity (OR: 0.238, 95% CI: 0.083-0.685, P=0.0008) of CAD. By ROC analysis, a level of FT3 < 4.2 predicted the presence of CAD with 69% sensitivity and 71% specificity (ROC area under curve: 0.744, 95% CI: 0.653-0.834, P<0.0001) in euthyroid patients.

Conclusions: Serum FT3 levels within the normal range were inversely associated with the presence and severity of CAD in patients referred for coronary angiography. Moreover, lower serum FT3 concentrations were correlated with the Gensini score and independently predicted the presence and severity of CAD in euthyroid patients. The FT3 levels may be used to indicate increased risk of CAD.

The importance of troponin I release curve in the Myocardial Infarction

L.V. Paiva. Hospital Center of Coimbra, Coimbra, Portugal

Troponin is a decisive biomarker in the diagnosis of myocardial infarction (MI) and has established prognostic power, differentiating MI from unstable angina. However, the best timing for the blood sample or the cut-off point, of troponin I (T) blood concentration, which gives the most prognostic information, is not yet established. We aimed to clarify the prognostic information given by the T release curve.

751 The subjects admitted with MI (68.9±13.0 years, 62.5% men, 44.9% STEMI, Variables analysed: admission T (Tadm), 2nd T measurement (Tmax), T slope between the 1st and 2nd measurement (Tslop) and the maximum T value at 24 hours from admission (T24h). Tadm and T24h were further divided (percentile05,50,75). Primary outcomes were in-hospital (IH) and 24-months mortality (24M).

IH (AUC, 95% CI)

- IHM 0.540 (0.47-0.62)
- IHF 0.581 (0.51-0.66)
- IH24h 0.541 (0.47-0.62)

IHM was 9.4% and 24M was 21.7%. ROC curve of Tadm, T2, Tmax, Tslop and T24h showed a weak relation with IHM and 24M. Only Tadm and Tmax related to IHM (46.5±8.4 vs 78.9±12.1, P=0.032) and Tadm to 24M (20.3±5.69 vs 28.4±7.14, P=0.028). Tadm and Tmax associated with LV systolic function post-MI (ANOVA, p=0.001). Neither the degree nor the direction (positive vs negative) of the Tslip related with IHM. Small [percentile 50:6.9ng/ml] or higher [percentile 75%-28ng/ml] Troponin variations between the 1st and the 2nd measurements had no association with IHM and 24M (p=0.05). The IHM24M predictor model on multivariate analysis did not include any of the studied variables. Grace score confirmed its high prognostic power in our cohort. The type of MI (STEMI: 5.9±13.3 vs. NSTEMI: 0.9±1, P=0.001) and patients undergoing coronary angioplasty (1.5±4.1 vs 4.6±12.1, P<0.001) significantly influenced Tslip values.

Conclusions: T release curve in the MI setting did not show discriminatory power to predict major adverse events. Our results suggested that T has its most value on the confirmation of MI and on LV systolic function compromise. It seems that
Phosphoglucomutase activity might be a useful diagnostic marker during the acute phase of ST-elevation myocardial infarction

M. Nishinari1, N. Aoyama1, Z. Ogawa2, S. Yukino3, S. Oka3, Y. Kurosaki4, I. Takeuchi4, R. Imai5, H. Takehara5, T. Izumi1, 1Kitasato University, School of Medicine, Department of Cardio-Angiology, Sagamihara, Japan, 2Kitasato University, School of Allied Health Sciences, Sagamihara, Japan

Purpose: In acute myocardial infarction (AMI) patients, the activity of phosphoglucomutase (PGM), a key enzyme in cellular glucose utilization and energy homeostasis, was previously found to be higher than that in patients with angina pectoris. Since PGM levels increased along with those of myocardial (creatinine phosphokine, aspartate aminotransferase, troponin-T, heart-type fatty acid-binding protein), thrombosis (total plasminogen-activator inhibitor type 1, D-dimer), and inflammatory biomarkers (C-reactive protein, pentraxin 3), PGM might be a useful diagnostic marker during the acute phase in these patients. Therefore, in the present study we aimed to evaluate CD31 expression on overall CD4+T cells in patients with STEMI.

Methods: We evaluated the PGM activity in 290 healthy adults. PGM activity in the range 4.8–29.0 U/l was considered normal. Then, we evaluated the levels of serum PGM activity in 62 patients with AMI (54 with STEMI and 8 with NSTEMI). Results: The levels of PGM activity were increased in AMI, especially in the STEMI group (49.6 U/l) on admission. Peak PGM activity was significantly higher in patients with STEMI compared with patients with NSTEMI. Conclusions: Our findings suggest that PGM activity can increase with the development of AT, moreover, it might be useful as a diagnostic and predictive marker in patients with STEMI.

Effects of CD31 expression on circulating CD4 T-cells in patients with unstable angina

P. Tourikis, D. Tousoulis, A. Katak, N. Papageorgiou, C. Mpri, K. Toulougouz, G. Siasos, C. Antoniades, C. Tzentolouris, C. Stefanadis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: CD4+CD28null T cells are considered to have a direct involvement in plaque destabilization and in occurrence of acute coronary syndromes. In addition, studies indicate that CD31 signal act as regulator of T cells activation and migration to the vascular wall. Therefore, in the present study we aimed to evaluate CD31 expression on overall CD4+T cells in patients with unstable angina compared to patients with STEMI and healthy controls.

Methods: CD4+CD28null T cells and CD4+CD28+ T cells, CD4+CD31null T cells and CD4+CD31+ T cells were analyzed by the same method and expressed as percentage of the whole number of T cells. At the same time CD4+CD31+ T cells, CD4+CD28+ T cells and total CD4+CD31- T cells were assessed by flow cytometry and expressed as percentage of CD4+ T cells. Nevertheless, the frequency of CD4+CD31+ T cells showed a significant increase in healthy controls (6.674±3.895 vs 11.227±7.709, p=0.0057).

Conclusions: We have shown that patients with unstable angina have significantly lower frequencies of circulating CD4+CD31+ T cells. However, no significant difference in the percentage of circulating CD4+CD28null T cells and total CD4+CD31- T cells was observed. Our results suggest that the presence of CD31 molecule seems to have a key atheroprotective role.

Glycated hemoglobin is associated with complexity of coronary artery disease even in non-diabetic patients

N. Ikeda1, R. Iijima2, H. Hara3, M. Mora1, M. Nakamura2, K. Sug1, 1National Center for Global Health and Medicine, Cardiology Division, Tokyo, Japan; 2Tokyo University, Onishi Medical Center, Department of Cardiovascular Medicine, Tokyo, Japan; 3Tongji Medical College of Huazhong University of Science and Technology, Wuhan, China, People’s Republic of China

Purpose: Glycated hemoglobin (HbA1c) value relates with risk factors cardiovascular events. However there is no previous study to evaluate the predictive value of HbA1c for the complexity of coronary lesions. The aim of this study is to evaluate the correlation between HbA1c and complexity of coronary artery disease using the SYNTAX score (SxScore).

Methods: We enrolled 513 consecutive patients who underwent first coronary angiography and were measured HbA1c from December 2008 to August 2011. The complexity of the coronary lesions were evaluated by the SxScore.

Results: The study patients were divided into quartiles according to HbA1c or FG (6.2–8.5, 8.5–9.6, 9.6–10.7, 10.7–12.8). The frequency of CD4+CD28null effector T cells, decreased frequency of CD3+CD4+CD45RA+CD62L+ naïve T cells and a compensatory increase of CD3+CD4+CD45RO+ memory T cells could be observed in aged normal group, compared with young normal group (<0.05 respectively). The frequency of CD4+CD25+CD62L- Treg cells showed no significant difference between the two groups. Compared with aged normal group, an expansion of CD3+CD4+CD28null effector T cells and decline of CD3+CD4+CD25+CD62L+ Treg cells, decreased CD3+CD4+CD45RA+CD62L+ naïve T cells and a compensatory increase of CD3+CD4+CD45RO+ memory T cells were observed in aged patients with ACS (p=0.05 respectively). The numbers of Tregs were similar between the three groups. These senescent changes in CD4+ T cell subpopulations were correlated with inflammation and chronic infection such as HP infection.

Conclusions: Our findings suggested an age-inappropriate CD4+ T cell disturbance in aged patients with ACS might be a phenomenon of immunosenescence, and chronic inflammation closely correlated with these changes in CD4+ T cells. They together formed a vicious circle which contributed to the pathogenesis of this disease.
In addition, higher HbA1c value presented independent predictive value for the patients with intermediate or high SxScore (the SxScore >23) after adjusted for age, sex, hypertension, dyslipidemia, creatinine and FG values (Odds ratio 1.564, 95% CI 1.202 to 2.034, p=0.0069) [Table].

Conclusions: HbA1c significantly associates with the complexity of coronary lesions. The association is observed even in non-diabetic adults. Higher HbA1c value is an independent predictor for the prevalence of complex coronary lesions.

**Endothelial function and circulating CD4-T cells in acute coronary syndromes**

P Tourikis, D Tououil, A Kakata, C Mipi, G Siasos, C Antoniadis, S Kioulaf, D Altnassan, K Toutouzas, C Stefanakis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece.

**Purpose:** Previous studies support the crucial role of immune responses in the development and progression of atherosclerosis. CD4+CD28null T cells and CD4+CD31+ T cells represent two specific subsets of circulating CD4+ T cells that affect endothelium. However, their accurate role on endothelial function remains controversial. Therefore, in the present study we examined the association between the frequencies of these T cells subsets and endothelial function in patients with unstable angina compared to healthy individuals.

**Methods:** Twenty-nine patients with unstable angina (23 males, mean age 61±2 years) and fifteen healthy controls (8 males, mean age 58±2 years) were studied. Endothelial function was evaluated by estimating the flow mediated dilatation (FMD) of the brachial artery. Venous blood samples were taken at the time of the index event for the patients with unstable angina. Circulating total CD4+ T cells, CD4+CD28null T cells, CD4+CD28+ T cells, CD4+CD31+ T cells and CD4+CD31- T cells were analyzed on fresh blood samples by flow cytometry.

**Results:** We compared the endothelial function and the levels of circulating CD4 T cells between patients with unstable angina and healthy controls. Patients with unstable angina had significantly impaired FMD than healthy controls (5.12±0.47 vs 8.246±0.713, p=0.001) that was correlated with a significant increase in the frequency of circulating CD4+CD31- T cells when these cells were expressed as percentage of CD4+ T cells (83.86±5.049 vs 72.76±4.803, p=0.002) and as percentage of the whole T cells (33.545±2.721 vs 24.493±3.3, p<0.002). However, there was no significant difference in the percentage of total CD4+ T cells between the two groups (37.06±5.942 vs 32.847±3.598, p=0.15), either in the frequency of CD4+CD31+ T cells (5.57±0.632 vs 8.83±1.773, p=0.534), CD4+CD28null T cells (6.1±0.949 vs 6.63±1.55, p=0.241) or CD4+CD28+ T cells (30.22±2.116 vs 25.513±3.652, p=0.157) when was expressed as percentage of the whole number of T cells.

**Conclusions:** The findings of the present study demonstrate that patients with unstable angina have significantly impaired FMD and significantly higher frequencies of CD4+CD31- T cells. These findings suggest that the increased levels of circulating CD4+CD31- T cells may significantly ameliorate endothelial function in patients with unstable angina.
Periprocedural ischemia in coronary bifurcation: relevance to intracoronary electrogrocardiography - influence on long-term results

D.I. Vassilev, A.A. Alexandrov, H.F. Mateev, M. Pehlivanova, E. Kostova, M. Hazan, S.L. Gobelevich, N. Gotcheva, R.J. Goër, National Heart Hospital, Sofia, Bulgaria: Central Hospital of the Internal Affairs and Administration Ministry, Warsaw, Poland

Background: There is uncertainty about influence of periprocedural ischemia and myocardrosis on long-term results of coronary artery bifurcation stenting (PCI). The aim of the study is to explore the influence of end-procedural ischemia (detected with intracoronary electrocardiography [ieCG]) and post-procedural myocardrosis (tropinin and creatine-phosphokinase – MB [CK-MB] elevation) on revascularization rates (TLR) and cumulative MACE (death, myocardial infarction, TLR, rehospitalization) rates at 9-12 months after PCI.

Methods: After placement of intracoronary guidewires in main branch (MB) and side branch (SB) an uninstrumented proximal ends of wires were connected to unipolar V leads. Intracoronary unipolar ECGs (ieCEG) were recorded before, during and after stent placement and at the end of procedure. The maximal ST-segment elevation during intervention and 5 min after the procedure was recorded in MB and SB. At the end, the coronary wire was placed in every distal vessels with reference value <1.0 mm, as well as in MB just below the stent, "mapping" the largest fibrotic area was found in OMI (<0.001 vs. CONTROL), whereas the highest from 60 patients with stable/unstable angina. Provisional T-stenting was a default strategy.

Results: 72% were males, age 66±8, diabetes 34%, 43% had previous myocardial infarction, 41% previous PCI. 58% had multivessel disease. The main treated vessel was LAD (72%). True bifurcation lesions (Medina ≥1) were 58%. On ieCEG, the maximal ST-segment elevation was 12±9 mm in MB and 8.7±7 mm in SB (p=0.04). At the end procedure 44 patients had residual ST changes (66%): OMI (75% male; 35 years) had no overt pathological myocardial tissue findings. The largest fibrotic area was found in OMI (p<0.001 vs. CONTROL), whereas the highest from 60 patients with stable/unstable angina. Provisional T-stenting was a default strategy.

Conclusion: The ieECG is a highly sensitive and specific method for differentiation of ischemia region, prediction of periprocedural myocardrosis and future adverse cardiac events.

Immunohistological analysis of coronary thrombus aspirate in STEMI patients: pathological and clinical findings


Purpose: Thrombus aspiration (TA) therapy allows the exploration of thrombus and atheroma fragments in ST elevation myocardial infarction (STEMI) patients. Our aim was to characterize these samples by immunohistology and to analyze the association between pathological findings and clinical data.

Methods: 153 samples were analyzed. Inflammation, fibrin and karyorrhexis were measured. Perls iron stain was performed in 111 cases to identify remnants of old intra-plaque hemorrhage. Samples were stained with antibodies against macrophages (CD68), platelet endothelial cell adhesion molecule (CD31) and actin filament (HF35). Clinical, angiographic and procedural data were prospectively collected. Anova, Student-T and chi-squared tests were used for comparisons. The hazard ratios are presented with their 95CI.

Results: Median weight of aspirated material was 0.049 g (range 0.001-0.992 g). Thrombi were: fresh (fibrin and intact granulocytes) in 39%, lytic (areas of colliquation necrosis and karyorrhexis of granulocytes) in 26%, heterogeneous (fresh and lytic areas) in 29%, and organized in 6% of the samples. Granulocytic infiltration and extracellular matrix presence and distribution were absent in 56%, were demonstrated in 54%, were present in 5% and hemorrhage was detected in 26% of cases. Positive of IHC stains was: CD68, 44%; CD31, 20%, and HF35, 10%.

The presence of the aspirate was inversely associated with the presence of atheroma plaque (mean diff 0.073, 95%CI 0.015-0.129, p=0.013) and of per-platelet hemorrhage (iron positivity) (mean diff 0.068, CI 0.025-0.112, p=0.002). Patients with chest pain 48 h after STEMI (pre-existing angina) were much less likely to have atheroma plaque in their aspirates (12% vs. 88%, p<0.001). Same finding, although less pronounced, was found in patients with previous history of CAD (21% CD68 positive vs. 46% in patients w. no previous CAD, p=0.078).

Regarding clinical outcomes, MACE were less frequent in patients with samples containing atheroma plaque (29% vs. 15%, HR: 1.9 (95% CI: 1.9-3)). Patients with fresh thrombus had more probability of re-infarction (2.9% vs. 10%, HR: 0.25 (0.5-1.2)).

Conclusions: The presence of atheroma plaque and inflammation in intracoronary aspirates might have clinical and pathophysiological implications. Immunohistological analysis of the thrombus aspirate in STEMI patients could be useful to understand the pathologic mechanisms of coronary thrombosis and needs further investigation.

Stage-dependent detection of CD14+ and CD16+ immune cells in human heart tissue after myocardial infarction: A post-mortem analysis

F.S. Czeplut, M. Schlegel, F. Bremmer, G. Hasenfuss, K. Schaefer. University Medical Center Göttingen, Göttingen, Germany

Human monocytes (Mo) consist of at least 2 functionally distinct subsets and can be classified into CD14+CD16– (CD16–mo) and CD14+CD16+ (CD16+mo) cells. Mo are crucial for wound healing after acute myocardial infarction (AMI). However, the functional relevance of CD16+mo and CD16–mo subgroups as well as their specific impact on post myocardial infarction coronary atherosclerosis is largely unknown. We investigated human myocardial tissue obtained during autopsy. Based on clinical data as well as macro- and microscopical criteria, tissues were classified as fresh myocardial infarction (fMI), organized myocardial infarction, or chronic cardiac fibrosis (CONTR).

In addition to serial cross sections, tissue microarrays were generated to allow co-localisation analyses of histochimical signals. Besides the number of CD14+ and CD16+ cells, the degree of cardiac fibrosis (Masson’s trichrome stain), angiogenesis (immunohistochemistry for von Willebrand factor [vWF]) or hypoxia (carbonic anhydrase IX [CAIX] stain) were quantified. A total of 45 persons were included in the study: 11 subjects (55% male; median age, 66 years) died of AMI and 15 persons (80% male; 73 years) of SAMI. In 16 individuals (75% male; 79 years), signs of OMI could be detected, whereas 8 persons (75% male; 35 years) had no overt pathological myocardial tissue findings. The largest fibrotic area was found in OMI (p<0.001 vs. CONTR), whereas the highest from 60 patients with stable/unstable angina. Provisional T-stenting was a default strategy.

Conclusion: The inflammatory and hypoxic signals in myocardial tissue is stage-dependent. The degree of hypoxia in fresh myocardial infarction was less pronounced compared to organized atherosclerosis. This effect might be due to a difference in vessel size and vessel density in the different infarction stages, which might be a reason for the higher degree of inflammation in fresh myocardial infarction compared to organized atherosclerosis.

Peripheral endothelial function predicts the presence of coronary atherosclerosis but not that of inducible ischemia

S. Schaefer, S. Mixel, A. Beutel, L. Himmrich, R.S. Von Barsdebel, J.D. Parker, T. Gor, T. Muenzel, University Medical Center, Department of Internal Medicine II, Mainz, Germany; Mount Sinai Hospital of the University Health Network, Toronto, Canada

Introduction: An association between markers of peripheral endothelial function and the extent of coronary atherosclerosis (CAD) has long been demonstrated. Along with the extent of atherosclerosis, other factors, which are also felt to be endothelium-dependent, determine coronary perfusion. These include for instance coronary spasm, platelet activation and microvascular tone. Whether peripheral endothelial dysfunction is associated with coronary ischemia during physical stress remains however unknown.

Methods and results: Flow-mediated dilation (FMD) and low-flow-mediated constriction (L-FMC) were measured in 200 consecutive patients before coronary angiography (age 68±11 years, 141 males) and 100 consecutive patients undergoing echocardiographic stress test with a modified Bruce protocol (age 67±11 years, 79 males). As previously published, there was a progressive decrease in both L-FMC and FMD with increasing severity of coronary artery disease (L-FMC from -3.5±2.3% in patient with no CAD to -2.4±2.3% in patients with ≥3 vessels disease, P<0.01; FMD from 5.4±3.4% in patients with no CAD to 3.4±2.8% in patients with 3-vessels disease, P<0.01). In contrast, absolutely no difference was found between patients with negative stress-echocardiography (L-FMC: 2.5±1.19%; FMD: 3.7±2.5%) and those with negative stress-echocardiography (n=22, L-FMC: -2.2±1.9%; FMD: 3.8±1.5%) in any of the endothelial function parameters (all P>0.5). Further, none of the endothelial function parameters showed any correlation with peak heart rate, METS, WMS at rest and at peak stress (all P>0.5).

Conclusion: Parameters of peripheral endothelial function correlate with (and help predict) the presence and the extent of coronary atherosclerosis; in contrast, they bear no correlation with the presence of inducible ischemia.
**P956**
Left circumflex coronary artery is underdiagnosed as culprit lesion in STEMI and increases both short- and long-term mortality

J.F. Vojacek1, M. Zelizko2, P. Kala3, J. Bisa1, J. Dusek1, P. Zdrahal1, M. Jakl1 on behalf of Registry of Cardiovascular Interventions, Czech Republic; 1Dept Cardiology I, Cardiology, Faculty Medicine, Charles University, Hradcany, Prague, Czech Republic; 2Institute for Clinical and Experimental Medicine, Prague, Czech Republic; 3Masaryk University, Faculty Hospital Brno, Department of Internal Cardiology Medicine, Brno, Czech Republic

**Background:** Left circumflex coronary artery (LCA) occlusion in the setting of acute coronary syndrome (ACS) is often difficult to diagnose and thus primary PCI in this subgroup of patients may be delayed.

**Methods and patients:** Altogether 24 894 patients enrolled into the nationwide Registry of Cardiovascular Interventions (RCI) in the years 2005 and 2006 were classified as having ACS. From this number 12 123 (mean age 65.8 yrs, 4 062 females) were classified as having no ST segment elevation myocardial infarction (NSTE) and 12 771 (mean age 63.9 yrs, 3 967 females) as ST segment elevation myocardial infarction (STEMI). RCI is connected to the official Institute of Health Information and Statistics and updates regularly information about the death of any subject in the RCI.

**Results:** Culprit lesion was identified as left anterior descending (LAD) in 35.1%, left circumflex (LCA) coronary artery in 28.7%, and aorto-coronary venous graft or left internal mammary graft in 2.89% in NSTE patients and in 1.25%, 42.52%, 15.1%, 40.35% and 0.81% in STEMI patients, respectively. Patients with LCA involvement were significantly more often represented in NSTE group as compared to STEMI patients (p < 0.05). Thirty-day survival rate in NSTE with LAD, LCA and RCA and STEMI patients with LAD, LCA and RCA culprit lesion was 97.8%, 96.9%, 97.8%, 91.8%, 86.9% and 96.1%, respectively; respectively; p<0.05, five-year survival rates in the respective subgroups were 81.0%, 76.2%, 79.7%, 75.3%, 67.8% and 79.9% (p<0.05) (Fig. 1).

**Conclusion:** Underdiagnosis of LCA involvement in STEMI translates into significantly worse both short- and long-term prognosis in these patients.

---

**P957**
Use of and impact of thrombectomy on outcome in primary percutaneous coronary intervention in patients with STEMI. Data of the prospective ALKK PCI registry

K. Schmidt1, M. Hochadel2, R. Zahn1, J. Brachmann3, B. Laufer4, C. Pfaffert5, H. Daruis6, T. Rundel7, B. Zrenner8, U. Zeymer9
1Heart Center Ludwigshafen, Department of Cardiology, Ludwigshafen am Rhein, Germany; 2Heart Attack Research Center at the University of Heidelberg, Ludwigshafen am Rhein, Germany; 3Klinikum Coburg, Department of Cardiology, Coburg, Germany; 4Central Hospital Bad Berka, Department of Cardiology, Bad Berka, Germany; 5Klinikum Ingolstadt, Department of Cardiology, Ingolstadt, Germany; 6Vivantes Hospital Neukolln, Department of Internal Medicine-Cardiology, Berlin, Germany; 7Clinic of Wetzlar, Department of Cardiology, Wetzlar, Germany; 8Hospital Landshut Aischhof, Department of Cardiology, Landshut, Germany

**Background:** Thrombus aspiration during primary PCI in patients with STEMI has been reported to result in better myocardial reperfusion and improved clinical outcome compared with conventional PCI. Little is known about the use of thrombectomy in primary PCI in clinical practice.

**Methods:** We used the data of the ongoing German ALKK PCI registry. Baseline data, procedural features and in-hospital events of all consecutive PCI in patients with STEMI were collected on standardized case record forms and centrally analysed by the Institut fuer Herzinfarktforschung Ludwigshaign. Only those ALKK participating hospitals, which actually performed thrombectomies, were included in this analysis.

**Results:** In 2010 the data of 2694 patients with STEMI were included in the ALKK PCI registry. A thrombectomy was performed in 12.6% of patients. Baseline characteristics, procedural features and outcomes are shown in the table.

---

**P958**
Unrestricted use of two new-generation drug-eluting stents in patients with acute myocardial infarction: a propensity score matched analysis

K.Y. Chen1, S.W. Rna2, W. Lin1, Y.J. Li1, G.P. Li1, 1Tianjin Medical University, Department of Cardiology, Tianjin, China, People's Republic of; 2Korea University Guro Hospital, Seoul, Korea, Republic of

**Objectives:** This study sought to compare everolimus-eluting stents (EES) with zotarolimus-eluting stents (ZES) in patients with acute myocardial infarction (AMI).

**Background:** A paucity of data has exclusively evaluated the safety and efficacy of second-generation drug-eluting stents (DES) in the setting of AMI.

**Methods:** The present study evaluated 3309 AMI patients treated with ZES (n=1,168) or EES (n=1,701) in a large-scale, prospective, multicenter Korea Acute Myocardial Infarction Registry (KAMIR). Propensity score matching was applied to adjust for differences in baseline and angiographic characteristics, producing a total of 2,168 patients (1,343 receiving ZES, and 1,343 receiving EES). Major outcomes at 1 year were compared between the 2 propensity score matched groups. Target lesion failure (TLF) was defined as the composite of cardiac death, recurrent nonfatal myocardial infarction (Re-MI), or target lesion revascularization (TLR).

**Results:** After propensity score matching, baseline clinical and angiographic characteristics were similar between the 2 groups. Clinical outcomes of the propensity score matched patients showed that despite of similar incidences of Re-MI, in-hospital and 1-year mortality, patients in the EES group had significantly lower incidences of TLF (6.5% vs. 8.7%, P=0.029), and probable or definite stent thrombosis (0.3% vs. 1.8%, P=0.001) as compared with those in the ZES group. Furthermore, there were numerically lower incidences of TLR (1.2% vs. 2.2%, P=0.51) in the EES group than in the ZES group.

**Conclusions:** In this propensity-matched comparison, EES appears to be superior to ZES in reducing TLF and stent thrombosis in patients with AMI.

---

**P959**
Characteristics of plaque composition which induce slow flow phenomenon during percutaneous coronary intervention: virtual histology-intravascular ultrasound study

T. Ohwada, T. Yokokawa, T. Sakamoto, K. Watanabe, Fukusima red cross hospital, Fukushima city, Japan

The aim of this study is to elucidate the characteristics of plaque composition (PC) which induce slow flow phenomenon (SFP) during percutaneous coronary intervention (PCI) using virtual histology-intravascular ultrasound (VH-IUS).

**Methods:** We assessed PC with VH-IUS in 160 consecutive patients (stable coronary disease, n=89; acute coronary syndrome, n=71) before PCI. Fibrotic (FI), necrotic core (NC), dense calcium (DC) regions were evaluated. We assessed culprit lesion area in the minimum lumen diameter and area in the entire segment. Angiographic slow-flow was defined as TIMI flow grade 2-3 after PCI. Patients were divided into slow-flow group (SFG, n=28) and normal-flow group (NFG, n=132). Peak level of creatine phosphokinase (CPK) was measured. Characteristics were compared between SFG and NFG using logistic regression analysis.

**Results:** In SFG compared with NFG, %DC area (4.1±4.6 vs. 6.8±7.0 mm², P=0.0162) and %DC volume (4.6±3.3 vs. 6.9±5.2 mm³, P=0.0057) of SFG were smaller than those of NFG. Multivariateregression analysis identified FI volume (OR: 1.357, 95% CI: 1.034-1.782, P=0.0278) as a significant predictor of SFP. Interestingly, peak CPK was correlated with FI volume (r=0.559, P=0.047).

**Conclusion:** SFP during PCI depends on plaque characteristics defined by VH-IUS. Moreover, myocardial damage after PCI could be estimated by FI volume with VH-IUS.
Significance of st-segment depression in patients with repertused st-segment elevation myocardial infarction.

Assessment by cardiac magnetic resonance

E. Valero1, C. Bonanad1, J. Sanchis1, J. Nunez1, A. Lacar1, E. Almenar1, O. Pons2, C. Bosch2, M. Valls2, O. Víctor1, J. Desco2, J. Pinós2, J. Riera2, J. Esteve2, J. Roca2, M. Sánchez-Vidriales2, J. Planas2, J. M. Fuster1, J. M. Grande1.

Purpose: The aim of our study was to evaluate by cardiac magnetic resonance (CMR), the dynamics of ST segment depression (STD) in patients with a repertused ST-segment elevation myocardial infarction (STEMI) and its association with the structural impact on the left ventricle (LV). A preliminary analysis of its prognostic significance was performed.

Methods: The study involved 191 consecutive patients admitted for a first STEMI. ECG was recorded at admission, 90 minutes, 24 and 96 hours after reperfusion. The sum of STD (sumSTD) in all leads was calculated. CMR was performed at one-week, and the ejection fraction (EF %), area at risk (% of LV mass with edema in T2 sequences), infarct size (% of LV mass with late gadolinium enhancement) and microvascular obstruction (MVO, % of LV mass with lack of late gadolinium enhancement in the core of the infarct area) were measured. ECG and CMR were quantified by independent observers. Patients were categorized according to sumSTD greater than the median at admission (1 sumSTD, anterior infarctions: > 2 mm; non-anterior infarctions: > 6 mm).

Results: SumSTD rapidly normalized in comparison with the ECG recorded at admission, 24 hrs (0.4±1 mm) and 96 hrs after reperfusion (0.3±1 mm), p < 0.001. Patients with an anterior myocardial infarction (n=85) exhibited less sumSTD at admission than those with a non-anterior infarction (1.6±1 vs 4.1±1.7 mm, p < 0.001). SumSTD was not associated with EF, infarct size nor MVO (p = 0.2) in neither anterior nor non-anterior in-farctions. (1 SumSTD did show association with a larger area at risk in both, anterior (42±14% vs 35±15%, p = 0.05) and non-infarction (25±10% vs 17±12%, p = 0.05). During the follow-up of 6 months, 13 re-infarctions and 17 re-admissions for acute heart failure: 34 patients (17%) had a first event. (1 SumSTD was not associated with outcomes neither in anterior (23% vs 29%, p = 0.6) nor in non-infarction myocardial infarctions (15% vs 10%, p = 0.3).

Conclusions: STD in patients with a STEMI tends to progress and rapidly normal-ize after reperfusion. At admission, STD is greater in non-anterior myocardial infarctions (n=85) exhibited less sumSTD at admission than those with a non-anterior myocardial infarction (1.6±1 vs 4.1±1.7 mm, p < 0.001). Patients with an anterior myocardial infarction (n=85) exhibited less sumSTD at admission than those with a non-anterior myocardial infarction (1.6±1 vs 4.1±1.7 mm, p < 0.001). }

Coronary artery calcification and the risk of heart failure in the elderly; The Rotterdam Study


Purpose: The purpose of this study was to determine the association of CAC with incident heart failure in the elderly, and examine its independence of overt CHD.

Methods: Within the Rotterdam Study, a prospective population-based cohort, 1,897 asymptomatic participants (mean age 69.9 years, 58% women) underwent CAC scoring and were followed for the occurrence of heart failure and CHD. Patients with a higher median CAC (sumCAC) exhibited a larger area at risk in both, anterior (42±14% vs 35±15%, p = 0.05) and non-infarction (25±10% vs 17±12%, p = 0.05). There was a significant correlation between tortuosity of coronary arteries (TCA) and carotid intima-media thickness (15% vs 10%, p = 0.3).}

Conclusions: CAC has a clear association with the risk of heart failure, independently of overt CHD. Since heart failure is highly prevalent in the elderly, it might be worthwhile to include heart failure as an outcome in future risk assessment programs incorporating CAC.

Coronal artery tortuosity: comparison with retinal arteries and carotid intima-media thickness

V. Davutoglu1, A. Dogan2, S. Okumus3, T. Demir4, M. Tatar5, B. Gurler5, S. Ercan3, I. San1, H. Alci1, Gaziantep University, Faculty of Medicine, Department of Cardiology, Gaziantep, Turkey; 2Gaziantep University, Department of Ophthalmology, Gaziantep, Turkey; 3Gaziantep University, University of Medicine, Department of Cardiology, Gaziantep, Turkey; 4Gaziantep Education Hospital, Department of Cardiology, Gaziantep, Turkey; 5Gaziantep University, Faculty of Medicine, Department of Physiology, Gaziantep, Turkey.

Purpose: We conducted a prospective study to investigate the possible relationship between tortuosity of coronary arteries (TCA) and carotid intima-media thickness and to compare TCA with retinal artery tortuosity.

Methods: A total of 105 participants (age 30–81 years) with non-significant coronary plaque or apparently normal coronary angiogram were included in the study. Group 1 consisted of 58 individuals with TCA and group 2 consisted of 47 individuals without TCA. The presence of TCA was identified by the finding of ≥4 tortuous coronary arteries and ≥3 tortuous carotid arteries and ≥1 tortuous retinal arteries. Retinal tortuosity was determined using the Optovue® Cirrus 4000 OCT scanner (Carl Zeiss Meditec Inc., Dublin, CA, USA) through the analysis of the OCT images. The presence of tortuosity was confirmed by a confirmed radiologist. The prevalence of TCA was compared with the prevalence of retinal tortuosity and carotid intima-media thickness.

Conclusions: The prevalence of TCA was higher in participants with TCA than without TCA (p = 0.001) and also presence of carotid intima-media thick was more common in patients with TCA than without TCA (p = 0.001). Rf=0.4, Rf=0.4 re-pectively. Carotid intima-media thickness was higher in participants with TCA than without TCA (p = 0.001) and also presence of carotid artery plaque was more common in patients with TCA (p = 0.001). There was a significant correlation between tortuosity of coronary arteries and TCA (p=0.005, R=0.3). Likewise, significant correlation were found between subclinical atherosclerosis and retinal artery tortuosity (p=0.02, R=0.3). Multivariate analysis identified female gender (p<0.008), retinal artery tortuosity (p=0.011) and carotid artery intima-media thickness (p=0.02) as independent predictors of TCA.

Conclusion: These results indicate that, whatever the mechanism is, 1) TCA is associated with retinal artery tortuosity and carotid intima-media thickness; 2) TCA is associated with subclinical atherosclerosis even in the present entirely normal appearance of coronary artery on angiography; 3) TCA correlated with retinal artery tortuosity implying that coronary tortuosity is a piece of systemic arterial tortuosity.
Comparison of levels of reperfusion induced apoptosis and cardiac myocyte necrosis during thrombolytic and primary percutaneous coronary intervention to treat ST-segment elevation myocardial infarction


Background: A recent study showed that stage 2 sleep, which includes sleep stages 2 to 4, is involved in the resolution of myocardial infarcts (1). This study investigated the role of stage 2 sleep in patients with acute myocardial infarction (AMI) in the early phase after mechanical reperfusion as a parameter of the rate of left ventricular remodeling.

Methods: We conducted a retrospective study on 5523 Chinese patients who were hospitalized with AMI. Clinical information collected from medical records, including age, sex, comorbidity disease, complication and clinical outcome, were statistically analyzed to determine the risk factors for cardiacogenic shock of patients with AMI. Then we evaluated the influence of cardiacogenic shock on the prognosis of AMI.

Results: Of 5523 hospitalized AMI patients, 197 (3.55%) progressed to cardiogenic shock. The independent risk factors for the development of cardiogenic shock were the presence of cardiogenic shock in patients with AMI and once AMI patients complicated with cardiogenic shock, their risks of 30-day mortality are increased. Early verified and managed AMI patients who were prone to cardiogenic shock may reduce 30-day mortality.

Conclusions: The novel finding is that the higher proportion of stage 2 sleep during non-REMP sleep may be related to the better recovery of LV systolic function.

Relationship of sleep structure and recovery of left ventricular systolic function in patients with acute myocardial infarction

H. Nakashima1, T. Henni1, Y. Uchida1, Y. Shiroma1, T. Nunohiro1, K. Maemura2, N. Nakamizo, K. Okamoto1

Aims: A few experimental studies have found that coronary flow dynamics is changed by sleep stages. However, there are no clinical studies that examine the relationships of sleep structure and cardiac function. We tested our hypothesis that the sleep structure estimated by polysomnography may have a significant impact on the recovery of left ventricular function in patients with ST-segment elevation myocardial infarction (STEMI).

Methods: This study included 346 STEMI patients who underwent primary percutaneous coronary intervention (PCI) within 12 h from the onset. Left ventricular ejection fraction (LVEF), regional wall motion (RWM), left ventricular size, perinfarct zone, and end-diastolic volume index (LVEDVI) were measured using left ventriculography after PCI and at 14 day. The distribution of sleep stage was quantitatively analyzed by polysomnography.

Results: The proportion of rapid eye movement (REM) sleep and the proportion of stage 1, 3, 4 during non-REM sleep did not show any relationship with the changes of LV function. Proportion of stage 2 sleep showed a significant weak correlation with changes of LVEF and RWM (r=0.163, p=0.009; r=0.145, p=0.026). Both LVEF and RWM showed stepwise good recovery across the quartile groups of stage 2 sleep. Multiple regression analysis showed that the proportion of stage 2 sleep was positively correlated with the recovery of LVEF and RWM (regression coefficient=0.13, p=0.039; regression coefficient=0.013, p=0.033). Presence or absence of sleep apnea syndrome could not modify the results.

Conclusions: STE enables quantification of regional myocardial function in patients with AMI. The longitudinal strain measured early after mechanical reperfusion may predict infarct size and LV remodeling. Thus, this data suggests that radial and circumferential strain in perinfarct and remote regions early after AMI may contribute to adverse left ventricular remodeling.
Clinical impact of pre and post PCI TIMI 3 flow on myocardial infarction vs control (38.1 ± 1.2% with LVEF (r2 0.33; p=0.0004) and EDV (r2 0.74; p=0.0001). There were no significant differences in 1-year recurrence of MI, repeated PCI were no significant differences in 1-year mortality, recurrence of MI according to initial TIMI flow. Final TIMI 3 flow means procedural success. Final TIMI 3 flow and EDWT may provide a simple and reliable method to monitor myocardial recovery in STEMI, expressed as reduced end diastolic LV volume and improvement of LVEF at 1 month.

Conclusions: This study confirms a progressive increase in EDWT following pPCI, as documented by pathological reports. Monitoring regional myocardial EDWT and ΔEDWT may provide a simple and reliable method to monitor myocardial recovery in STEMI. Time chest pain onset to balloon in subjects with and without RVMI was 318±188 min and 272±185 min, respectively (p=NS). All patients with RVMI demonstrated regional RV wall motion abnormalities. Comparing subjects with and without RVMI, the former had lower left ventricular (LV) ejection fraction (EF) (35±8% vs 42±12%, p<0.05), higher LV end diastolic volume index (EDVI) (88±19 ml/m² vs 77±20 ml/m², p<0.05), higher volume of LVGE (56±36 ml vs 38±26 ml, p<0.05) and LV microvascular obstruction (6±12 ml vs 4±4 ml, p<0.05). Patients with RVMI had more frequently postinterventional TIMI flow (70% vs 50% and 21% vs 30%, p<0.05) and distal embolization of left anterior descending artery (6 (30%) vs 8 (10%), p<0.05).

Conclusions: Right ventricular involvement is not uncommon in anterior STEMI and is associated with larger extent of left ventricular myocardial infarction and suboptimal outcome of percutaneous coronary intervention.

Conclusions: This study demonstrates that initial TIMI 3 flow significantly decrease 1-year MACE. Also final TIMI 3 flow significantly decrease in-hospital mortality, 1-year mortality, 1-year MACE rate in patients with STEMI in Korea.
Figure 1A. There is good agreement between the two methods with a bias of -5.7% LV (95% CI -33.2 to 21.9). However, when assessing the association between the AAR and IS, there is much stronger association between the IS with the AAR by CMR (r=0.46) (Figure 1B) than the AAR by APROACH (r=0.41) (Figure 1C).

Conclusion: Although there is a good agreement between AAR assessed by anatomic and delayed enhancement cardiac magnetic resonance (DE-CMR) studies were performed ≥24hrs apart. The relative amount of DE tissue per segment was used to define: no necrosis (0% DE), transmural necrosis (51-100% DE). All subjects were selected for good image quality, sinus rhythm and adequate 2D/3D speckle-tracking in at least 14 of 17 LV segments. LV function was assessed from three apical LV 2D views by measuring 2D longitudinal strain (2D-Ls), and from 4-beat LV full-volume data sets, assessing wall motion score (WMS) and measuring 3D longitudinal (Ls), circumferential (Cs), and radial (Rs) strains.

Results: Among all parameters, 3D WMS (AUC= 0.87, 95%CI 0.83-0.90) and 2D-Ls (AUC= 0.83, 95%CI 0.80-0.87) were the best predictors of transmural extent of myocardial necrosis. The predictive value of 3D WMS was significantly higher than 2D-Cr (AUC= 0.85, 95%CI 0.76-0.84, p<0.05). As (AUC= 0.81, 95%CI 0.77-0.84, p<0.05), Rs (AUC= 0.81, 95%CI 0.77-0.84, p<0.05), Ls (AUC= 0.73, 95%CI 0.69-0.77). The incremental predictive value of 2D and 3D strain parameters over 3D WMSI was significant, but small (Figure). However, the AUC of the predictive model for transmural necrosis at DE-CMR which included 3D WMS, 2D Cr and 3D Cs was 0.91 (95%CI 0.88-0.93; p<0.0001).

Conclusions: Despite a good accuracy for both 3D Cr and 2D Ls, visual wall motion assessment by experienced reader on good-quality 3D LV data sets was found to be superior than strain quantification to predict transmural necrosis at DE-CMR.

Detection of unstable plaques in STEMI patients

P. Cervinka, R.S. Spacek, M.B. Bystron, M.K. Kvasnak, P.K. Kala on behalf of grant of IGA Ministry of health of the Czech Republic no. NS 9804-4-II0808, Masaryk Hospital, Department of Cardiolog, Unit nad Labern, Czech Republic

The aim: Using an optical coherence tomography (OCT) to assess plaque characteristics of culprit lesion of infarct related vessel and to detect possible unstable plaques of noninfarcted vessel in patients with STE elevation myocardial infarction (STEMI) treated with primary PCI (pPCI).

Method: 30 consecutive patients with single vessel disease and STEMI were enrolled in the study. OCT study of the culprit lesion of infarct related vessel was performed initially after the insertion of intracoronary wire either with or without lesion predilatation. Final OCT of culprit lesion after stenting/aspiration and also other two non-infarcted vessels was performed 3 days after primary PCI.

Results: Plaque rupture of culprit lesion was found in 10 (70%) patients. In the infarct-related culprit lesion, TFCA and trombus was found in 100% of cases. Plaque rupture was recognized in 70% of lesions. In the OCT findings of non-infarct vessels, the frequency of unstable plaques was 47%. In the majority of cases (37%), only 1 non-infarct related vessel was involved. However, 3 patients (10%) have unstable plaques in both non-infarcted arteries. Moreover, plaque rupture and thrombus formation were found in 23% of cases of non-infarcted related vessels. 30-day, 6-month and 9 month follow-ups were uneventful. At 9 month follow up, the number of unstable plaques (according to OCT) significantly decreased from average 2.9 to 1.4. Furthermore, both total cholesterol and LDL cholesterol also decreased significantly (from 5.7 to 4.26 mmol/l and from 3.58 to 2.44 mmol/l respectively). HsCRP decreased significantly at 9 month to (from 7.5 to 2.5 mg/l). We found a strong correlation between the number of unstable plaques and smoking. Patients who did not quit smoking, the number of plaques was significantly higher.

Conclusions: Present study demonstrates high frequency of OCT-derived TCFa, plaque ruptures and thrombus of both, infarct and noninfarct-related coronary vessels in patients with evolving STEMI. Fortunately, at 9 month follow up, the number of unstable plaques significantly decreased.

The ICALOR home-nurse led disease management programme in heart failure prevents hospital readmission: a French nationwide time-series comparison

N. Agrinier1, C. Ailler2, F. Allain3, N. Jay4, D. Dobre5, N. Thierry6, F. Zamad7 on behalf of ICALOR. 1INSERM, CIC-EC CIE 6E; CHU Nancy, Epide quiologie et Evaluation Cliniques; EA 4860 Amecin, Nancy, France; 2ICALOR, Nancy, France; 3INSERM, CIC-EC CIE 6E; CHU Nancy, Département d’information médicale, Nancy, France; 4Département de Cardiologie, INSERM, CIC8051 and U061, CHU Nancy, Hypertension and Heart Failure Unit, Vandoeuvre les Nancy, France; 5Department of Cardiology, INSERM, CIC8051, CHU Nancy, Hypertension and Heart Failure Unit,ICALOR, Vandoeuvre les Nancy, France

Purpose: Insufficiency CArdiaque en LORraine (ICALOR), a multidisciplinary management programme for heart failure (HF) was established in 2006 in Lorraine, a French region of 1.5 million adult inhabitants. Our purpose was to describe the implementation of the ICALOR programme, and to assess its effectiveness on the incidence of HF hospitalisations and related costs from a population perspective.

Methods: Patients were admitted in ICALOR after an index hospitalisation for worsening HF. Patients were provided a patient education programme and then...
followed by a HF trained home nurse (average 10 home visits/year) who monitored simple health indicators that were conveyed by a web-based medical record to primary care physicians and cardiologists who also received automatic alerts generated by the computer system. We used the ICALOR information system and national hospitalisation database to conduct the analyses. Two quasi-experimental methods were used to assess HF hospitalisations rates: one individual before-and-after analysis and one time-series trends comparison of the French national to the Lorraine region data using the national hospitalisation database.

Results: The median age of the 1222 patient recruited before 2010, was 76 years and 65.5% were male. Upon enrolment, patients essentially presented with NYHA class II (n=537, 48.4%) or class III (n=359, 32.4%) symptoms. One-year mortality rate was 20.3%. The mean number of hospitalisations was significantly lower during the 6-month period after inclusion in the programme than during the 6-month period preceding inclusion (40%). The difference between the number of hospitalisations observed in the Lorraine region and that expected had it been similar to that observed in the whole country was -7.19% in 2010. The annual hospital cost avoided by ICALOR was estimated to €1,766 < €2,299 per patient.

Conclusions: Disease management of HF based on patient education and HF trained home-nurse patient monitoring with automated feedback to primary care physicians improve outcome cost-effectively in France. Lower rate of HF hospitalisations in patients included in ICALOR had a significant population impact and could prevent in Lorraine the concomitant continuous rise of the annual HF hospitalisations rate otherwise observed in France.

**Epidemiology and management programmes**

**Table 1. Prevalence of heart failure in percentage from 1990 to 2007 by age**

<table>
<thead>
<tr>
<th>Year</th>
<th>19-54</th>
<th>55-64</th>
<th>65-74</th>
<th>75-84</th>
<th>85-99</th>
</tr>
</thead>
<tbody>
<tr>
<td>1990</td>
<td>0.040</td>
<td>0.43</td>
<td>4.5</td>
<td>25.4</td>
<td>10.9</td>
</tr>
<tr>
<td>1994</td>
<td>0.047</td>
<td>0.52</td>
<td>1.8</td>
<td>5.1</td>
<td>10.9</td>
</tr>
<tr>
<td>1998</td>
<td>0.055</td>
<td>0.63</td>
<td>1.9</td>
<td>5.2</td>
<td>11.5</td>
</tr>
<tr>
<td>2002</td>
<td>0.055</td>
<td>0.49</td>
<td>1.7</td>
<td>5.0</td>
<td>11.0</td>
</tr>
<tr>
<td>2007</td>
<td>0.060</td>
<td>0.50</td>
<td>1.5</td>
<td>4.4</td>
<td>10.1</td>
</tr>
</tbody>
</table>

Fig. 1: Trends in number of HF patients

**Conclusions:** Overall, prevalence of HF peaked in the late 90s and then decreased. In the three oldest age groups, containing most HF patients, prevalence peaked in 1998 followed by a decrease until 2007. Prevalence increased in the two youngest age groups, most markedly among people <55 years. In absolute numbers the age group 85-99 years increased, mainly due to demographic changes.

**Economic burden of patients with various etiologies of chronic systolic heart failure analyzed by resource use and costs**

J. Biermann1, A. Neumann2, C.E. Angermann1, R. Erbel1, B. Masch1, V. Regitz-Zagrosek1, T. Scherf1, R. Wachter1, G. Gelbrich3, T. Neumann4 on behalf of German Competence Network Heart Failure. 1Clinic of Cardiology, University Hospital Essen, Essen, Germany; 2University of Duisburg-Essen (UDE), Essen, Germany; 3Department of Internal Medicine I and Comprehensive Heart Failure Center, University Hospital, Würzburg, Germany; 4University Hospital Giessen and Marburg, Department of Internal Medicine, Marburg, Germany; 5Charité - University Medicine Berlin, Campus Mitte, Institute for Gender in Medicine (GiM), Berlin, Germany; 6Institute for Heart and Circulation Research, Dortmund, Germany; 7Department of Cardiology and Pneumology, Georg-August University Göttingen, Göttingen, Germany; 8Center for Clinical Trials (KKS), University of Leipzig, Leipzig, Germany

**Purpose:** Chronic heart failure is a major cardiac disease, going along with a high economic burden. Diagnostic and therapy differ depending on etiology of chronic heart failure. The present work analyses disease-related resource use and associated costs of systolic chronic heart failure with respect to the etiology of the disease.

**Methods:** From the database of the German Competence Network Heart Failure, 2,710 individuals with systolic chronic heart failure (mean age 62.9 years ± 13.6, 25.2% female, 89.8% NYHA II/III) were included into analyses. Resource use was assessed with regard to outpatient contacts, hospitalisations including rehabilitation, and drug utilization.

**Results:** Overall care costs per patient were 3,150 € per year. Costs of inpatient care were the largest component of direct costs (2,622 €) thus representing 83% of total costs. Costs of medication (290 €) and outpatient physician contacts (238 €) were significantly lower. Lower average costs of heart failure care appeared in patients with hypertrophic cardiomyopathy (4,681 €) and dilated cardiomyopathy (3,596 €), while patients with heart failure due to coronary artery disease (3,046 €) and arterial hypertension (1,039 €) showed significantly lower resource use and costs per year.

**Conclusions:** Heart failure is associated with a high economic burden. Patients with non-vascular forms of heart failure require an over-average resource use primarily due to hospital admissions. Efficient treatment strategies have to consider these aspects for optimizing care and to delimitate the economic costs of heart failure care.

**Patients with chronic systolic heart failure require individualised care also for non-cardiac problems**

S. Kreiss1, S. Stoerk1, G. Gelbrich3, M. Hanke1, H. Faller1, G. Ertl1, C.E. Angermann1, 1Department of Internal Medicine I, University Hospital Würzburg; Comprehensive Heart Failure Center, Würzburg, Germany; 2Clinical Trial Centre, University of Leipzig, Leipzig, Germany; 3Comprehensive Heart Failure Center; University of Würzburg, Würzburg, Germany; 4Institute of Psychotherapy and Medical Psychology; University of Würzburg, Würzburg, Germany

**Purpose:** The Interdisciplinary Network for Heart Failure (INH) Study developed a novel nurse-coordinated program, HeartNetCare-HF (HNC), which provides telephone-based structured monitoring and education. HNC uses a standardised 19-item protocol allowing indicators of worsening heart failure, symptoms, compliance, state of mood and health care utilisation. Educational modules cover e.g. medication, nutrition and physical activity. Further, patients are invited to raise questions themselves. According to the INH protocol nurses documented telephone contacts during follow up (FUP, 180 days) were categorised regarding monitoring, education and medical problems addressed by the patients.

**Results:** 411 contacts with a mean duration of 12.5 min took place between nurses and HNC-patients. 85% of the 329 HNC patients received at least one intervention and were thus included into the analysis. Contents of telephone contacts during follow up (FUP, 180 days) were categorised regarding monitoring, education and medical problems addressed by the patients.

**Conclusions:** Our study highlights the importance of outcome-relevant non-
cardiac co-morbidities in HF patients. Solely technically based telemedical strategies can obviously not meet results patient needs. Individualised risk assessment and tailored integration of appropriate cardiac telemonitoring with comprehensive individualisation care is required to improve outcomes in HF.

Heart failure, ventricular dysfunction and risk factor prevalence in a young Aboriginal population: The Heart of the Heart Study

M. Mogrady1, H. Krum1, M. Carrington2, S. Stewart1, C. Zelti2, M. Marwick2, T. H. Marwick1, B.A. Haikursa1, A. Brown1, Monash University, Melbourne, Australia; 2Baker IDI, Melbourne, Australia; 3University of Adelaide, Adelaide, Australia; 4Cleveland Clinic, Cleveland, OH, United States of America; 5University of Queensland, Brisbane, Australia; 6Baker IDI, Alice Springs, Australia

Purpose: Heart failure (HF) has a grim prognosis, with Indigenous populations having poorer outcomes and HF mortality 2-3 times greater than non-Indigenous counterparts. Despite this there has been little evaluation in this group, thus we sought to document HF, asymptomatic left ventricular dysfunction (ALVD), risk factor prevalence and associations in a young Indigenous population.

Methods: Comprehensive cardiovascular assessments, including clinical examination, echocardiography, ECG, hemoglobin, anaemia, and medical record review were used to determine heart failure status (independently adjudicated), ALVD and underlying risk factors in participants enrolled across 6 Indigenous communities.

Results: Of 436 participants (mean age 44±14 years, 64% women) enrolled, 23 were diagnosed with HF (5.3%; 95% CI: 3.2-7.2%), only 8 had a pre-existing HF diagnosis. ALVD was observed in 53 (syntocic 11, diastolic 42); participants (13%, 95% CI: 9.4-15.7%). HF risk factor prevalence was as follows: hypertension 42% (95% CI: 37-47%), diabetes 34% (95% CI: 30-39%), coronary artery disease (CAD) 7.4% (95% CI: 4.9-9.9%), obesity (BMI≥30kg/m²) and history of acute rheumatic fever or rheumatic heart disease 7.3% (95% CI: 4.9-9.8%). The mean HbA1c was 6.9±1.1%, with 37% (95% CI: 33-42%) of subjects having an elevated HbA1c (>6.5%), 18% (95% CI: 15-28%) of these without diabetes diagnosis. Elevated BP (systolic >140mmHg and/or diastolic >90mmHg) was measured in 34% (95% CI: 29-38%) with 68% (95% CI: 61-70%) without hypertension diagnosis. In logistic regression (adjusted for age and gender), HF was associated with CAD (OR 6.1, p=0.0001), hypertension, and obesity (BMI≥30) the 9.6, p<0.001: 5.4, p<0.002: 4.8, p=0.06: 2.9, p=0.02, respectively. All of the above HF risk factors were associated with both systolic and diastolic dysfunction. In multivariate models (adjusted for age, sex, HF risk factors, BNP and creatinine), only CAD (p=0.04) and BNP (p=0.001) remained independently associated with impaired systolic dysfunction (LVEF <50%) and age (p =0.001), diabetes (p=0.006) and BNP (p=0.006) with diastolic dysfunction.

Conclusion: The burden of HF, a large proportion undiagnosed, along with ALVD, and risk factors in this young population were high. Impaired glucose metabolism and high BP were also noted in a significant proportion without a history of diabetes or hypertension. BP was independently associated with both systolic and diastolic dysfunction. These findings may have implications for developing appropriate strategies to improve the high rates of premature morbidity and mortality within Indigenous populations.

A comparative study of exposure to ambient air particles in patients hospitalized for heart failure: preserved versus depressed ejection fraction

E. Arroyo-Ucár1, A. Domínguez Rodríguez2, J. Abruña-Monsoro2, S. Rodríguez1, R. Juárez-Prera1, Y. González2, C. Hernandez-García1, M. Carillo-Pérez Tome1, P. Albrué-González2, P. Avanzas1,1University Hospital of Canarias, Tenerife, Spain; 2Department of Physic, Valencia, Spain; 3Center for Atmospheric Research, Tenerife, Spain; 4University of La Laguna, Tenerife, Spain; 5Hospital Central de Asturias, Oviedo, Spain

Purpose: Previous studies using administrative data have reported a positive association between short-term increases in ambient particles and the risk of hospitalization for heart failure (HF). Our objective was to study whether the contemporaneous exposure to ambient air particles at the time of hospital admission due to HF in patients with HF with preserved ejection fraction (HF-PEF) and reduced ejection fraction (HF-REF).

Methods: We studied 335 consecutive patients admitted into a tertiary care hospital with a diagnosis of HF. Patients with ejection fraction of ≥45% were classified as having HF-PEF and those with an ejection fraction of <45% were classified as having HF-REF. We determined the average concentrations of different sizes of PM (≤10, ≤2.5, and <1μm) and the concentrations of gaseous pollutants (carbon monoxide, sulphur dioxide, nitrogen dioxide and ozone) from 1 day up to 7 days prior to the admission.

Results: According to the pre-established criteria, 124 patients were classified as HF-PEF (Table). The HF-PEF population was exposed to higher nitrogen dioxide concentrations compared to the HF-REF population (12.9±5.8 vs 24.5±3.24 μg/m³, p<0.001). When comparing 30 values of PM between patients with HF-PEF and HF-REF, the first group tended to have lower values of PM10 (21[13-30] vs 25[17.5-32] μg/m³; p=0.02). We carried out multivariable binary logistic regression analysis, using a stepwise selection model.

This analysis showed that nitrogen dioxide was a significant predictor of HF-PEF (OR ranging from [1.403, CI 95% 1.003-2.007, p=0.04] to [1.669, CI95% 1.043-2.671, p=0.03].

Variables HF-PEF (n=124) HF-REF (n=213) P-value
Age (years) 69±12 66±12 0.01
Male gender, n (%) 56 (45.2) 154 (72.7) <0.001
Hypertension, n (%) 75 (60.5) 84 (38.7) <0.001
Hypochloro/leucemia, n (%) 35 (28.2) 52 (24.2) 0.25
Smokers, n (%) 14 (11.3) 40 (17.5) 0.12
Diabates, n (%) 45 (36.3) 104 (45.4) 0.09

Clinical variables of 353 consecutive patients with HF.

Conclusions: This is the first study to demonstrate that short-term nitrogen dioxide exposure is independently associated with HF admission in the HF-PEF population.

What is the burden of hospitalizations for Heart Failure in France in 2010?

M. Galinier1, B. Bouvet4, M. Roch0, P. De Groot5, J.N. Trochu4, 1University Hospital of Toulouse - Rangueil Hospital, Department of Cardiology, Toulouse, France; 2BGé Conseil, Paris, France; 3Hospital Regional University of Lille - Cardiological Hospital, Department of Cardiology, Lille, France; 4University Hospital of Nantes, Institut of the Thorax, Clinic Cardiologic, Nantes, France

Background: Chronic heart failure (HF), common to multiple disease areas (arterial hypertension, diabetes, atrial fibrillation...), has a high medical unmet need (due to its morbidity/mortality) and high economic burden. Despite its severity, there is a lack of data on this disease in France, and particularly on the burden linked to HF-related hospitalizations.

Objective: Our objective was to assess the number of hospitalizations related to HF in France over one year and to estimate its burden.

Methods: Data were extracted from the French national hospital database (PMSI MCO database) covering 96% of all hospitalizations in France. For this study, all hospitalizations with an ICD-10 code related to HF as principal diagnosis for 2010 were included. Over this one-year period, we looked at the number of hospitalizations, the number of patients, the duration of hospital stay, and patients’ age and outcomes.

Results: In 2010, there had been 210,490 hospitalizations in France with a code related to HF as principal diagnosis. 9.1% of them were hospitalizations of less than 2 days. A hospital stay for HF had an average duration of 9.6 days (10.5 after exclusion of hospital stay shorter than 2 days). This number of hospitalizations was linked to 160,092 patients (mean age: 79.0 years), corresponding to a number per patient of hospitalizations of 1.3 and of days spent in the hospital of 12.7 (13.4 after exclusion of hospital stay shorter than 2 days). For 17.5% of the hospitalizations, patients spent on average 4.2 days in an intensive care unit. 92.2% of the patients came to hospital directly from home (via emergency room for 58.2% of them). Hospitalization mortality rate was 7.5%; 71.5% of the patients went back home directly after their hospitalization, and 20.6% were discharged to skilled nursing facilities.

Conclusion: In applying the 2009 average cost for hospitalization due to HF (4,455€), the annual cost associated with HF-related hospitalizations in France is close to €1 billion. Any intervention that would significantly reduce HF-related hospitalization rate will consequently have a major impact on costs related to this disease.

A novel model to increase the rate of cardiac rehabilitation in patients after acute heart failure

C.H. Wang, N.L. Yang, M.J. Hung, M.H. Liu, T.C. Fu, C.C. Hsu, Chang Gung Memorial Hospital Keelung, Department of Internal Medicine, Division of Cardiology, Keelung, Taiwan

Background: Heart failure (HF) is a major cardiovascular syndrome. Cardiac rehabilitation (CR) was shown to lower the rehospitalization rate, and improve cardiac remodeling and the health-related quality of life. Nevertheless, the recruitment rate of patients who undergo CR is low. This study demonstrated a novel design to improve the CR rate.

Methods: In total, 218 patients hospitalized due to acute cardiogenic pulmonary edema were consecutively enrolled. For 60 patients in the beginning, CR was arranged in a traditional way (TW). For the following 158 patients, CR was arranged using integration (INT) of extensive admissions including a CR room design (a glass room incorporated in the cardiovascular ward), coordination with a clinical pathway-based disease manager, exercise prescription according to non-invasive hemodynamic monitoring during cardiopulmonary exercise testing (CPET), adaption of aerobic interval training (AIT), and change to a community-based system.

Results: There were no significant differences in the demographics between the INT and TW groups. In the INT group, compared to the TW group, patients' knowledge of CR benefits and the motivation to engage in CR significantly improved. Our design provided a chance for patients in the acute stage to interact with those undergoing CR. The physical therapists were fully supported to perform CR since
Quantifying circadian variation of multiple physiologic signals in ambulatory heart failure patients

J. Boehmer, Y. Zhang, R. Sweeney, R. Waria, Q. An, P. Thakur, V. Averina, J. Thompson, Penn State Milton S. Hershey Medical Center, Hershey, United States of America, Boston Scientific, St Paul, United States of America

Introduction: Physiologic variables exhibit diurnal variation due to changes in activity, posture and neural activity. HF and other diseases may influence this variation. Quantifying the variation, however, has been difficult due to limited availability of ambulatory data. MultiSENSE, a feasibility study designed to gather data from implanted CRT devices, enables evaluation of diurnal patterns in HF patients (pts).

Method: Heart rate (HR, bpm), tidal volume (TV, l), respiration rate (RR, bpm) and RV-can intra-thoracic impedance (Z, Ohm) were collected throughout the day while 3rd heart sound (S3 measured by accelerometer, mg) was collected in at least 2-3 pts. Circadian variation of a variable (CV, %) was defined as the difference between the day-time and night-time mean normalized by the daily mean. A t-test was used to compare the mean CV in all pts with 0.

Results: 115 pts with > 30 days of data were analyzed. The figure shows one pt with a lower HR, TV, RR and Z at night related to reduced activity and a more supine posture. Mean CVs (%; mean±SD) are: HR 7.1±6.8, TV 46.4±20.8, RR 7.6±8.8, Z 21.6±4.3 and S3 342±31.7 (all p < 0.001).

Conclusion: Simultaneous chronic measurements from an implanted device permitted quantification of diurnal variation of multiple physiologic variables. Further evaluation is warranted to determine its clinical value in HF patient management.

Non-invasive cardiac output monitoring during cardiopulmonary functional testing provides additional prognostic value in patients after acute heart failure

M. Anguita, J. Comín-Colet, F. Formiga, L. Almenar, M. Crespo, L. Marciano, J. Chaves, G. De Frutos, on behalf of the VIDA-IC investigators. 1Cardiology, Hospital Universitario Reina Sofía, Córdoba, Spain; 2Cardiology, Hospital del Mar, IMIM, Barcelona, Spain; 3Internal Medicine, Hospital Univ Bellvitge, Barcelona, Spain; 4Cardiology, Hospital Univ La Fe, Valencia, Spain; 5Cardiology, Hospital Universitario A Coruña, A Coruña, Spain; 6Internal Medicine, Hospital Univ Ramón y Cajal, Madrid, Spain; 7Medical Department, Pfizer, Madrid, Spain

Purpose: Previous studies suggest that, despite positive clinical evidence and guidelines recommendations, elderly with HF receive a less optimal treatment than younger patients. The aim of our study was to analyze differences between patients below and above 75 years presenting with HF with depressed systolic function (LVEF ≤ 40%).

Methods: The VIDA-IC was designed to include 1200 consecutive ambulatory patients with systolic HF by 120 investigators in Spain during 2011.

Results: Mean age was 71.2 years, 32% were female. 65% had previous hospitalizations due to HF and 40% of patients evaluated were older than 75 years. NYHA class III/IV was assigned in older patients more than in younger patients (53% vs 37%, p < 0.001). Older patients had more previous admissions for HF (74% vs 55%, p < 0.001), atrial fibrillation (57% vs 45%, p = 0.026), anemia (26 vs 17%, p = 0.05) and renal failure (31 vs 18%, p = 0.002). Prevalence of risk factors, ischemic heart disease and other comorbidities were similar in both groups. LEVF was 33.6% in both groups. No differences in drug therapy were observed for the majorities of drugs: diuretics (94% vs 93%), ACE (57% vs 65%), ARB (35 vs 37%), j-blockers (72% vs 75%), aldosterone blockers (69 vs 75%) for ivabradine (10% vs 5%) or oral anticoagulants (45% vs 41%). Only 52% of patients were receiving optimal HF therapy (defined as j-blocker, ACEi/ARBs and aldosterone blockers each) and the difference between older patients and younger patients is close to be statistically significant (52% vs 61%, p = 0.086), preliminary analysis of 400 patients); the final analysis with all the patients included is required to have enough sample to clarify the age differences in optimal therapy. Ybbradine was used less (4 vs 13%, p = 0.007) and digoxin more (34 vs 22%, p = 0.009) in older patients, in relation to the higher proportion of atrial fibrillation present in these subgroup of patients. Non-pharmacological therapy was also similar (ICD: 7% vs 10%, CRT therapy: 65% in both subgroups; NS). Younger patients were followed more frequently in HF units (26 vs 14%, p = 0.008).

Conclusion: Despite advanced disease in elderly patients, only digoxin treatment was intensified in older patients. Additional data are needed to demonstrate if older patients have different HF pharmacological optimal therapy. The rate of ICD and CRT implants are perhaps lower than indicated, but without differences between both subgroups of age. These “real world” data suggests that there is sub-optimal transfer of clinical trial evidence into clinical practice in systolic CHF patients below and above 75 years in Spain.
E. Joshi, G.W. Holt, B.T. Fitzgerald, G.M. Scala. Heart Care Partners, Brisbane, Australia

**Background:** Takotsubo cardiomyopathy (TC) is typically considered reversible, though recent findings with 2D strain imaging demonstrate persisting late wall motion abnormalities. The pattern, timeframe and completeness of improvement remain to be determined. This study utilises the new parameter - the Takotsubo Index (TTI) = length of level of hypokinesia (cm)/total length of LV apex (cm) and analysis of standard 16 segment wall motion scoring on sequential follow-up of TC patients.

**Methods:** 69 patients (4 male, 67±12 yrs) with TC were evaluated with transthoracic echocardiography at Day 1 of presentation and follow up period (514±74 days). Chest pain was the most common presentation (79%). Complications included arrhythmias (6), death (1) and recurrent TC (2). Causes included emotional stress (38%), acute medical illness (31%), post-operative (13%) and other (18%). ECG changes included STEMI (59%) and Non-STEMI (41%). Echocardiography showed ejection fraction at diagnosis of 47±3.5% rising to 56±14% at late follow-up [1-1422, mean 513 days]. The Takotsubo Index increased from 0.52 to 0.98 (6.8 mm to 74.8 mm, p <0.001) with TTI <0.66 in 29 patients (42%) and TTI <0.8% in 14 patients (20%). A multi-parametric score apically with time. Apical wall motion improved but did not normalise (see Fig. 1B).

**Conclusion:** Apical hypokinesia incompletely resolves after Takotsubo episodes. Surprisingly, the line of hypokinesia moves apically as the curtain of dysfunction lifts on these ventricles.

---

**Conclusions:** NICOM during the CPET was demonstrated to provide prognostic information in addition to traditional risk factors, biomarkers, and other well-established CPET parameters.

**Methods:** This study enrolled 960 patients in 12 Italian ICUs (n=40 in each group). The ICU, a management algorithm was designed based on the measured EI. The analyzed end points included HF-, and all cause-related events during the 6-month follow-up period. In the 6 months, there were 13 (6.9%) deaths from all-cause related rehospitalizations. Compared to the control (24.6%) and CM groups (15.1%), the EI group had a lower rate of HF-related death and rehospitalizations (8%, p=0.004). A multivariable approach was demonstrated to provide prognostic information in addition to traditional risk factors and secondary endpoints.

**Conclusion:** NICOM during the CPET was demonstrated to provide prognostic information in addition to traditional risk factors, biomarkers, and other well-established CPET parameters.

---

**Echocardiographic assessment of acute hemodynamic response during optimization of resynchronization pace-maker improves long term prognosis**

S. Salinger Martinovic, Z. Perisic, S. Apostolovic, M. Pavlovic, M. Zivkovic, N. Krsic, T. Kostic, N. Bozinovic, M. Damjanovic, D. Stanjevic. Clinic for Cardiovascular Diseases, Nis, Serbia

**Purpose:** Resynchronization therapy (CRT) is used in treatment of patients (pts) with advanced heart failure in NYHA III-IV class with LVEF < 35% and left bundle branch block who have echocardiographically confirmed asynchrony and are on optimal drug treatment. There are four types of cardiac asynchrony (atrio-ventricular, inter-ventricular, intra-ventricular and intramural) and CRT improves all of them. The aim of study was to examine acute and hemodynamic changes one year after implantation of CRT device with different configurations during optimization procedure.

**Methods:** We enrolled 62 patients (EF 24.6±4.4%, QRS duration 154±7.1ms, NYHA class III/IV 75.8%±24.2%) with implanted CRT device. Before hospital discharge all pts underwent optimization procedure guided by Doppler echocardiography. Left (LVPEI) and right (RVPEI) ventricular pre-ejection intervals, inter-ventricular mechanical delay (IVD), maximal rate of ventricular pressure rise during early systole (max dP/dt) and stroke volume derived from the left ventricular outflow tract: velocity-time integral (VTI) of left ventricular outflow tract were measured during left and biventricular pacing with three different atrioventricular (AV) delays (150 ms, 120 ms and 90 ms). Six-minute walking distance (6MWD) at hospital discharge and after one year was measured as well.

**Results:** After CRT device optimization, optimal AV delay and CRT mode were defined. Left ventricular pre-ejection intervals changed from 175.4±21.5 to 142.6±16.7 ms (p <0.001), RVPEI from 108.6±18.9 to 127.3±18.3 ms (p <0.001), IVD from 71.3±14.8 to 24.7±7.6 ms (p <0.001) and dP/dt from 532±7.4 to 675±2.1 ms (p <0.001). Left ventricular outflow tract VTI increased after optimization of resynchronization, from 1.1±0.4 to 2.2±1.5 cm (p <0.001). Shortened AV delay of 90 ms was optimal in the majority of patients (46.7%). After one year we found significant reduction of the end-diastolic diameter of the left ventricle from 71.9±7.5 mm to 67.4±6.8 mm (p <0.001) with significant improvement in NYHA functional class [NYHA II: 0% at baseline to 74.2%, NYHA III: 75.8% at baseline to 22.6% and NYHA IV:24.2% at baseline to 3.2% of pts after one year (p <0.001)] and in 6MWD [at baseline 222.3±40.35 increased to 302.38±74.86, p <0.001].

**Conclusion:** Echocardiographic assessment of the acute hemodynamic response to CRT is a useful tool in optimization and the variability of Doppler parameters emphasizes the necessity of individualized approach. This improves long-term prognosis, not just left ventricle geometry, but clinical status, NYHA class and life quality as well.
Relationship of reduced cerebral blood flow and heart failure severity in elderly males

G. Loncarević, B. Bozic, T. Lepić, S. Dimkovic, N. Prodanović, Z. Radujović, V. Vuković, B. Putniković, V. Popović

Clinical Center Zvezdara, Department of Cardiology, Belgrade, Serbia; 2Military Medical Academy Belgrade, Belgrade, Serbia; 3Cardiology Department, Clinical Medical Center Zvezdara, School of Medicine, University of Belgrade, Belgrade, Serbia; 4Institute for Statistics, Faculty of Organizational Sciences, University of Belgrade, Belgrade, Serbia; 5Clinical Hospital Center Zemun, Belgrade, Serbia; 6Institute of Endocrinology, Clinical Center of Serbia, University of Belgrade, Belgrade, Serbia

Introduction: Brain detrimental effects are underrecognized complication of chronic heart failure (CHF). One of the major causes may be cerebral hypoperfusion. This study was designed to investigate the relationship between cerebral blood flow (CBF) and severity of CHF as well as to evaluate its determinants among different parameters of cardiac dysfunction.

Methods: Seventy-one CHF males with NYHA class II and III and 20 control subjects aged 55 years were recruited. CBF was evaluated by color duplex sonography of extracranial arteries. Echocardiography, 6-minute walk test, quality of life and endothelial function were also assessed. Serum NT-pro-BNP and adipokines levels (adiponectin and leptin) were measured.

Results: CBF was significantly reduced in elderly CHF patients compared to healthy controls (677 ± 170 vs 783 ± 128, mmHg, p = 0.01). Reduced CBF was associated with reduced left ventricular ejection fraction (LVEF) (r = 0.271, p = 0.022), lower 6-minute walk distance (r = 0.339, p = 0.004), deteriorated quality of life (r = -0.327, p = 0.005), increased serum adiponectin (r = -0.359, p = 0.002), and NT-pro-BNP levels (r = -0.375, p = 0.001). In multivariate regression analysis, LVEF and adiponectin were independently associated with reduced CBF in CHF patients (R2 = 0.269).

Conclusion: CBF was reduced in elderly males with mild to moderate chronic heart failure, and was associated with factors that reflected the severity of CHF including high serum adiponectin and NT-pro-BNP levels, decreased LVEF, impaired physical performance, and deteriorated quality of life.

Acoustic cardiology helps to identify heart failure and its phenotypes

S. Wang, Y.Y. Lam, F. Fang, M. Liu, Q. Shang, X.K. Luo, J. Wang, J.E. Sanderson, P.J. Sun, C.M. Yu, Div. of Card. Dept of M&T. VM, LiHS, SH Ho Cardio Disease & Stroke Ctr, PWH, CUHK, Hong Kong, China, People’s Republic of

Purpose: Despite recent advances in its management, heart failure remains a major cause of death and its rapid bedside diagnosis and phenotypes identification are still challenging. We sought to determine whether acoustic cardiology can accurately identify heart failure and its phenotypes.

Methods: Three cohorts of patients were studied [84 with hypertension, 109 with heart failure and normal ejection fraction (HFNEF, EF>50%) and 89 with heart failure and reduced ejection fraction (HFRF, EF<50%)]. All participants received acoustic cardiological and echocardiographic examinations. Acoustic cardiological parameters included S3 score (probability that the third heart sound exists), electromechanical activation time (EMAT, interval from Q wave to the first heart sound; %EMAT is the proportion of cardiac cycle that EMAT occupies), and systolic dysfunction index (SDI, a combination of %EMAT and S3 score). Receiver operative characteristics curves were used to determine diagnostic utility of acoustic cardiology.

Results: There was significantly differentiated HFNRF from hypertension (area under curve [AUC], 0.83; 95% confidence interval [CI], 0.77-0.89) with a %EMAT > 11.54% yielded 55% sensitivity and 90% specificity. Similarly, an echo-measured E/e’ > 15 yielded 55% sensitivity, 90% specificity and 0.84 AUC in detecting HFNRF. Whereas SDI out-performed the other acoustic cardiological parameters in differentiating HFNRF from HFNEF (AUC, 0.81; 95% CI, 0.75-0.87), an SDI > 5.43 yielded 53% sensitivity and 91% specificity. The E/e’ ratio had a similar diagnostic performance.

Conclusions: Our study demonstrates this bedside technology may be helpful in identifying heart failure and its phenotypes, especially when other tests are not immediately available.

Feasibility and validity of chair based exercise in heart failure patients

N.A. Razab, P.J. Doherty. York St John University, York, United Kingdom

Purpose: A recent cardiac rehabilitation (CR) audit showed that on average 42% of patients accessed rehabilitation programmes in the UK. The mode of CR exercise tends to be classic aerobic group-based using predominately standing exercise but recent innovations by health service providers aimed at increasing uptake have included chair based exercise (CBE) for patients with low exercise capacity. Therefore, this study set out to determine the physiological demand associated with CBE in HF patients and determination the appropriateness of CBE to clinical practice.

Method: Prospective cohort study investigating CBE in HF patients involved 30 patients patients, mean age(years) was 69.4 (SD 12.84) with NYHA I-II. The study was approved by NHS ethics and informed consent was obtained. All patients attended all three sessions/familiarisation, test 1 and test 2. Test 1 involved breathing with six minutes walking test (SMWT), leg incremental test, leg steady state and CBE while test 2 involved arm incremental test, arm steadystate, repeated BNP, repeated CBE. Both arm and leg incremental ergometers were used to assess fitness, expressed as oxygen consumption (VO2) and metabolite equiva- lents (METs) at 60 minutes per participant. Participants were required to wear a small light weight face mask that analysed the air breathing (Quanox BZ) in all exercise testing. Participants were divided into tertiles based on their performance on their VO2 submaximal value. Using SPSS ver- sion 18, repeated ANOVA was used to evaluate the mean differences between the CBE, SMWT, LVEF and ARMI. A Spearman correlation was performed between BNP and SMWT with CBE level to evaluate their relationship to CBE levels.

Results: CBE has level and the average patient in each level was 4 (SD 2). This data showed the overall mean metabolic range of METs during main part (MP) of CBE was 1.6 to 4.86 METs. The average percentage on MP CBE of arm and leg submaximal testing specifically on heart rate (HR) was 88% and 83%, systolic blood pressure (SBP) was 87% and 96%, rate pressure product (RPP) was 77% and 72%, VO2 and METs was 63% and 81% respectively.

CBE level was highly correlated with SMWT (r0.89, p < 0.001) and negatively correlated (r0.25) with BNP. All statistical comparison showed that HR and pulmonary arterial pressure on CBE was significantly lower than SMWT, LVEF and ARMI. Conclusion: This study provides data suggesting that CBE, if well designed, is safe and offers a range of exercise intensities to enable exercise prescription for HF patients. The level of performance on CBE is predictive of function using the SMWT.

Preoperative prediction of post-operative right ventricular function in patients referred for left ventricular assist device implantation

M. Dandel, E. Potapov, T. Krabatsch, A. Stepanenk, H.B. Lehmkhui, H. Sinaweski, C. Riosalita, Y. Hetzer. German Heart Center Berlin, Berlin, Germany

Background: Prolongation of waiting times for transplantation and growing numbers of non-transplantable patients with end-stage heart failure increase the need for mechanical cardiac support systems. Left ventricular assist devices (LVADs) provide better quality of life and survival than biventricular devices (BVADs) or total artificial hearts. Because many patients with severely impaired right heart function before ventricular assist implantation show relevant improvement in RV function after LVAD implantation, BVAD implantation is not necessary in all patients with global heart failure. However, it is still a challenge to reliably evaluate right ventricular (RV) function and to predict its time-course during LV support. We assessed this issue.

Methods: We evaluated all patients with preoperatively severe left and right heart failure who received a “long-term” LVAD between 1/2006 and 1/2011 designed as bridge to transplantation or permanent therapy. RV anatomic and functional parameters collected prospectively before LVAD implantation and invisibly obtained data on pulmonary hemodynamics were tested for relationship with post-implantation RV function and patient outcome. Echocardiography, including tissue Doppler and 2D strain imaging, was used to evaluate RV size, geometry and function.

Results: After LVAD implantation, 36 (19.4%) of the 186 evaluated patients with preoperatively reduced RVF (r ≤ 25%) showed further worsening of RV function which necessitated mechanical support also for the RV. Whereas before LVAD implantation the RVF was similar in patients with and without postoperative improvement of RV function there were significant differences in preoperative RV short/long axis (L/S) ratio, tricuspid annulus peak systolic velocity (TAPSM) and peak global RV systolic strain rate (RVSsr) between the two patient groups (p < 0.01). L/S ratio ≤ 0.86, TAPSM > 8cm/s and peak global RVSsr > 0.71 measured before LVAD implantation in patients with tricuspid regurgitation (TR) grade ≥ 2 and systolic pulmonary arterial pressure > 50mmHg appeared predictive for optimal RV function after LVAD implantation (predictive values up to 94.0%). Al- tered RV geometry (high sphericity) and TR grade ≥ 2 appeared to be highly relevant risk factors for postoperative right heart failure in patients with systolic pulmonary arterial pressure below 50mmHg before LVAD implantation.

Conclusion: RV geometry, velocity of RV wall motion and myocardial shortening before LVAD implantation are highly predictive for RV function after LVAD implantation ii pulmonary arterial pressure and tricuspid regurgitation are also considered.

Lung ultrasound may be useful in predicting cardiac filling pressures and PVR

E. Platz, A. Lattanzi, C. Agbo, F. Resnic, S. Solomon, A. Desai. Brigham and Women’s Hospital, Boston, United States of America

Purpose: Bedside assessment of filling pressures in patients with heart failure remains challenging. This study set out to determine the physiological demand associated with CBE in HF patients and determination the appropriateness of CBE to clinical practice.

Method: Quantification of linear ultrasound (LUS) artifacts (B-lines) represents a novel, noninvasive approach to assessment of extravascular fluid. We assessed the relationship between the number of B-lines (vertical artifacts arising from the pleural line) and intracardiac filling pressures.
Importance of lung impedance monitoring in the correction of dyssynchrony, as assessed using thoracic ultrasonography (TUS).

**Methods:** Prior to scheduled right heart catheterization (RHC), 100 subjects (median age 60 years, 33 women, median LVEF 58%, 50 with history of heart failure, 23 post cardiac transplantation) underwent LUS of 8 zones. A reviewer blinded to the hemodynamic data quantified the number of sonographic B-lines.

**Results:** Of 92 subjects who underwent RHC, 79 had adequate LUS data of all zones. The number of sonographic B-lines correlated with measured right atrial pressure (r=0.32), pulmonary artery diastolic pressure (PAPD) (r=0.34), mean pulmonary artery pressure (MAPAP) (r=0.43), and pulmonary artery systolic (PASP) (r=0.48) pressures and pulmonary vascular resistance (PVR) (r=0.51) (p<0.005 for all), but not pulmonary capillary wedge pressure. There was a graded association between tertiles of B-line number and increasing PAPD, MAPAP, PASP and PVR (p for trend <0.001 for all) (Figure). The associations were robust in the subgroup of patients without a history of cardiac transplantation.

**Conclusions:** Early predictive LI-guided treatment is effective for prevention of hospitalizations and reducing mortality.

**Figure 1**

**P997 Importance of lung impedance monitoring in the outpatient clinic for predicting and preventing hospitalizations of patients with Chronic Heart Failure**

M. Shochat, A. Shotan, A. Asif, M. Kazatsker, T. Sigalov, Y. Levy, I. Shochat, I. Dahan, D. Blondheim, S. Meisel. Hillel Yaffe Medical Center, Heart Institute, Hadera, Israel

**Background:** Implantable intra-thoracic impedance device has shown that lung fluid accumulation in patients with decompenated chronic heart failure (CHF) begins several days before admission, but predicts hospitalizations with only 50-76% accuracy.

**Aim:** We evaluated the ability of the new a non-invasive method for lung impedance monitoring to predict decompensation in CHF patients and to trigger early therapy in order to prevent hospitalizations.

**Methods:** Lung impedance (LI) was measured by device based on transverse distribution of electromagnetic energy through the chest. Changes in the clinical status of patients, LI and NT-proBNP levels were concurrently recorded at each outpatient heart failure clinic visit (20±18 days).

**Results:** 172 CHF patients (72±10 years) at NYHA II/III/IV (72/70/30) were followed in an outpatient clinic. Patients were treated with diuretics, beta blockers and ACE/ARB/aldosterone. An LI decrease >15% from normal baseline was used to initiate early preventive therapy since we have shown previously that clinical decompensation occurred at this level of LI decrease. 200 CHF patients were recruited. 28 patients stopped their participation in the study after less than 3 months of follow up and were excluded. 81 of 172 patients were treated as usually by clinical evaluation (Gr. 1) and 91 according to LI (Gr. 2). LVEF and NT-proBNP in groups 1 and 2 were 23.7±5.6820±2434 pg/ml, and 23.6±5.868±2532 pg/ml respectively (p=NS). 172 episodes of LI decrease >15% occurred in Gr. 1 with changes in treatment administered according to clinical signs only. These LI decrease episodes included 144 AHF hospitalizations and 23 deaths. In Gr. 2, 192 episodes of LI decrease >15% were recorded. Treatment was immediately intensified. In 161 cases LI increased as the result of treatment intensification and only 31 AHF hospitalizations were required (p=0.01) and 15 patients died (p=0.045). Time elapsed between LI decrease >15% and hospitalization in both groups was 16±6 days. Free time between hospitalizations was longer in LI-guided treated Gr.2 than in Gr. 1 (p<0.01).

**Conclusions:** Early predictive LI-guided treatment is effective for prediction of hospitalizations and reducing mortality.
**P1000** Measuring only septal and lateral wall systolic velocities using tissue doppler velocities is an easy and reproducible method to determine contractile reserve

**J.J. Van Zalen**, R. McIntosh, P. Raju, L. Beale, G. Brickley, S. Poddi, N. Patel, G.W. Lloyd, Eastbourne District General Hospital, Eastbourne, United Kingdom; University of Brighton; Chelsea School, Eastbourne, United Kingdom

**Purpose:** The average Spectral Tissue Doppler (TDI) from 6 basal myocardial segments on exercise is an established method of determining contractile reserve during exercise stress echocardiography (EXE) in heart failure patients. It can however be challenging to acquire. TDI velocity may be influenced by both cardiac contraction and tethering of non-contracting segments which might render two walls a less accurate measure of global function than six. We sought to establish how closely the mean systolic velocity of the septum and lateral wall was related to the mean of six myocardial segments.

**Methods:** Patients with heart failure underwent EXE. Spectral TDI peak systolic velocity (s’) measurements were made at rest and peak exertion in six perannular left ventricular locations. The results of the septal and lateral walls were compared to the mean of all six segments.

**Results:** 70 patients (72±9 years, 65.8% IHD; 48 males) underwent EXE. 100% of the septal and lateral walls were measured at rest. In 74 patients (97.4%) s’ was measurable from the septal and lateral walls were determined at exercise. Measuring all 6 walls was possible in 56 patients (73%) at rest and in 30 patients at exercise (39%). At exercise it was not possible to measure 1 wall in 12 patients (16%), 2 walls in 26 (34%) patients, 3 walls in 3 patients (4%) and in 5 patients (7%) 4 walls were not determined. Both septal and lateral s’ correlated highly with the mean of all segments both at rest (r = 0.94; p <0.0001) and exercise (r = 0.92; p <0.0001).

In the subgroup of patients with IHD the results were similar (rest: r = 0.92; p <0.0001; exercise: r = 0.91; p <0.0001).

**Conclusion:** Septal-lateral TDI is easier to acquire successfully, and is closely related to the mean s’ in all walls, with and without IHD.

**P1001** The effects of telemonitoring on heart failure patients’ knowledge, self-care, self-efficacy and adherence: a randomized controlled trial

**J. Bayne**, H.J.M. Vrijhoef, M. Speuwenberg, J. Kragten, G. Deweerdt, A.P.M. Gorgels, Maastricht University Medical Center, Maastricht, Netherlands; Atrium Medical Centre Parkstad, Heerlen, Netherlands; Orhis Medical Centre, sittard, Netherlands

**Background:** Education of heart failure patients by health care professionals is an essential part of the treatment. Perspectives of an increasing number of patients and lack of professionals force healthcare to explore new strategies in supporting patients.

**Methods:** Patients with heart failure were randomly recruited in the outpatient clinics of 3 institutions and assigned to the telemonitoring or usual care group. The device used for this study was the Health Buddy® system, without transfer of vital signs. Follow-up time was one year; patients received four postal questionnaires to assess level of knowledge, self-care, self-efficacy and adherence. Analysis was performed by generalized estimating equations analysis to assess effects of telemonitoring during the follow-up of one year.

**Results:** Of the 382 patients included, 197 were allocated to the intervention group and 185 to the usual-care group. Mean age was 72 ±SD 11.2 years and 46% were ≥75 years old; 59% were male, 65 lived with a partner; 57% were in functional class II, 40% of the patients was in class III, and 3% in class IV. Patients in the telemonitoring group had a significant improved knowledge level, and increased with 0.9 point on the 15-points Dutch HF knowledge scale (p<0.001). Despite randomization baseline differences in favor of the intervention group were found for self-care (p<0.001) and self-efficacy (p<0.024) for which correction was performed. Self-care abilities improved on the 10-item HF self-care behavior scale with 1.5 point in the intervention group whereas no changes were found in the controls (p>0.001). Self-efficacy, measured with the Barmason Efficacy Expectation Scale, improved significantly after three and six months, yet was not significantly different after one year. Adherence improved for daily weighing (p<0.001) during whole follow-up; fluid intake results varied from p=0.019 after three months to p=0.086 after twelve months. Adherence for activity recommendations improved (p=0.023) after three months and importance of medication adherence increased after six (p=0.012) and twelve months (p=0.037). No effects were found appointments with caregivers, diet, smoking and use of alcohol. Adherence was measured with the HF compliance questionnaire. The overall daily compliance using the telemonitoring system was 95%.

**Conclusions:** This telemonitoring system improved education and empowers patients, and therefore supported patients and healthcare professionals in their interactions.

**P1002** Significant improvement in functional status and quality of life in heart failure patients who received EECP

**N. Kataria, S. Mittal, N. Trehan, R. Kasliwal. Medanta Heart Institute, Gurugram, India

**Purpose:** EECP therapy has been studied in refractory ischemic cardiomyopathy and heart failure patients with good results in the past. However, the mechanism and potential indications remain unexplored.

**Methods:** We did a retrospective analysis of defined end points in 60 heart failure patients who received EECP therapy at our centre. Comorbidities include diabetes mellitus, hypertension, obesity, smoking, and coronary artery disease. The mean age of the patients was 64 years. The EECP therapy included daily sessions of one hour duration for 35 days. The Canadian Cardiovascular Society (CCS) angina class and the Medical Research Council (MRC) breathlessness scale were used to study improvement in symptoms. Quality of life indicators were (a) reduction in symptoms (b) improvement in activity (c) improvement in psychological parameters. The objective parameters studied were ejection fraction and 6 minute walk distance.

**Results:** There was a significant improvement in all study parameters after EECP therapy (Table-1).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Pre-EECP</th>
<th>Post-EECP</th>
<th>Difference</th>
<th>Z value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CCS Class</td>
<td>3.3 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.3 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRC Class</td>
<td>3.7 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCS Total</td>
<td>3.3 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.3 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRC Total</td>
<td>3.7 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCS 3-6 M</td>
<td>3.3 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.3 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRC 3-6 M</td>
<td>3.7 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCS 6-9 M</td>
<td>3.3 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.3 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRC 6-9 M</td>
<td>3.7 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CCS 9-12 M</td>
<td>3.3 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.3 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>MRC 9-12 M</td>
<td>3.7 ± 0.3</td>
<td>2.0 ± 0.3</td>
<td>1.7 ± 0.3</td>
<td>-1.87</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusions:** EECP therapy is an excellent treatment option for heart failure patients who are at the end of the road in terms of medical and interventional therapies. Our hypothesis is that EECP therapy works not only through a mechanism of improved collateral circulation but also improves endothelial function with potential benefit in all vasculopathies. Large randomized trials to validate the hypothesis are proposed.
Left cardiac sympathetic denervation for treatment of symptomatic systolic cardiac heart failure patients - 3 years follow-up


Objective: To evaluate the feasibility, safety and potential beneficial effects of additional Left Cardiac Sympathetic Denervation (LCSD) in systolic HF patients.

Methods: In this prospective randomised pilot study, inclusion criteria were: NYHA functional class II or III, left ventricular ejection fraction (LVEF) ≤40%, sinus rhythm and resting heart rate ≤65 bpm, despite optimal medical therapy (MT). Fifteen patients were randomly assigned either to MT alone or MT plus LCSD. Primary endpoint was safety, measured by mortality in first month follow-up and morbidity according to predefined criteria. Secondary endpoints: exercise capacity, quality of life, LVEF, LV/HF ratio, 123-methiothepin/guanadine scintigraphy (MBG), muscle sympathetic nerve activity (MSNA), BNP levels and 24h-Holter mean heart rate before and after 6 months. We studied clinical effects in long term follow-up.

Results: 10 patients underwent CT. There were no adverse events attributable to surgery. No one died in both groups during the first month of follow-up. ST LVEF improved from 25±6.6 to 33±5.2% (p<0.03); ST 6 min walking distance improved 167±35 to 198±47m (p=0.02). ST MLHFQ score physical dimension tended to improve from 21.5±5 to 15.7±p (p=0.068). The remainder analysed variables were unchanged. During the follow-up of 48±549 days, in MT group most patients either died or underwent CT, while in ST group most were alive without CT.

Conclusions: LCSD was feasible and seemed to be safe in SHF patients. Its beneficial effects warrant the development of a larger randomized trial.

3D echocardiography for predicting response to cardiac resynchronisation therapy in patients with congestive heart failure

D.V. Krinichkin, V.A. Kuznetsov, N.N. Mnihkov. Tyumen Cardiology Center, Tyumen, Russian Federation

Purpose: To assess the significance of the real-time 3D echocardiography for predicting response to cardiac resynchronisation therapy (CRT) in patients with congestive heart failure

Materials and methods: 38 patients were examined with 3D echocardiography prior to CRT and in 5-7 days after implantation when the optimization of the device was performed. All the patients with reduction in LV end-systolic volume ≥15% after the implantation (along with improvement in LV systolic function) were considered CRT responders. Cardiac dyssynchrony was evaluated with systolic dyssynchrony index (SDI) which is used as a marker of global LV dyssynchrony.

Results: Right after the implantation in 26 patients (68%) there was found a reduction in LV end-systolic volume ≥15% from baseline which was considered as an acute response to CRT and these patients were assigned to the group of responders. Baseline characteristics of both groups were not different with exception of SDI (p<0.0001). Responders demonstrated a significant reduction in SDI right after the implantation (from 10.3±6.6 to 5.6±3.02; p<0.0001), whereas in non-responders SDI remained unchanged (from 3.6±0.32 to 3.1±0.23; p=NS).

To determine an optimal threshold value for SDI as an echocardiographic predictor of CRT acute response, ROC analysis was performed. A threshold value of 5.6% with 96% sensitivity and 92% specificity predicted acute reduction in LV end-systolic volume of ≥15% (area under the curve: 0.90, 95% CI 0.77-1.04, p<0.0001). Result of SDI threshold value in 26 patients showed a decrease in LV end-systolic volume following CRT.

Conclusions: Real-time 3D echocardiography is a relatively new and highly effective method for diagnosis of dyssynchrony degree calculation of six volumes and ejection fraction. SDI of ≥3.6% can be used as a criterion for revealing CRT responders.

Peripheral arterial stiffness and reactivity in heart failure

M. Popovici, V. Cobet, N. Ciobanu, V. Ivanov, I. Popovici, L. Ciobanu, I. Moraru, M. Todras on behalf of Popovici M. Institute of Cardiology. Chisinau, Moldova, Republic of

Purpose: Assessment of the arterial stiffness and reactivity in heart failure.

Materials and methods: The large (C1) and small artery (C2) elasticity indices were evaluated in patients with systolic (60 men with supported acute myocardial infarction,mean age 57±2 years) or diastolic (26 men with arterial hypertension, mean age 57±2 years) heart failure (HF) using technical disposable Pulse Wave CR-2000. The obtained outcomes were compared with normal indices accepted for this ageand gender (C1<11, and C2>7). The assayed in vitro vascular reactivity study included the constricting and relaxing aortic rings response determining in endothelium-intact and endothelium-denuded aortas on various stimuli action (NE, Phe, ET-1, Ang II, Ach, Ang 1-7 concentration of 10-7 M) using Computer TSE Acquisition System.

Results: Arterial stiffness significantly decreased in HF especially in hyperten-

sive patients: C1and C2 measured 5,03±0,31 mmHg H1 and x10 respectively and 3,77±0,21 mmHg H100 that is consisting almost 50% from normal values. In systolic HF C1 and C2 differences were found slightly higher, however below by 25-25% concerning normal parameters. Blood pressure in HF patients was 167±35 to 198±47 mmHg (p=0.02), ST MLHFQ score physical dimension tended to improve from 21.5±5 to 15.7±px (p=0.068). The remainder analysed variables were unchanged. During the follow-up of 48±549 days, in MT group most patients either died or underwent CT, while in ST group most were alive without CT.

Conclusions: LCSD was feasible and seemed to be safe in SHF patients. Its beneficial effects warrant the development of a larger randomized trial.

New devices and diagnostic techniques 167

A new algorithm to assess cardiac performance in heart failure patients: the Bodyguard device

P. Brown, A.M. Marsh, R. Lotto, C. Peers, B. Grundy, M. Jeilan, G.A. Ng. University of Leicester, Department of Cardiovascular Sciences, Leicester, United Kingdom

Background: The Optima-Life Bodyguard is a small, wearable device that uses software algorithms to derive estimates of cardiac performance (as VO2) and heart rate variability. The system is validated in athletes and normal healthy individuals, but has not previously been studied in a heart failure population. This pilot study compares results generated by the Bodyguard device with those derived from standard techniques. The results presented from this pilot study focus on estimation of VO2.

Methods: 34 patients with documented NYHA class II or III heart failure were recruited. The Bodyguard Holter monitor was fitted for 24 hours. A cardiopulmonary bicycle exercise (CPEX) test was performed. The data from the Bodyguard device and the other tests were compared; measured and estimated maximum heart rate (HRmax) and VO2max were compared as inputs to the Bodyguard algorithm. Inaccuracy was calculated as the difference between Bodyguard result and conventionally measured result, expressed as a percentage of the conventionally measured result. Results are expressed as an average of all patients (means±SEM).

Results: Patient age 61±11 yrs. NYHA II=22, III=6, not available=6. Measured VO2max 15.6±6.1 ml/kg/min. The Bodyguard device measured the heart rate accurately with a calculated inaccuracy of ≤0.1% in all conditions. When both HRmax and VO2max were estimated, the calculated VO2 over the duration of the CPEX test gave mean calculated inaccuracy of 44±18%; if HRmax was estimated, and measured VO2max used inaccuracy was 48±15%; if estimated VO2max used with measured HRmax, 20±19%; if both parameters measured, 22±18%.

Conclusions: This first experience of the Bodyguard device in a heart failure patient population shows promise, but some measured variables are necessary inputs to improve accuracy. HRmax was more valuable in this regard than VO2max, probably because of the considerable difference in HRmax between a normal population and a heart failure population on optimal medical treatment including beta-blockade. HRmax is readily measured in clinical practice via maximal exercise testing. Our experience was that patients found the device very tolerable due to its small size and weight. Further work will be needed to explore the potential of the device as a motivational tool in heart failure rehabilitation.

Two-dimensional vs three-dimensional deformation parameters to estimate infarct size and global left ventricular function after STEMI: which parameter is better?


Purpose: To comparatively assess the role of 2D longitudinal strain (2D Ls) and 3D strain parameters (longitudinal, Lc; circumferential, Cc; radial, Rl and area strain, Aa) to estimate infarct size and global left ventricular (LV) function (in terms of ejection score index, WSII) after STEMI.

Methods: In 77 pts with recent STEMI (58±13 years), 3 apical LV views for measuring 2D Ls (70±9 ps) and 4-beat LV full-volume data sets (31±4 vps) for measuring 3D Ls were acquired 8±3 days after primary PCI using Vivid E9 scanner and analyzed with dedicated softwares (BT11, GE Healthcare, Horten, Norway). All subjects were selected for good image quality, sinus rhythm and adequate 2D/3D speckle tracking in at least 14 of all 17 segments. In 46 pts, global infarct size index was calculated from delayed-enhancement cardiac magnetic resonance (DE-CMR),
performed ≤24h apart from the echo study and compared with global strain values. In all pts, global strain values were compared against peak troponin I (Tnl), 3D EF and 3D WMSI at predischarge.

Results: Among all strain components, global 2D Lc and 3D Cv had the closest correlation with 3D EF, 3D WMSI and Tnl, while 3D Lc showed the weakest correlation with the same parameters. At multivariable analysis, 3D Cv (R2=0.76) and 3D WMSI (R2=0.70) were significantly correlated with global strain in terms of 3D LVEF (p<0.001 for both). 2D Lc and 3D Cv showed the closest correlation with infarct size index at DE-CMR (Table).  

Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Peak Tnl</th>
<th>3D LVEF</th>
<th>3D WMSI</th>
<th>Infarct size index (DE-CMR)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2D longitudinal strain</td>
<td>0.40</td>
<td>-0.60</td>
<td>0.57</td>
<td>0.36</td>
</tr>
<tr>
<td>3D circumferential strain</td>
<td>0.61</td>
<td>-0.84</td>
<td>0.74</td>
<td>0.60</td>
</tr>
<tr>
<td>3D radial strain</td>
<td>0.56</td>
<td>-0.79</td>
<td>0.72</td>
<td>0.53</td>
</tr>
<tr>
<td>3D area strain</td>
<td>0.51</td>
<td>-0.76</td>
<td>-0.67</td>
<td>-0.53</td>
</tr>
<tr>
<td>2D longitudinal strain</td>
<td>0.62</td>
<td>-0.69</td>
<td>0.76</td>
<td>0.64</td>
</tr>
</tbody>
</table>

p<0.0001 for all, except *p=0.01.

Conclusions: Global 3D Cv, as well as 2D Lc could be used as an objective and accurate estimate of LV damage and overall function at bedside in patients with recent STEMI. Since infarct size is a strong prognostic marker, prospective follow-up studies are warranted in order to verify the ability of 2D Lc and 2D Lc to improve risk stratification early after STEMI.

Echocardiographic assessment of biventricular pacing effects on right ventricular function

A. Kusiak, J. Wilinski, W. Wojciechowska, M. Jastrzebski, T. Sondel, B. Bączor, M. Kłos-Bieńek, D. Czarnecka, Jagiellonian University Medical College, 1st Department of Cardiology and Hypertension, Krakow, Poland

Aim: Most of the studies assessing effects of cardiac resynchronization therapy (CRT) have focused on left ventricle (LV). Little is known about how CRT affects right ventricular (RV) performance. The aim of this study was to evaluate a short term effect of CRT on RV function assessed by echocardiography with tissue Doppler imaging techniques (TDI) and complex RV evaluation.

Materials and Methods: The data of 57 consecutive patients (54 men, 95%), aged 66.4 (± 8.7 years) with HF were analyzed. All patients were in NYHA III-IV functional classes, despite optimal pharmacological treatment according to the current guidelines, had LVEF <35% and RVSP complex ≥ 120 ms in a standard electrocardiogram. At baseline and three months after CRT implantation patients’ history was taken, echocardiographic measurements, anthropometrical examination, laboratory tests including the level of NTproBNP and ECG were performed.

Results: In the whole study group mean NYHA class and QRS duration diminished and 6-minute walk test distance increased. Echocardiographic parameters results are presented in Table.

Table 1

<table>
<thead>
<tr>
<th>Echocardiographic parameter</th>
<th>At baseline</th>
<th>At 3 months follow-up</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RV wall thickness (mm)</td>
<td>5.47±1.20</td>
<td>5.12±1.02</td>
<td>0.028</td>
</tr>
<tr>
<td>RV basal dimension (mm)</td>
<td>28.74±4.47</td>
<td>28.32±4.04</td>
<td>0.266</td>
</tr>
<tr>
<td>RV end-diastolic area (cm²)</td>
<td>15.72±5.00</td>
<td>15.62±4.56</td>
<td>0.927</td>
</tr>
<tr>
<td>RV end-systolic area (cm²)</td>
<td>10.94±4.51</td>
<td>10.22±4.25</td>
<td>0.007</td>
</tr>
<tr>
<td>RV fractional area change (%)</td>
<td>31.35±10.32</td>
<td>30.46±10.35</td>
<td>0.001</td>
</tr>
<tr>
<td>TAPSE (mm)</td>
<td>13.95±2.80</td>
<td>15.79±2.33</td>
<td>-0.001</td>
</tr>
<tr>
<td>S’ (cm/s)</td>
<td>8.84±4.45</td>
<td>11.00±3.43</td>
<td>-0.001</td>
</tr>
<tr>
<td>RV fractional area change (%)</td>
<td>2.02±0.95</td>
<td>1.86±0.91</td>
<td>0.013</td>
</tr>
<tr>
<td>RVSP (mm Hg)</td>
<td>31.07±20.43</td>
<td>27.75±17.36</td>
<td>-0.001</td>
</tr>
</tbody>
</table>

Conclusions: This study showed that in the whole study population CRT improves RV systolic function evaluated with classic and TDI derived echocardiographic parameters assessed three months after the therapy initiation.

Heart Failure: Biomarkers and Prognosticators

The time course of the pulmonary edema development during ST elevation Myocardial Infarction

M. Shochat, A. Shohat, M. Kazatker, A. Asif, Y. Levy, E. Shochat, I. Dahan, D. Blondheim, T. Sigalov, S. Meisel. Hillel Yaffe Medical Center, Heart Institute, Haifa, Israel

Development of pulmonary congestion-edema (PEd) in course of ST elevation myocardial infarction (STEMI) is frequent. The epidemiology of PEd development is well known but dynamics of PEd development are less known.

The aim was to characterize the time course of PEd evolution in STEMI patients and to develop new risk markers for early diagnosis of PEd. In order to find this correlation, patients were divided into 3 groups. Gr.1 (n=178) - patients without PEd, Gr.2 (n=240) - patients with mild PEd (Killip class I), Gr.3 (n=103) - patients with severe PEd (Killip class II-IV). In all patients, a standard clinical examination, clinical symptoms and periodic chest X-ray (CXR) examinations. In Gr. 2 patients, cardiac catheterization was performed and PEd was confirmed at cath lab. In Gr. 3 patients, PEd was confirmed at cath lab and in the others there was resolution of PEd under treatment.

The mean time between admissions to development of Killip class II of PEd was 12 hrs and 99% of patients were asymptomatic at this stage. Only 6 hours after appearance of lung rales patients complains on dyspnea were carried.

The best and earlier parameter which predicted PEd development at preclinical stage was LI.

P1009 Benefits of a probiotic therapy with Saccharomyces boulardii in heart failure patients

E.T. Mesquita, A.C. Costanzia, S.D. Moscovitch, H.C.C. Faria Neto, Universidade Federal Fluminense, Niterói, Brazil; Oswaldo Cruz Institute, FIOCRUZ, Rio de Janeiro, Brazil

Background: A cardio-intestinal syndrome has been described in heart failure patients (HF), with intestine morphofunctional alterations, increased bacteria concentration and translocation, inflammatory activation, contributing to injury and disease progression. In clinical practice, probiotics have showed benefits in inflammatory conditions; however, its effects have never been tested in chronic HF patients.

Purpose: To evaluate the impact of the therapy with Saccharomyces boulardii (SB) in HF patients with reduced ejection fraction (HFrEF).

Methods: A prospective randomized double-blind, placebo-controlled study. Twenty HF patients with left ventricle ejection fraction (LVEF) ≤50%, New York Heart Association class I or II were randomized to daily treatment with SB (1000 mg/day) or placebo for 3 months. By echocardiography (ECHO), the left atrial diameter and LVEF (Simpson’s) were estimated. Tolerability and safety were monitored. The sample distribution was tested by the Shapiro-Wilk’s test was used for variables with normal distribution and Mann-Whitney test for variables without. The survival rate considered was 0.05. The results are represented by the mean difference between the study’s beginning and end data of each variable.

Results: The SB group showed a significant reduction in uric acid levels (SB: -4.25 mg/dL vs. Placebo: -0.22 mg/dL, p= 0.009), and in high-sensitivity C-reactive protein levels (SB: -2.3 mg/L vs. Placebo: -4.4 mg/L, p= 0.007), in total leucocyte count (SB: -101.7/mm3 vs. Placebo: +541.1/mm3, p= 0.032), and in creatinine (SB: +0.9 mg/L vs. Placebo: +1.08 mg/L, p= 0.009), on high-sensitivity C-reactive protein (SB: -1.02 mg/L vs. Placebo: -0.02 mg/L, p= 0.007), and in creatinine (SB: +0.9 mg/L vs. Placebo: +1.08 mg/L, p= 0.009). There was also a decrease in left atrial diameter (SB: -0.27 cm vs. Placebo: 0.22 cm, p= 0.007). LVEF was improved but did not reach significance. The SB group reported improvement in gastrointestinal symptoms, and no adverse effects.

Conclusions: The use of probiotic SB in chronic HF patients with reduced LVEF suggests a beneficial effect on immune-inflammatory activation (C-reactive protein, uric acid, total leucocyte count). (ClinicalTrials.gov registration: NCT01500343)

P1010 Warfarin use is associated with increased survival in patients with left ventricular systolic dysfunction and pulmonary hypertension

D.H.J. Elder, A. Goudel, B. Szwiejkowski, A. Choy, A. Smuthers, C.G. Lang, Ninewells Hospital, Dundee, United Kingdom; University of Dundee, Dundee, United Kingdom

Background: Pulmonary hypertension carries an increased mortality rate in those with left ventricular systolic dysfunction (LVSD). In pulmonary hypertension pathologic changes within the lung microcirculation include thrombosis, even in the absence of clinically manifest thromboembolic disease. However, anticoagulation for pulmonary hypertension in those with LVSD is controversial, unless consistent thromboembolic disease or atrial fibrillation is evident.

Methods: The泰格side echocardiography database was linked to dispensation pre-
The implication of surgical parameters as predictors of development of perioperative heart failure in patients undergoing non-cardiac surgery.

**Purpose:** Perioperative heart failure is important cause of morbidity in patients undergoing non-cardiac surgery. The role of perioperative echocardiographic biomarker, and clinical risk factors such as Revised Cardiac Risk Index (RCRI) for the risk stratification has been investigated. However, surgical data as predictors of perioperative heart failure have not been as well investigated.

**Methods:** A total of 734 consecutive patients (64 ± 12.7 g/dl, 415 males) who performed cardiac consultation for elective non-cardiac surgery were studied. We evaluated the clinical risk factors including RCRI, echocardiographic and laboratory findings. Surgical data included type of surgery and anesthesia, surgical times, transfusion, hemoglobin levels before and after surgery. The primary end-point was a development of heart failure within 30 days after surgery.

**Results:** There were 58 (7.9%) perioperative heart failures. Age (72.0 ± 11.0 years versus 66.0 ± 12.7 years, P < 0.001) was significantly older in patients with perioperative heart failure than those without. Clinical risk factors and comorbidities such as hypertension, diabetes, hyperlipidemia, current smoking, and pulmonary hypertension. Adequately designed prospective randomised controlled trials are required to validate this finding given the limitations of this observational study.

**Conclusion:** Warfarin use is associated with improved in those with LVSD and pulmonary hypertension. Adequately designed prospective randomised controlled trials are required to validate this finding given the limitations of this observational study.

**P1015**

**Role of osteopontin and lipoprotein-associated phospholipase A2 as biomarkers in heart failure patients**

O. Vittos1, D. Marta2, M. Serban2, A. Vittos2, E. Moldoveanu2.

1Medcenter, Bucharest, Romania; 2Victor Babes National Institute, Department of Pathology, Bucharest, Romania.

**Purpose:** Both forms of heart failure (HF), with reduced ejection fraction (HFrEF) and with preserved ejection fraction (HfPEF) are present in approximately the same proportion between HF patients. We have investigated osteopontin (OPN), a pleiotropic cytokine implicated in vascular remodeling and fibrosis and lipoprotein associated phospholipase A2 (LpPLA2), an enzyme which is now recognized as a marker of vascular inflammation.

**Methods:** The study included 208 HF patients and 20 healthy controls. Baseline evaluation for patients included clinical examination, 12-lead ECG, estimation of NYHA functional class, transthoracic echocardiography (left ventricular ejection fraction, left ventricular end diastolic diameter, and routine laboratory tests). LpPLA2 activity was determined by spectrophotometric method and OPN by ELISA method.

**Results:** HFrEF patients represented 42.31% from all HF patients. OPN was higher in HFrEF patients (43.9±7.17±0.5 mg/ml) than in normal (21.4±9.4±1.8 mg/ml) and was higher in HfPEF patients (46.0±3.15±6.6 mg/ml) than in HfPEF patients (42.4±7.17±9.2 mg/ml). LpPLA2 activity was higher in HFrEF patients (414.2±5.17±0.6 mg/ml) than in normal (255.6±2.0±0.8 UL). LpPLA2 activity was higher (442.4±11.6±2.6 UL) in HfPEF patients than in HfPEF patients (393.6±5.36±0.3 UL).

**Conclusion:** Elevated plasma values of LpPLA2 in HFrEF patients are in concordance with elevated values of OPN and with exacerbated inflammation status existing in these patients, which is confirmed by higher incidence of left ventricular hypertrophy (LHV) in the HfPEF patients compared with HFrEF patients.

**P1014**

**Prognostic value of CA-125 circulating levels in stable heart failure patients**

A. Mendez Fernandez1, J. Ordonez2, M. Noguero1, N. Ribas1, T. Miró1, G. García1, M.T. Domingo1, A. Bayés1, S. Mirabel1, E. Roig1.

1Hospital de la Santa Creu i Sant Pau, Department of Cardiology, Barcelona, Spain; 2Hospital de la Santa Creu i Sant Pau, Department of Biochemistry, Barcelona, Spain

CA-125 is a high-molecular weight glycoprotein used as tumor marker. Increased levels of CA-125 correlated with the severity of congestion and systemic inflammatory activity in heart failure (HF) patients (P<). Increased levels of CA-125 have been associated with poor prognosis in acute HF. To assess the prognostic value of increased circulating levels of CA-125 in stable chronic HF, 154 pts were studied. Pts were in stable condition in NYHA functional class II-III and followed in a HF Unit. New hospital admissions for worsening HF and death were evaluated. NT-proBNP values were also assessed on the same day.

**Results:** Mean age was 72.1±11.2 years, 62% were men. The etiology of HF was hypertension in 22%, ischemic heart disease in 35%, dilated cardiomyopathy in 8%, valve heart disease 19%, congenital 2% and others 14%. Mean ejection fraction (EF) was 48±17% with 53% of pts having preserved EF. Pts were treated with ACEI or angiotensin antagonists in 77% of pts, diuretics in 83%, beta-blockers in 58% and aldosterone antagonists in 48%. CA-125 levels correlated with NT-proBNP levels (p<0.001). During follow-up (18±8 months), 105 pts required a hospital admission for worsening HF (68%) and 28 died (18%).

**Conclusion:** Patients with CA-125 levels ≥50 UK/L identified patients with worsening HF and high mortalit.
decreased only in systolic HF patients, which means that the atrio-ventricular matching differ substantially. Our data suggests that atrio-ventricular matching is preserved in diastolic HF, but the progression in systolic HF is mediated by the manifestation of atrio-ventricular mismatching.

Increased incidence of heart failure after the great East Japan earthquake and tsunami disaster in iwate

M. Homma, M. Nakamura, Y. Koeda, S. Nakajima, F. Tanaka, T. Sakai, H. Endo, M. Kawakami, K. Sakata, T. Onoda on behalf of Northern Iwate Heart Disease Registry Consortium, iWate Medical University, Iwate, Japan

Background: On 11 March 2011, a massive 9.0 magnitude earthquake occurred on the northeastern coast of Japan. Just after the earthquake, a massive tsunami struck the coast area and caused extensive and severe damage. Although several previous studies have shown an increased incidence in cardiovascular disease after natural disasters, the impact of tsunami remains unknown.

Methods: We have investigated the incidence and clinical characteristics of hospitalized patients with HF in the coastal area hit by the tsunami (Iwate area) for two months after the disaster (from 11 March 2011 to 10 May 2011). For comparison with the period before the disaster, the incidence of HF was investigated retrospectively in the same area and period for two months during 2009 and 2010. In addition, to elucidate the impact of the tsunami, incidence of HF was also assessed from a remote area with minimal effect from the tsunami (control area).

To capture HF as defined by the Framingham criteria, medical charts from all hospitals located in these areas were reviewed. The tsunami area was defined by an officially published tsunami invasive area/town area greater than 10%.

Results: Trends in the number of HF cases are shown in the figure. There was a significant increase in the number of HF cases after the disaster within the tsunami area (Z = 7.99, p = 0.0018), but not in the control area (Z = 2.94, p = 0.026). No significant difference in age or the percentage of new onset HF were observed before and after the disaster in either area.

Conclusion: After the catastrophic earthquake and tsunami, the incidence of HF in the tsunami area increased significantly compared to the control area.

Heart rate does not predict post-discharge events in patients hospitalized for heart failure with reduced ejection fraction in the EVEREST trial

J. Wilcox1, S.J. Greene2, M. Ghereghadeh1, M.E. Harinstein3, M.J. Kwansy4, A. Fought1, M.A. Konstam5, F. Zannad6, A.P. Maggi2, K. Sweder1, 1Feinberg School of Medicine, Division of Cardiology and Cardiovascular Surgery, Chicago, United States of America; 2Northwestern University, Feinberg School of Medicine, Chicago, United States of America; 3University of Pittsburgh, Cardiovascular Institute, Pittsburgh, United States of America; 4Yale School of Medicine, Division of Cardiology and the CardioVascular Center, Boston, United States of America; 5Inserm, CIC9501, U961, CHU, Nancy, France; 6AMCO Research Center, Florence, Italy;

Purpose: Elevated resting heart rate (HR) is associated with worse outcomes in patients (pts) with stable chronic heart failure (HF). HR may predict post-discharge outcomes (PDO) in pts hospitalized for worsening HF.

Methods: The Efficacy of Vasopressin Antagonism in Heart Failure Outcome Study with Tolvaptan (EVEREST) trial examined the effects of tolvaptan (TLV), a vasopressin antagonist, in pts with worsening HF and ejection fraction (EF) <40%. We analyzed 1894 pts in sinus rhythm and not pacemaker dependent. Baseline demographic, medication history, physical exam and laboratory findings were compared across quartiles (Q) as well as hazard ratios for (1) all-cause and (2) cardiovascular (CV) mortality, and (3) CV mortality or HF re-hospitalization.

Results: Baseline data are shown in Table 1. TLV had no effect on HR. Higher HR was not associated with any endpoint. Adjusted multivariate analysis showed no significant difference by in-hospital HR change or baseline HR.

Conclusion: In chronic HF pts hospitalized with worsening HF and reduced EF, baseline HR did not predict mortality or PDO. HR in this unstable situation may reflect different conditions compared with stable states.

P1019

Relation between heart rate and quality of life in chronic heart failure patients

A. Torrens Oses, C. Enjuanes Grau, J. Comín Colet, G. González, M. Cladellas, J.M. Verdu, A. Linas, J. Brugera Cortada. Hospital del Mar, Department of Cardiology, Heart Failure Program, Barcelona, Spain

Purpose: Recent data from the SHIFT study suggests that heart rate (HR) is a key determinant of health-related quality of life (HRQoL). After proving the concept in a clinical trial, the relation between heart rate and HRQoL in “real-world” CHF patients from the community with higher age and high prevalence of preserved LVEF has not been explored. The aim of our study was to evaluate the relationship between HR and HRQoL in this “real-world” non-selected patients with CHF.

Methods: Up to 684 consecutive stable CHF patients with reduced or preserved LVEF referred to a comprehensive nurse-based heart failure programme were included. At inclusion, relevant clinical and demographic information were obtained. HRQoL was measured using the Minnesota Living with Heart Failure Questionnaire (MLWHFQ) (range of scores from 0, best QoL, to 105, worst QoL). HR was calculated from a resting ECG at inclusion and classified into 3 different groups: <70 beats per minute (bpm), ≥ 70 and < 90 bpm, and ≥ 90 bpm.

Results: Mean age was 72 ± 11, with a 57% of male patients. Mean LVEF was 43.14 ± 25.41, with a 42% of hypertensive cardiomyopathy. Sinus rhythm was present in 55.5% of patients, and chronic atrial fibrillation in 33%, with a mean HR of 79.9 ± 20.3. Mean overall summary score of the MLWHFQ was 43.14 ± 25.4. All-Cause Mortality (n=388) and CV Death or HF hospitalization (n=659) had no effect on HRQoL. CV or HF hospitalization (n=82) had no effect on HRQoL.

Conclusions: As expected, patients with higher HR had worse HRQoL. The overall summary score of the MLWHFQ for the groups <70 bpm, 70-90bpm, ≥90 were 40.75 ± 26, 42.9 ± 25 and 49.02 ± 26, respectively (p-value = 0.005). In the multivariate analysis (multiple linear regression), HR was an independent predictor of worse scores in the HRQoL evaluation (beta standardized = 0.11; p-value = 0.004). When we analyzed the subgroups created according LVEF, higher HR was associated with worse HRQoL in the reduced LVEF group (overall MLWHFQ: <70 bpm = 40.75 ± 26.7, 70-90bpm = 46.07 ± 25.3, ≥90 = 49.3 ± 21.6; p-value = 0.024) and this relation didn’t exist in the preserved LVEF group (overall MLWHFQ: <70 bpm = 40.75 ± 26, 70-90bpm = 45.9 ± 24.5, ≥90 = 44.6 ± 22.3; p-value = 0.23).

Conclusion: As shown in the SHIFT study, higher HR is associated with worse QoL in real-world non-selected CHF patients. However, this association appears to be mostly due to the effects of HR in patients with reduced LVEF. Additional studies are needed to confirm this hypothesis and to establish whether this differential effect according to LVEF is driven by differences in pathophysiological mechanisms between patients with CHF with reduced or preserved LVEF.

P1020

Urinary acid base imbalance in patients with chronic heart failure

Y. Otaki, T. Watanabe, H. Takahashi, T. Narumi, S. Kadowaki, T. Arimoto, T. Shioshiodo, T. Miyashita, T. Miyamoto, I. Kubota. Yamagata University, Yamagata, Japan

Purpose: Renal dysfunction is reported to be associated with poor outcome in patients with chronic heart failure (CHF). A recent study showed that acidic urine is related to chronic kidney disease (CKD), which is a risk factor for the development of CHF. However, it remains to be determined whether urinary acid base imbalance is associated with a poor outcome in patients with CHF.

Methods and Results: We measured urine pH using dipsticks in 592 patients with CHF. Patients were prospectively followed and divided into three groups based on their urine pH level (acidic urine, urine pH ≤ 5.5, normal urine, urine pH ≥ 6.0).
6.0 to 7.0; alkaline urine, urine pH ≥ 7.5). There were 170 cardiac events during a median follow-up period of 522 days. Patients with acidic urine or alkaline urine had severe New York Heart Association (NYHA) functional class compared to those with normal urine. Prevalence of acidic urine increased with worsening CKD stage. In the univariate analysis, the presence of acidic urine or alkaline urine was significantly associated with cardiac events. Further, age, NYHA functional class, estimated glomerular filtration rate, brain natriuretic peptide, hemoglobin, uric acid, proteinuria, and left ventricular ejection fraction were significantly related to cardiac events. In the multivariate Cox proportional hazard analysis, both acidic urine and alkaline urine were independent predictors of cardiac events. A Kaplan-Meier analysis demonstrated that the rate of cardiac events was higher in patients with acidic urine or alkaline urine than in those with normal urine.

Figure 1. Kaplan-Meier analysis of cardiac events free rate among patients with acidic urine, alkaline urine, and normal urine.

Conclusion: The presence of urinary acid base imbalance can reliably identify patients at high risk of future cardiac events in patients with CHF.

Diastolic and systolic mechanical dysynchrony in patients with heart failure

F.Q. Huang, R.S. Tan. National Heart Centre Singapore (NHCS), Singapore, Singapore

Objectives: We aimed to evaluate the cardiac mechanical dysynchrony in patients with heart failure (HF).

Methods: 75 patients with HF (mean age: 61.6±10.5y) and 30 healthy controls (mean age: 59.8±6.5y) were involved. Subjects were divided into: group 1 (LVEF<50%), group 2 (LVEF≥50%) and group 3 (controls). The time intervals of R wave on ECG to the onset of mitral annulus velocities S' and E' at septal (R-sS', R-sE'), lateral (R-lS', R-lE') and tricuspid annulus velocities S' and E' (R-rS', R-rE') were recorded.

Results: R-sS' of mitral annulus at septal, lateral and tricuspid annulus significantly prolonged in patients with HF in comparison to the controls (46.43±8.43 vs. 34.17±9.54 ms, p<0.001). In HF patients, R-sS' was significantly higher in HF patients with severe NYHA functional class than in those with mild NYHA functional class (49.37±10.30 vs. 39.54±9.90 ms, p<0.001).

P1021

<table>
<thead>
<tr>
<th>Group</th>
<th>R-sS'(ms)</th>
<th>R-lS'(ms)</th>
<th>R-rS'(ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group1</td>
<td>49.37±10.44</td>
<td>67.47±24.63</td>
<td>43.37±26.85</td>
</tr>
<tr>
<td>Group2</td>
<td>64.10±15.69</td>
<td>46.85±62.44</td>
<td>34.37±26.85</td>
</tr>
<tr>
<td>Group3</td>
<td>61.81±26.13</td>
<td>74.89±37.54</td>
<td>19.34±11.85</td>
</tr>
<tr>
<td>Controls</td>
<td>46.54±15.34</td>
<td>46.07±64.48</td>
<td>43.81±33.03</td>
</tr>
</tbody>
</table>

Conclusions: There were significant LV electromechanical time delay in both systole and early diastolic in HF patients compared to normals and more severe in patients without HFPEF. In patients with HFPEF, there was a regional systolic mechanical dysynchrony between septal and lateral mitral annulus, whereas in patients without HFPEF, it occurred in the tricuspid annulus and mitral annulus.

Elevated arterial stiffness is correlated with BNP levels in HF patients. Moreover novel biomarkers of renal function are associated with arterial stiffness and biomarkers of cardiac remodeling. These findings highlight a possible common pathogenetic mechanism of arterial, cardiac and renal dysfunction in HF.

P1022

Serum neutrophil gelatinase-associated lipocalin and cystatin-c levels are associated with arterial stiffness in patients with heart failure

S. Michalos1, G. Sissas1, D. Toussoulis1, E. Gkonou1, C. Kolia1, S. Koutsis1, A. Miliou1, N. Gouliopoulos1, A.G. Papavassiliou1, C. Stefanadis1, 2.1. University of Athens Medical School, Hippokration General Hospital, Department of Cardiology, Athens, Greece; 2. University of Athens Medical School, Department of Biochemistry, Athens, Greece

Purpose: Patients with heart failure (HF) have a significant decline of renal function. Measurement of arterial stiffness is well validated in large population studies as strong predictor of adverse cardiovascular outcomes. In the present study we investigate the association between novel biomarkers of renal dysfunction and indices of arterial function in HF.

Methods: We enrolled 78 consecutive patients with HF (mean age 65) and 79 healthy subjects (CI) adjusted for age and sex. We collected pulse velocity (PWV) was measured as an index of aortic stiffness and augmentation index (AIx) as a measure of arterial wave reflections. Serum levels of Neutrophil gelatinase-associated lipocalin (NGAL), Cystatin-C, Brain natriuretic peptide (BNP) and Matrix metalloproteinase-9 (MMP-9) were measured by ELISA. Creatinine clearance was estimated using Cockcroft-Gault formula (eCcl).

Results: In HF patients, logCystatin-C levels was negatively correlated with eCcl (r=-0.214, p=0.049) and logMMP-9 levels were positively correlated with serum creatinine levels (r=0.458, p<0.001). Patients with HF compared to CI, had significantly higher PWV (9.95±2.80 m/sec vs. 9.02±1.78 m/sec, p=0.027) and higher AIx (23.35±9.54% vs. 19.82±8.04%, p=0.047). Interestingly, in HF patients, AIx was correlated with logCystatin-C levels (r=0.261, p=0.029) while, PWV was correlated with logBNP levels (r=0.304, p=0.049).

Conclusions: Elevated arterial stiffness is correlated with BNP levels in HF patients. Moreover novel biomarkers of renal function are associated with arterial stiffness and biomarkers of cardiac remodeling. These findings highlight a possible common pathogenetic mechanism of arterial, cardiac and renal dysfunction in HF.

First-degree atrioventricular block is a reliable risk factor of cardiac prognosis in patients with chronic heart failure

S. Kadowaki, T. Watanabe, T. Narumi, Y. Otaki, T. Arimoto, M. Takahashi, T. Shindo, T. Hamamoto, T. Kubota. Yamagata University School of Medicine, Yamagata, Japan

Background: First-degree atrioventricular block (AVB) is frequently encountered in clinical practice. Previous studies have proved that first-degree AVB is a benign finding in healthy patients. However, it has been recently reported that first-degree AVB is associated with atrial fibrillation, pacemaker implantation, and cause mortality among outpatients in the Framingham heart study. The purpose of this study was to elucidate whether first-degree AVB can predict cardiac events in patients with chronic heart failure (CHF).

Methods and Results: We measured the PR interval in 306 CHF patients and divided into 2 groups based on presence of first-degree AVB (PR interval ≥220 ms). Patients were prospectively followed with end points of cardiac death or rehospitalization for worsening CHF. There were 82 cardiac deaths, including 13 cardiac deaths and 69 re-hospitalization during median follow-up period of 463 days. Patients with cardiac events were older, had more severe NYHA functional class and the prevalence of first-degree AVB was compared to those without cardiac events. Furthermore, patients with cardiac events showed more renal dysfunction, and higher levels of brain natriuretic peptide and uric acid compared to those without cardiac events. Kaplan-Meier analysis showed that cardiac event rate was higher in patients with first-degree AVB than in those without. Multiple Cox hazard analysis revealed that first-degree AVB was independently associated with cardiac events.

Conclusions: First-degree AVB may be a reliable prognostic factor in CHF patients.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790 by guest on 11 March 2019
The enormous earthquake hit Japan on March 11 increased acute heart failure -analysis of remote monitoring of intrathoracic impedance-

H. Suzuki, S. Yamada, M. Kamioka, Y. Kamiyama, S. Saito, T. Takeshi. Fukushima Medical University, Fukushima, Japan

Background: The enormous earthquake which hit Japan on March 11, 2011, induced physical and mental stressors to residents in Fukushima Prefecture, Japan. Several studies have revealed that stress in catastrophic disasters can trigger cardiovascular events such as myocardial infarction and fatal arrhythmia, however, little is known about the association with the occurrence of acute heart failure. Recently, remote monitoring of implantable device allows us earlier detections of clinical problems including pulmonary congestion and arrhythmic events. Objectives: The purpose of this study was to determine whether the March 11 earthquake and subsequent disasters including tsunami and radiation leaks from damaged nuclear power plants increased the incidence of acute decompensated heart failure in patients with chronic heart failure.

Methods: Forty chronic heart failure patients (mean age 62±13 years, mean left ventricular ejection fraction 30±8%) who lived in Fukushima Prefecture on March 11 were enrolled in this study. All subjects received implantable cardioverter defibrillator or cardiac resynchronization therapy with defibrillator which can check intrathoracic impedance using remote monitoring. When accumulated impedance under reference impedance got over 60 ohms (threshold of fluidindex), we defined the existence of pulmonary congestion. We compared the incidence of pulmonary congestion and arrhythmic events between one month before and after March 11. Results: Three patients were excluded because of monitoring discontinuation by evacuation (n=2) and crushed death under collapsed house (n=1). In the one month after March 11, 9 patients (24%) exceeded the threshold of fluid index compared with only 2 patients (5%) in the preceding one month, representing a 4.5 fold increase in relative risk (P=0.04). On the contrary, arrhythmic events did not change significantly in the one month following March 11.

Conclusions: These results suggest that earthquake-induced stress causes an increased risk of worsening heart failure without changes in fatal arrhythmia. In addition, remote monitoring of intrathoracic impedance may be a useful tool for the management of chronic heart failure patients in catastrophic disasters, but have some limitation of network system during evacuation.

Omega-3 supplementation modulated beneficially the adverse effect of depressive symptomatology on 1-year prognosis in patients with chronic heart failure


In the clinical course of chronic heart failure severe short term depressive symptoms have been recognised to confer to adverse outcome through various mechanisms. Many studies have shown long-chain omega-3 polyunsaturated fatty acids (n-3 PUFAs) are a potential treatment of depressive disorders. The purpose of this study was to evaluate the role of n3-PUFA supplementation on the clinical course of patients with chronic heart failure and depressive symptomatology.

Methods: We enrolled 256 consecutive patients (mean age 61±13 years old) with chronic compensated heart failure, due to ischemic or dilated cardiomyopathy, NYHA classification II-III, under optimal medical treatment. They were randomized to receive 1000 mg n-3PUFA supplementation. Detailed information regarding their medical records, anthropometric data, physical activity, nutrition and smoking habits, and adverse cardiovascular events (death or re-hospitalization due to cardiac events such as myocardial infarction, arrhythmia events) were recorded; while depression was assessed using the Zung’s Depression scale (ZDRS range 20-80).

Results: Thirty five percent of patients experienced an adverse event during the 1-year of follow up. Logistic Regression analysis revealed that depressive symptomatology increased the risk by 2.8% (95% CI 1-1.065, p=0.05), after taking into account several founders. A significant interaction was observed between omega-3 intervention and depression (p<0.001). Thus the analysis was repeated by intervention group. Depression symptomatology was associated with increased risk of adverse events only in patients who did not receive omega-3 supplementation (OR=1.074, 95%CI<1.05–1.107); while depression did not influence outcomes in the omega-3 intervention group (p=0.54).

Conclusion: Omega-3PUFA supplementation seems to mediate the adverse effect of depression on the 1-year clinical course of patients with chronic heart failure under usual medical treatment. This finding may illustrate another potential beneficial effect of omega-3 supplementation in patients with heart failure.


dever, influence of myocardial tissue characteristics after myocardial infarction on regional or global myocardial mechanics has not been fully investigated.

Methods: Consecutive twenty-six reperfused acute myocardial infarction patients (55±12 years, 22 men) underwent cardiac magnetic resonance (CMR) imaging with cine, T2 weighted imaging (T2WI), resting 1st pass perfusion and delayed enhancement (DE) imaging 2 or 3 days after percutaneous coronary revascularization. Extent of edema, scar, presence of microvascular obstruction, perfusion defect were measured based on 17 myocardial segment model and degree of transmurality. At the same day with CMR, echocardiography was also done. Using 20 speckle tracking analysis, longitudinal, circumferential strain and torsion were measured. Serial blood cardiac biomarkers and electrocardiography were done until discharge.

Results: Twelve patients had left anterior descending culprit lesion, 11 had right coronary and 3 had circumflex artery culprit lesions. Extent of myocardial scar and edema measured by DE-CMR and T2WI was significantly correlated with peak level of CK-MB (r=0.755, p<0.001) and 12 lead ECG-derived extent of Q-wave (r=0.677, p<0.001). Extent of edema significantly correlated with global longitudinal strain (r=0.627, p=0.001) and torsion (r=0.429, p=0.029). But extent of myocardial scar or edema did not correlated with diastolic function as represented by E/e' and early diastolic longitudinal strain rate. E/e' is correlated with average non-infarct circumferential myocardial wall strain (r=0.452, p=0.031).

Conclusions: Extent of myocardial scar and edema is correlated with LV longitudinal strain and torsion but not with diastolic function in reperfused acute myocardial infarction. Diastolic function in acute myocardial infarction is determined not only by infarct extent but also noninfarct myocardial tissue characteristics.

Predictors of worsening left ventricular hypertrophy in 42 patients with aortic stenosis

1National University Health System, Singapore, Singapore; 2National University Heart Centre, Department of Cardiology, Singapore, Singapore; 3National Heart Centre Singapore (NHCS), Singapore, Singapore; 4Aunong General Hospital, Singapore, Singapore

Background: Left ventricular hypertrophy (LVH) is a maladaptive effect of aortic stenosis (AS) and portends worse outcomes. We aim to determine predictors and course of LVH progression.

Methods: We analysed 509 consecutive patients with AS who underwent paired echocardiographic studies >180 days apart. One hundred and eighty-eight patients (37%) had significant increase (>20%) in left ventricular mass index (LVMI). We compare their baseline echocardiographic parameters to the group without progression.

Results: The mean time interval between the paired studies, LV ejection fraction and aortic valve area (AVA) were 1252±910 days, 60±12% and 1.29±0.44cm² respectively and were not significantly different between the two groups. One hundred and forty patients (28.8%) had mild AS (AVA<1.5cm²), 217 (44.7%) had moderate AS (AVA 1.5-2cm²) and 129 (26.5%) had severe AS (AVA<1.0cm²); there was no significant difference in the degree of progression of LVH between the 3 groups (8.3% vs. 9.9% vs. 9.6%, P=NS). Despite similar LV systolic function and aortic valve parameters, progression of LVH was noted in the group with smaller baseline LV mass index and volumes but increase end-systolic wall stress (ESWS) (Table).

Table 1

<table>
<thead>
<tr>
<th>Echocardiographic parameters</th>
<th>Group A (n=188)</th>
<th>Group B (n=321)</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time interval (days)</td>
<td>1272±897</td>
<td>1147±853</td>
<td>NS</td>
</tr>
<tr>
<td>LVMI (cm²/m²)</td>
<td>40.6±12.8</td>
<td>45.8±16.1</td>
<td>0.01</td>
</tr>
<tr>
<td>Left ventricular ejection fraction (%)</td>
<td>60.3±7.8</td>
<td>60.0±11.9</td>
<td>NS</td>
</tr>
<tr>
<td>AVA (cm²)</td>
<td>1.28±0.43</td>
<td>1.30±0.44</td>
<td>0.30</td>
</tr>
<tr>
<td>Aortic valve dimensions index</td>
<td>0.37±0.10</td>
<td>0.39±0.11</td>
<td>0.34</td>
</tr>
<tr>
<td>Peak transaortic velocity (m/s)</td>
<td>291±75.3</td>
<td>284±75.0</td>
<td>0.48</td>
</tr>
<tr>
<td>Mean transaortic pressure gradient (mmHg)</td>
<td>20.7±13.6</td>
<td>20.6±20.3</td>
<td>0.30</td>
</tr>
<tr>
<td>Aortic valve resistance (dyne s/cm⁵)</td>
<td>122±92.7</td>
<td>126±152.2</td>
<td>0.15</td>
</tr>
<tr>
<td>End-systolic wall stress/end-systolic volume</td>
<td>2.19±0.78</td>
<td>1.90±0.76</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Comparison between initial parameters.

Conclusion: ESWS appears to predict progression of LVH in patients with AS. Regular monitoring is warranted.
Prosthesis-patient mismatch (P-PM) is an important determinant of morbidity and mortality after aortic valve replacement. The aims of this study were to report the frequency of P-PM and its relation to the clinical outcome after transcatheter aortic valve implantation (TAVI).

Between April 2008 and December 2011, 166 patients with symptomatic severe aortic stenosis, who had undergone successful transcatheter aortic valve implantation with the CoreValve prosthesis, the indexed effective orifice area (EOA) at baseline and discharge was measured. P-PM was defined as severe (indexed EOA < 0.65 cm²/m²) or moderate (0.65 cm²/m² ≤ indexed EOA < 0.85 cm²/m²). Clinical, echocardiographic, and procedural factors relating to P-PM were studied.

Mean age was 79.3±6.2 years and 59.6% were female. The indexed EOA increased from 0.35±0.1 to 0.94±0.2 cm²/m² (P<0.001) after TAVI. Moderate and severe P-PM occurred in 74 (44.6%) and 15 (9%) of patients, respectively. Mortality beyond 30 days was more in patients with severe P-PM than those with moderate or no P-PM (35.9% vs. 8.8%, P=0.003) but was no significant different between the groups with regard to LV-EF (median 34% (IR 25-47) vs. 45%; p=0.04), and spironolactone therapy (12% vs. 23%; p=0.01). Cox regression model corrected for age, LV-EF, beta-blocker, spironolactone, heart rate, heart rhythm, and underlying heart disease revealed as independent risk factors for mortality: indexed EOA < 0.65 cm²/m² (HR 6.28 (1.84-21.42) p=0.003). P-PM was related to death in a population with reduced ejection fraction.

Incidence and clinical outcome of Prosthesis patient mismatch after transcatheter aortic valve implantation with the CoreValve prosthesis

YOUNG INVESTIGATORS AWARDS SESSION: BASIC SCIENCE

Deficiency of mitogen-activated protein kinase activated protein kinase 2 (MK2) prevents maladaptative vascular remodeling and promotes endothelial regeneration after injury of the carotid artery

P. R. Kapopara, J. Von Felden, K. Sonnenschein, J. Bausersch, B. Schiefer, U. Baveniek, Hannover Medical School, Department of Cardiology and Angiology, Hannover, Germany

Background: Maladaptive vascular remodeling after mechanical injury of the arterial wall (e.g. angioplasty) is characterized by neointima formation and media hypertrophy causing narrowing of the affected artery. Moreover, mechanical injury of the arterial wall results in a loss of the vessel protecting endothelial cell layer. The MAP kinase-activated-protein kinase 2 (MK2) regulates expression of inflammatory mediators, cell migration, and cell proliferation; processes known to be important for vascular remodeling and endothelial regeneration after vascular injury. Therefore, we hypothesized an important role of MK2 in vascular remodeling and endothelial regeneration after injury of the arterial wall.

Methods & Results: The functional role of MK2 in arterial remodeling after vascular injury was investigated in hypercholesterolemia low-density-lipoprotein-receptor-deficient mice (LDLRKO) subjected to wire injury of the common carotid artery (CCA). MK2-deficiency (LDLRKO/MK2KO) almost completely protected against neointima formation, media hypertrophy and luminal stenosis (n=8, p<0.01). Histomorphometry, day 28 post-injury. To elucidate potentially underlying mechanisms cell proliferation (BrdU-assay; expression of p53 and histone H3) and angiogenesis and mitophagy via cyclic AMP elevation (Western blot) was analyzed in cultured smooth muscle cells (SMC) isolated from aortas of wildtype (WT) and MK2-deficient mice (MK2KO).

MK2-deficiency significantly reduced cell proliferation as well as increased expression of Brdu and p53. Westernblot) was analyzed in cultured smooth muscle cells (SMC) isolated from aortas of wildtype (WT) and MK2-deficient mice (MK2KO). MK2-deficiency significantly reduced cell proliferation (BrdU-assay; expression of p53 and histone H3) and impaired migration (wound scratch assay) induced by P53 and MK2KO. Further, MK2-deficiency decreased migration of SMC (wound scratch assay) induced by PDGF and FCS (n=8, p<0.01). However, inflammation and cell proliferation processes known to be important for vascular remodeling and endothelial regeneration after vascular injury. Moreover, mechanical injury of the arterial wall results in a loss of the vessel protecting endothelial cell layer. The MAP kinase-activated-protein kinase 2 (MK2) regulates expression of inflammatory mediators, cell migration, and cell proliferation; processes known to be important for vascular remodeling and endothelial regeneration after vascular injury. Therefore, we hypothesized an important role of MK2 in vascular remodeling and endothelial regeneration after injury of the arterial wall.

Heart Failure: biomarkers and prognosticators / YIA Session: Basic Science 173

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790/173 by guest on 11 March 2019
thermore, employing endothelial cells isolated from WT and MKO2KO mice MK2-deficiency increased cell proliferation, expression of p-Rb and cyclinD1 as well as cell migration induced by endothelial growth medium (EGM) or FCS (n=3-5, p<0.05).

Conclusion: Deficiency of mitogen-activated proteinkinase activated proteinkinase 2 (MK2) prevents maladaptive vascular remodeling and promotes vascular regeneration after vascular injury.

Secretome of apoptotic peripheral blood cells (APOSEC) attenuates microvascular obstruction in a porcine acute myocardial infarction model: role of platelet aggregation and vasodilatation

K. Hoetzenecker1, A. Assinger1, M. Lichtenauer1, M. Mildner1, T. Schewe1, Z. Petrase1, C. Plass1, M. Gyogyoss1, I. Vol1, H. Anker1, S. Koleskik2

1 Christian Doppler Laboratory for the Diagnosis and Regeneration of Cardiac and Thoracic Diseases, Vienna, Austria; 2 Medical University of Vienna, Institute of Physiology, Vienna, Austria; 3 Medical University of Vienna, Department of Dermatology, Vienna, Austria; 4 University of Kaposvar, Kaposvar, Hungary;

Medical University of Vienna, Department of Internal Medicine II, Division of Cardiology, Vienna, Austria.

Early repulsion of the culprit coronary artery within a narrow time window has significantly improved early mortality after acute myocardial infarction (AMI). However, a lack of adequate repulsion at the microvascular level is often a limiting prognostic factor. Our group has recently found that paracrine factors secreted from apoptotic peripheral blood mononuclear cells (APOSEC) attenuate the size of AMI. The aim of this study was to determine the influence of APOSEC on microvascular obstruction (MVO) in a porcine AMI model. Cell culture supernatants derived from irradiated apoptotic peripheral blood mononuclear cells (APOSEC) were collected and injected intravenously after induction of AMI. MVO was determined by magnetic resonance imaging and cardiac catheterization. Platelet function and platelet-associated parameters were monitored in vitro and in vivo by means of ELISA, flow cytometry, aggregometry, and western blots. Effects of APOSEC on pathophysiology and coronary vascular tone were determined by ELISA, western blot and myographic experiments, respectively.

Treatment of AMI with APOSEC resulted in a significantly improved microvascular perfusion (Myocardial blush grade: 1.3±0.3 vs. 2.5±0.5, p=0.003) Platelet activation markers (P-selectin, CD40L, PF-4, TSP-1) were reduced in plasma samples, suggesting an anti-aggregatory capacity of APOSEC. This finding was confirmed in vitro by showing that activation and aggregation of both porcine and human platelets were significantly impaired by co-incubation with APOSEC, paralleled by vasodilator-stimulated phosphoprotein (VASP)-mediated inhibition of platelets. In addition, APOSEC evidenced a significant vasodilatory capacity of coronary arteries. HUVECs co-incubated with the compound significantly upregulated iNOS expression. Treatment of isolated coronary arterial segments with APOSEC resulted in a dilation of the vessels in a dose dependent manner (APOSEC from 5x10^-6 cells: 29% dilation; 1x10^-6 cells: 26%; 5x10^-7 cells: 34%). These findings were corroborated by in vivo data showing heightened vasodilatory mediators 40min after administration of APOSEC in the porcine AMI model (NO: VIP, PGII).

Our data give first evidence that APOSEC reduces the extent of MVO during AMI. This explains the improved long-term outcome after APOSEC treatment in AMI as previously described.

Vascular hyperglycemic memory is driven by p66Shc by protein kinase C β II (PKCβII) persisted after returning to normoglycemia. Sustained p66Shc upregulation and mitochondrial translocation were associated with continued ROS production, reduced NO bioavailability and apoptosis. We found that p66Shc gene overexpression was epigenetically regulated by promoter CpG hypomethylation and increased histone 3 (H3) acetylation. Indeed, pharmacological inhibition of H3 acetyltransferase restored basal expression levels of p66Shc. Furthermore, p66Shc-derived ROS production maintained PKCβII-dependent inhibitory phosphorylation of eNOS at Thr-495, leading to a detrimental vicious cycle despite restoration of normoglycemia. In vivo and in vitro silencing of p66Shc, performed at the time of glucose normalization, blunted ROS production and restored Ach-induced relaxation. Vascular apoptosis persisted even after intensive glycemic control with insulin whereas concomitant i.v administration of p66Shc siRNA abolished this event by limiting mitochondrial cytochrome c release and caspase 3 activation.

Conclusions: p66Shc is the key effector driving vascular hyperglycemic memory in diabetes. Our study provides molecular insights for the progression of diabetic vascular complications despite intensive glycemic control.

YOUNG INVESTIGATORS AWARDS SESSION: POPULATION SCIENCES

Obesity is associated with improved survival in patients with atherosclerotic heart disease

A. Azimi1, G.P. Torp-Pedersen1, M.C. Chart1, G.G. Gilsson1, L.J. Jensen1, H.T. Tilsted1, J.R. Ravkilde1, J.L. Lassen2, P.T. Thaysen3, L.T. Thuesen3,1 Gentofte Hospital - Copenhagen University Hospital, Heart Department, Hellerup, Denmark; 2 Odense University Hospital, Department of Cardiology, Odense, Denmark; 3 Aalborg Hospital of the Aarhus University Hospital, Department of Cardiology, Aalborg, Denmark; 4 Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark.

Purpose: We examined the influence of obesity on survival in patients with proven atherosclerotic heart disease to further examine the paradox that obesity may appear protective in patients with established cardiovascular disease.

Methods: A cohort study based on registry data from the Western Denmark Heart Registry (WDHR). We included all patients in WDHR with coronary atherosclerosis confirmed by coronary angiography from February 2000 to August 2011. Patients were divided into eight groups according to body mass index (BMI): Group 1: BMI < 18.5 kg/m²; group 2: 18.5 ≤ BMI < 23 kg/m²; group 3 (reference group) 23 ≤ BMI < 25 kg/m²; group 4: 25 ≤ BMI < 27.5 kg/m²; group 5: 27.5 ≤ BMI < 30 kg/m²; group 6: 30 ≤ BMI < 35 kg/m²; group 7: 35 ≤ BMI < 40 kg/m² and group 8: BMI ≥ 40 kg/m². Cox proportional hazard models were used to estimate the hazard ratios (HR). The models were adjusted for following variables: sex, age, prior heart surgery, prior PCI, smoking, diabetes, LVEF and prior MI, use of statins and antihypertensive drugs as well as degree of vessel disease.

Results: The study included 46,247 patients with mean age 66.5±11 years, 33,085 (72%) men. During the 11.6 years of follow-up 6,785 (15%) patients died. The highest incidence rate of mortality was equal to 115 death/1000 patient year (95% CI 100.5 -131.7) for the underweight (BMI < 18.50 kg/m²) and the lowest 29 death/1000 patient year (95% CI 24.77-34.1) for the pre-obese (27.5 ≤ BMI < 30 kg/m²). Regression multivariable analysis demonstrated that the risk was lowest among the pre-obese and increased with both lower and higher BMI (Fig. 1).

Figure 1. Hazard ratio for all-cause mortality

Conclusions: Patients with documented atherosclerotic heart disease that are overweight have improved survival compared with normal BMI. Underweight and severely obese patients have high mortality.
1037 Clustering of cardiovascular diseases in family members of young sudden cardiac death victims: a Danish nationwide cohort study

M.F. Ranthe1, B.G. Winkel2, E.W. Andersen1, B. Risgaard2, J.R. Mohlmann1, H. Bundgaard1, M. Melbye1, J. Thiel-Hansen1, H.A. Boyd3, Statens Serum Institut, Department of Epidemiology Research, Copenhagen, Denmark;4Rigshospitalet - Copenhagen University Hospital, Laboratory of Molecular Cardiology, Copenhagen, Denmark;5Rigshospitalet - Copenhagen University Hospital, Heart Center, Unit for Inherited Cardiovascular Diseases, Copenhagen, Denmark

Purpose: Descriptive studies have indicated clustering of cardiovascular diseases (CVDs) in families with victims of sudden cardiac death (SCD). These studies included highly selected cases often from tertiary referral centers and had no control groups. This population-based cohort study, aimed to prospectively describe the occurrence of CVDs in young relatives of young SCD victims, compared to the background population.

Methods: In Denmark, 2000-2006, all cases of SCD aged 1-35 years were identified. We compared the incidence of CVD in young persons related to those victims of SCD, with the background population in a follow-up study using Standardized Incidence Ratios (SIRs) to estimate relative risks.

Results: For 463 victims of SCD we identified a nationwide cohort of 1,591 first- and second-degree relatives aged <35 years, and followed for more than 7,000 person-years in 2000-2008. The observed number of CVDs were 32 and the expected number 34.5, corresponding to a SIR of 0.91 (95% CI 0.52-1.61). Type of CVD: Person-years Number of outcomes SIR (95% CI)

<table>
<thead>
<tr>
<th>Type of CVD</th>
<th>Person-years</th>
<th>Number of outcomes</th>
<th>SIR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Heart Disease</td>
<td>3270</td>
<td>3</td>
<td>0.91 (0.52-1.61)</td>
</tr>
<tr>
<td>Cardiomyopathies</td>
<td>3254</td>
<td>4</td>
<td>1.11 (0.76-1.71)</td>
</tr>
<tr>
<td>All Arrhythmias</td>
<td>3239</td>
<td>6</td>
<td>2.13 (1.06-2.98)</td>
</tr>
<tr>
<td>Ventricular Arrhythmias</td>
<td>3265</td>
<td>6</td>
<td>2.13 (1.06-2.98)</td>
</tr>
<tr>
<td>Other CVDs</td>
<td>3227</td>
<td>7</td>
<td>1.41 (1.26-1.58)</td>
</tr>
</tbody>
</table>

Conclusion: CVDs in young first-degree relatives co-aggregated strongly with SCD in families. These results may be useful for the development of recommendations regarding timing and content of cascade screening in families experiencing SCD in the young.

1039 Impact of everolimus-eluting stents on stent thrombosis as compared to conventional bare metal stents in patients with ST-segment elevation myocardial infarction: insights from the EXAMINATION trial

S. Brugalla1, M. Saba1, A. Cequeru2, A. Iniguez2, A. Serra2, R. Hernandez-Antolín1, V. Mainar1, M. Valgimigli1, G. VanEst5, P. Serruy5, A. L. Cardocillas Bautista, Hospital Clinico San Carlos, Madrid, Spain;3Rigshospitalet - Copenhagen University Hospital, Heart Center, Unit for Inherited Cardiovascular Diseases, Copenhagen, Denmark;5Rigshospitalet - Copenhagen University Hospital, Heart Center, Unit for Inherited Cardiovascular Diseases, Copenhagen, Denmark

Purpose: Second generation drug eluting stents have shown better performance as compared to first generation in terms of reduced clinical events, including stent thrombosis (ST). Nevertheless, few data are available about its safety in a STEMI all-comer population. We sought to investigate the incidence, predictors and clinical implications of ST occurring within 1 year after primary percutaneous coronary intervention (PCI) among patients with STEMI, randomized to everolimus eluting stent (EES) vs. cobalt-chromium bare metal stent (BMS).

Methods: The Examination trial is an all-comer prospective, randomized 1:1 controlled trial, assessing in patients with stable angina undergoing PCI, whether pre-treatment with intracoronary enalaprilat as compared with control patients (9.9 [2.7-19.0] ng/ml vs. 26.6 [6.3-60.5] ng/ml; p=0.035).

Conclusions: In patients with stable angina undergoing PCI, intracoronary infusion of enalaprilat improves microvascular function and protects from the occurrence of myocardial necrosis.

1041 Intracoronary enalaprilat to reduce microvascular damage occurring during elective percutaneous coronary intervention trial (Promicro trial): a randomized double-blind controlled study

F. Mangiacapra, A. Peace, L. Di Serafini, S.A. Pyxaras, J. Bartunek, E. Wytiefs, G.H. Heyndrickx, W. Wijns, B. De Bruyne, E. Barbatko. OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

Angiotensin converting enzyme (ACE)-inhibitors improve coronary flow and reduce ischemic events during percutaneous coronary intervention (PCI). However, the mechanisms leading to this protective effect are unknown. We aimed at assessing the effects of pre-treatment with intracoronary enalaprilat on coronary microvascular resistance (IMR) and coronary hyperconstricting responses as compared with SES in pigs in vivo, and intracoronary serotonin (10 and 100 nM) before and after enalaprilat infusion as compared with SES in pigs in vivo.

Results: For 463 victims of SCD we identified a nationwide cohort of 1,591 first- and second-degree relatives aged <35 years, and followed for more than 7,000 person-years in 2000-2008. The observed number of CVDs were 32 and the expected number 34.5, corresponding to a SIR of 0.91 (95% CI 0.52-1.61). Type of CVD: Person-years Number of outcomes SIR (95% CI)

<table>
<thead>
<tr>
<th>Type of CVD</th>
<th>Person-years</th>
<th>Number of outcomes</th>
<th>SIR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ischemic Heart Disease</td>
<td>3270</td>
<td>3</td>
<td>0.91 (0.52-1.61)</td>
</tr>
<tr>
<td>Cardiomyopathies</td>
<td>3254</td>
<td>4</td>
<td>1.11 (0.76-1.71)</td>
</tr>
<tr>
<td>All Arrhythmias</td>
<td>3239</td>
<td>6</td>
<td>2.13 (1.06-2.98)</td>
</tr>
<tr>
<td>Ventricular Arrhythmias</td>
<td>3265</td>
<td>6</td>
<td>2.13 (1.06-2.98)</td>
</tr>
<tr>
<td>Other CVDs</td>
<td>3227</td>
<td>7</td>
<td>1.41 (1.26-1.58)</td>
</tr>
</tbody>
</table>

Conclusion: CVDs in young first-degree relatives co-aggregated strongly with SCD in families. These results may be useful for the development of recommendations regarding timing and content of cascade screening in families experiencing SCD in the young.

1042 New generation biolimus A9-eluting stent suppresses coronary hyperconstricting responses and inflammation through rho-kinase pathway inhibition in pigs: comparison with a Sirolimus-Eluting Stent

K. Nishimya1, Y. Matsunoto1, J. Takahashi1, R. Tsuhrayu1, Y. Ito1, K. Ito1, H. Ishibashi-Ueda1, S. Yasuda1, H. Shimokawa1, T. Toboku University Graduate School of Medicine, Miyagi, Japan;2National Cerebral and Cardiovascular Center Hospital, Department of Pathology, Suita, Osaka, Japan;3National Cerebral and Cardiovascular Center Hospital, Department of Cardiovascular Medicine, Suita, Osaka, Japan

Purpose: 1st generation durable polymer coated drug-eluting stents (DES), such as sirolimus-eluting stent (SES), enhance coronary vasoconstricting and inflammatory responses. Biolimus A9-eluting stent (BES) has been developed as a new generation DES with a bioresorbable polymer from which biolimus A9, an analogue of sirolimus, is eluted. However, it remains to be elucidated whether new generation DES exert beneficial effects on coronary vasoconstriction and inflammatory changes. In the present study, we thus examined whether BES inhibits coronary vasoconstricting responses as compared with SES in pigs in vivo, and if so, whether Rho-kinase pathway (a central molecular pathway of coronary vasoconstriction) is involved.

Conclusions: In patients with stable angina undergoing PCI, intracoronary infusion of enalaprilat improves microvascular function and protects from the occurrence of myocardial necrosis.
Morphological characteristics by optical coherence tomography of ruptured neatherosclerotic plaques in patients with very late stent thrombosis
Erasmus Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, Netherlands

Purpose: Neatherosclerotic plaque rupture has recently emerged as a substrate for very late stent thrombosis (VLST). However, the morphological characteristics associated with neointimal rupture have not yet been determined in vivo. We investigated by frequency domain optical coherence tomography (OCT) the differences in morphological characteristics and stent-related factors in patients with VLST due to neointimal rupture (NR) and patients with VLST without rupture.

Methods: From 1/1/2009 to 31/1/2012, 29 patients underwent cardiac catheterization in our institution for VLST and underwent OCT assessment of the culprit stented segment following thrombus aspiration. Neointimal rupture was identified as a fibrous cap disruption with cavity formation inside the stent and adjacent thrombus. Criteria used in nativeatherosclerosis were used for neointima characterization. Lipid content of the neointima was measured as a percentage of vessel circumference. A neointima with lipid content in >90% was characterized as lipid-rich. In cases where a fibrous cap could be identified over a lipid necrotic core, fibrous cap thickness (FCT) was measured. The presence of calcifications, neovascularization or dense macrophage infiltration was also assessed. Stent struts were assessed for coverage and malapposition. Stents with >30% uncovered struts were considered uncovered, while struts with >5% malapposed struts were considered malapposed.

Results: Median interval from the initial implantation was 5.5 years (range 2-16). OCT revealed 14 cases with VLST due to NR. A fibrous cap was identified in 13 cases with NR and in 9 cases without NR. OCT and lipid content were lower in the NR group compared to the non-NR group (FCT: 47.2±25μm vs. 66.2±35μm, p=0.001; lipid content: 254±108µg/m2 vs. 105±101µg/m2, p<0.01). Lipid-rich plaque was more often in the NR group (92.9% vs. 46.7%, p<0.05). The NR group had a trend for higher macrophage infiltration and calcifications compared to the non-NR group (macrophage infiltration in the NR group was 64.3% vs. 33.3%, p>0.05; calcifications: 42.9% vs. 13.3%, p<0.01). There were no differences in the incidence of neovascularization between the two groups (14.3% vs. 6.7%, p=0.60). There was a significantly less incomplete coverage and malapposition in the NR group (incomplete coverage: 18.8% vs. 86.7%, p=0.01; malapposition 0% vs. 53.5%, p<0.05).

Conclusions: Neointimal rupture is an important mechanism of very late stent thrombosis, occurring more frequently in lipid-rich neointima covered by a thin fibrous cap. This mechanism seems to be independent of incomplete coverage or stent malapposition.

Endothelial progenitor cells, microvascular obstruction and left ventricular remodeling in patients with ST-elevation myocardial infarction undergoing primary percutaneous intervention
Catholic University of the Sacred Heart, Rome, Italy

Background: Endothelial progenitor cells (EPC) are bone marrow derived elements with regenerative properties, known to be released in ST elevation myocardial infarction (STEMI). We assessed EPC in the intracoronary and peripheral blood during primary percutaneous coronary intervention (pPCI) for STEMI and pPCI peripheral levels at one year follow up, and correlated them with angiographic reperfusion and with left ventricular remodeling (LVR).

Methods: In 78 STEMI patients undergoing pPCI, blood samples were sequentially drawn from the aorta and the culprit coronary artery for cytofluorimetric EPC (CD34+CD45dimKDR+ cells) detection. Myocardial blush grade (MBG) was calculated at the end of pPCI. In 40 of the 78 enrolled patients echocardiographic follow up was completed at one year, and peripheral EPC levels were re-measured. LVR was defined as an increase in end diastolic volume > 20% compared to baseline.

Results: EPC levels (expressed as absolute percentage of cells per total number of cytometric events) during pPCI were significantly higher in the intracoronary than in the aortic blood samples (0.043% (0.004-0.154) vs 0.006% (0.001-0.083) p<0.001). Both intracoronary and aortic EPC were inversely related to MBG (p=0.01 for linear trend). Peripheral EPC levels at one year follow up were significantly lower in patients with LVR (0.001% (±0.001%) vs. 0.003% (±0.002% (p=0.01)). At multivariate analysis, EPC levels at follow up and post pPCI MBG were independently associated with a lower risk of LVR (OR 0.10 CI 0.01-0.94, p=0.02 and OR 0.21 CI 0.05-0.89, p=0.03, respectively).

Conclusion: A rapid intracoronary EPC recruitment takes place in the earlier phases after STEMI onset, possibly in the attempt to overcome ongoing microvascular dysfunction. The relationship of peripheral EPC levels at one year follow up with LVR suggests their role in preserving myocardial integrity.

YOUNG INVESTIGATORS AWARDS SESSION: THROMBOSIS

Chronic kidney disease in atrial fibrillation: risks of stroke and bleeding and the effect of antithrombotic treatment
J.B. Olesen1, G.Y.H. Lip2, A.-L. Kampert3, K. Hommel3, L. Kobr3, D.A. Lane1, J. Lindhardt1, G.H. Gislason1, C. Torg-Pedersen1.
1Copenhagen University Hospital Gentofte, Department of Cardiology, Copenhagen, Denmark; 2University of Birmingham Centre for Cardiovascular Sciences, Birmingham, United Kingdom; 3Rigshospitalet - Copenhagen University Hospital, Copenhagen, Denmark

Purpose: Both atrial fibrillation (AF) and chronic kidney disease (CKD) increase the risk of stroke and thromboembolism. However, the risk of stroke/thromboembolism and bleeding associated with CKD in AF patients has not been thoroughly investigated, nor has the effect of antithrombotic treatment in such patients.

Methods: From nationwide Danish registries, we identified all patients discharged with non-valvular AF between 1997-2008. The risk of stroke/thromboembolism and bleeding associated with non-end-stage CKD and end-stage CKD (i.e. patients in renal replacement therapy [RRT]), was estimated using Cox regression analyses. Furthermore, the effect of warfarin and aspirin treatment was investigated in CKD (non-end-stage and RRT) patients, and compared to patients with no renal disease.

Results: We included 132,372 patients, of these 3,587 (2.7%) had non-end-stage CKD and 901 (0.7%) were on RRT at inclusion. During follow-up, 4,538 (3.6%) developed non-end-stage CKD and 477 (0.4%) commenced RRT. The risk of stroke/thromboembolism was increased in both non-end-stage CKD patients (hazard 1.34, 95% CI 1.26-1.44) and RRT patients (1.83, 1.57-2.14); this risk was significantly decreased with warfarin (0.76, 0.64-0.91) but not with aspirin. The risk of bleeding was increased in both non-end-stage CKD patients (2.24, 2.10-2.38) and RRT patients (2.70, 2.38-3.07). Among CKD patients, this risk was significantly increased with both warfarin (1.33, 1.16-1.53) and aspirin (1.17, 1.02-1.34).

Conclusions: CKD increased the risk of stroke/thromboembolism and bleeding in AF patients. Warfarin decreased the risk of stroke/thromboembolism in CKD patients, while both warfarin and aspirin increased the risk of bleeding.

Figure 1. Risk with chronic kidney disease
Thrombolytic therapy of prosthetic heart valve thrombosis in pregnancy with low dose slow infusion of t-PA (TROIA-PREG)

A.E. Oguz, B. Cakal, S. Gunduz, M.A. Astarloa, M.O. Gursuy, F. Kaynam, M. Kalik, S. Karakurum, M. Yildiz, S. Ozkan, Karatay Kasımpaşa Heart Education and Research Hospital, Department of Cardiology, Istanbul, Turkey

Purpose: Prosthetic valve thrombosis (PVT) during pregnancy requires urgent therapy but there is still controversy about how to treat this life-threatening complication. Cardiac surgery in pregnancy is reported to be maternal mortality and morbidity of 6% and 24% and fetal mortality and morbidity of 9% and 30%, respectively. Thrombolytic therapy (TT) has been rarely used in pregnancy with only 32 cases of PVT reported in the literature so far. The aim of this study is to evaluate safety and efficacy of administration of t-PA for PVT during pregnancy.

Methods: Transthoracic echocardiography guided TT was administered to 22 consecutive patients with PVT in 27 different episodes (mean age: 29; gestation: 15, nonobstructive: 12) between 2005 and 2012. The principal agent used was t-PA (25 mg, 6-hours without bolus, repeat if needed). Anticoagulation with i.v unfractionated heparin was withheld during TT.

Results: The success rate of TT was 100%. The rate of abortion (15%) after TT was comparable to that of general population. One patient had placental hemorrhage with pretum live birth occurred at 30th week. None of live born children suffered a permanent defect. The average dose of t-PA used was 45±22 mg.

Conclusion: Low dose, slow infusion of t-PA with repetition as needed without bolus provides effective and safe thrombolysis in both mother and fetus. TT can be considered as first-line therapy in pregnant complicated with PVT.

Critical role for PI3K/p110alpha in arterial thrombosis and vascular smooth muscle cell activation: implications for drug-eluting stent design

E.W. Hoy1, A. Akhmedova2, T.F. Luerscher1, F.C. Tanner1, 1University Hospital Zurich, Zurich, Switzerland; 2University of Zurich-Inchtel, Department of Anatomy and Physiology, Cardiovascular Research, Zurich, Switzerland

Background: Impaired neoinnervation and stent thrombosis remain safety concerns associated with the use of drug-eluting stents (DES) despite a reduction in restenosis rates. Phosphoinositol-3-kinase p110alpha (PI3K/p110alpha) controls cellular processes such as proliferation and chemotaxis and thus represents an emerging drug target. However, its effect on arterial thrombus formation and activation of vascular smooth muscle (VSMC) as well as endothelial cells (EC) is not known.

Methods: PI3K/p110alpha was inhibited by treatment with the small molecule inhibitor PIK 75 or, alternatively, a specific siRNA. Arterial thrombus studies were performed in a murine carotid artery photochemical injury model. Proliferation and migration of VSMC and EC were assessed by cell number and Boyden chamber, respectively. Endothelial senescence was evaluated by β-galactosidase assay, endothelial dysfunction by organ chambers for isometric tension recording as well as Western blots for analysis of eNOS, TF, and PAI-1 expression.

Results: Male C57Bl6 mice were either treated with PIK 75 (10 mg/kg/d for 7 days) or vehicle. Arterial thrombus formation was delayed in mice treated with PIK 75 as compared to controls (n=8, p<0.005). PIK 75 impaired arterial expression and activity of TF and PAI-1 as well as NFκB activity (n=8, p<0.05); in contrast, plasma clotting and tail bleeding times did not differ (n=8, p=NS). In human vascular smooth muscle and endothelial cells, PIK 75 inhibited expression and activity of TF as well as protein levels as compared to controls (n=8, p<0.05). Furthermore, inhibition of PI3K/p110alpha with PIK 75 or a specific siRNA selectively impaired proliferation and migration of VSMC while sparing EC completely. Treatment with PIK 75 did not induce endothelial senescence nor inhibit eNOS expression or endothelium-dependent relaxations. In contrast to PIK 75, both rapamycin and siRNA inhibited arterial proliferation and migration; moreover they induced expression of TF and PAI-1.

Conclusions: PI3K/p110alpha inhibition delays arterial thrombus formation via inhibition of TF and PAI-1. In addition, PI3K/p110alpha inhibition impairs proliferation and migration of VSMC. PI3K/p110alpha inhibition exhibits a very interesting profile of action and may offer new options for DES design.

An alternative pathway for hypofibrinolysis in type 2 diabetes: the role of complement C3

1University Hospital Aachen, RWTH, Internal Medicine I, Cardiology, Pulmonology & Vascular Medicine, Aachen, Germany; 2University of Leeds, Leeds, United Kingdom; 3University of Edinburgh, Edinburgh, United Kingdom; 4Western General Hospital, Metropolitan Unit, Edinburgh, United Kingdom; 5Bern University Hospital, Bern, Switzerland

Purpose: Plasminogen activator inhibitor (PAI)-1 has been regarded as the main antifibrinolytic protein in diabetes but recent work indicates that complement C3, an inflammatory protein, directly modulates fibrinolysis in type 1 diabetes (T1DM).

Therefore, we investigated the role of complement C3 in fibrinolysis in a large cohort of T2DM subjects.

Methods: Fibrin clot lysis was determined in 875 patients enrolled on the Edinburgh type 2 diabetes study using a turbidimetric assay. Plasma levels of complement C3, C-reactive protein (CRP), PAI-1 and fibrinogen were analysed by ELISA.

Results: Clot lysis time showed a highly significant correlation with C3 and PAI-1 plasma levels (r=0.25, p<0.001 and r=0.15, p<0.0001; respectively). In contrast, a relatively weak correlation was detected with CRP (r=0.08, p=0.02) and fibrinogen (r=0.08, p=0.01). Plasma levels of C3, CRP, fibrinogen or PAI-1 did not differ in the presence of previous history of myocardial infarction or cerebrovascular disease. Plasma levels of all four proteins correlated with body mass index, but only fibrinogen showed an interaction with age and duration of diabetes. In a regression model involving these proteins, C3 was a predictor of lysis time [predictive value for 0.1 mg/ml change in plasma levels 14.4 (95% CI 7.9, 21.0) p<0.001], as was PAI-1 (predictive value for 0.1 mg/ml change in plasma levels 8.2 (4.2, 12.1; p<0.001) with a smaller effect shown for 0.1 mg/ml change in fibrinogen levels [5.3 (0.10-10.5; p=0.049] and none detected for CRP [-2.5 (-9.7, 4.8; p=0.50].

No correlation was demonstrated between C3 and PAI-1 plasma levels indicating the two proteins affect different pathways in fibrin clot lysis. In multivariable analysis, drug therapies failed to predict C3 plasma levels, although a trend was observed in men towards a positive and negative association with sulphonylurea and antiplatelet therapy, respectively.

Conclusions: C3 is at least as strong as PAI-1 at predicting fibrin clot lysis in subjects with T2DM. Therefore, future studies should analyse C3 plasma levels as a surrogate marker of fibrinolysis potential in this population.

Multivessel primary percutaneous coronary intervention in acute myocardial infarction complicated by cardiogenic shock and resuscitated cardiac arrest: friend or faux?

D.M. Mylotte1, M.C. Morice1, H. Eltchaninoff2, G. Garot1, Y. Louvard3, T. Lefeuvre4, P. Garlot5, 1Cardiovascular Institute Paris-Sud (ICPS), Massy, France; 2Hôpital Charité de Berlin, Berlin, Germany; 3Hospital Centre Regional de Reims, Reims, France

Purpose: Survival in patients with ST-segment elevation myocardial infarction (STEMI) complicated by cardiogenic shock (CS) and resuscitated cardiac arrest (CA) is poor, despite primary percutaneous coronary intervention (PCI). Most of these patients have multivessel (MV) coronary disease, however the safety and efficacy of primary MV PCI is unknown. We sought to compare outcomes between primary MV and culprit-only PCI in these patients.

Methods: Between 1998 and 2010, we prospectively collected data from consecutive STEMI patients in 5 French centres. The study population was derived from 11,530 patients admitted with STEMI, among whom 2.3% (n=266) were eligible for study inclusion, having presented with both resuscitated CA and CS. The primary end point was 6-month survival.

Results: The mean age was 62.1±13.6 years. CAs occurred most commonly at home (35.4%) and the median interval to first responder CPR was 5.0 [2.0, 14.0] minutes. Ventricular fibrillation was the initial arrhythmia in 60.2%, and the baseline ECG demonstrated STEMI in 86.5%. Pre-hospital thrombolysis was performed in 14.6%. On angiography, most patients had MVD (63.5%). Baseline characteristics were similar in patients undergoing either culprit-only (60.9%) or MV (39.1%) PCI. Six-month survival was significantly higher in patients undergoing MV PCI compared to those undergoing culprit-only PCI (43.9% versus 20.4%, P=0.0017). A reduction in the composite of recurrent CA and shock death (P=0.024) mediated this difference. On multivariate analysis, MVP was associated with improved 6-month survival (OR 3.19; 95% CI, 1.15-6.45, P=0.005).

Figure 1. Six month survival

Conclusions: In STEMI patients with MV disease complicated by CS and CA, primary MV PCI appears to improve outcomes compared to culprit-only PCI. Randomized trials are required to verify these results.
Tertiary centres have improved survival compared to other hospitals in the Copenhagen area after out-of-hospital cardiac arrest

H. Soeholm 1, K. Wachtel 2, S. Loumman Nielsen 2, J. Bro-Jeppesen 1, F. Pedersen 1, M. Warscher 4, S. Boesgaard 1, J. Elfer Möller 1, C. Hassager 1, J. Kjaergaard 1, Righospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark; 2Copenhagen University Hospital Gentofte, Department of Cardiology P, Gentofte, Denmark; 3Righospitalet - Copenhagen University Hospital, Dept. of Anaesthesia, Centre of Head & Orthopaedics, Copenhagen, Denmark; 4Righospitalet - Copenhagen University Hospital, Heart Centre, Department of Anaesthesia, Copenhagen, Denmark

Purpose: Out-of-hospital cardiac arrest (OHCA) has been reported to carry varying mortality. It remains unclear whether it is caused by intrinsic factors or due to in-hospital care. The aim of this study is to compare 30-day and long-term mortality after OHCA at tertiary heart centres vs. non-tertiary hospitals.

Methods: 1,234 consecutive patients treated by the Copenhagen mobile emergency care unit (MECU) with either return of spontaneous circulation (ROSC) or on-going resuscitation at hospital arrival were included (2002-2010). Patients are transported to the nearest hospital or to a tertiary heart centre for acute coronary angiography if ECG shows ST-segment elevations. To reduce referral bias patients with ST-elevations were excluded (n=198).

Results: 30-day mortality was 56% vs. 76% (Fig.1, left) and long term mortality was 76% vs. 94% (Fig.1, right) for tertiary and non-tertiary hospitals, respectively (p<0.01, p=0.01). Multivariable analysis showed that admission to a non-tertiary hospital was independently associated with increased risk of death (HR=1.27 [95%CI: 1.06-1.53, p=0.009]). Longer time to ROSC, age and asystole or pulseless electric activity as initial arrhythmia are significant predictors of death, whereas bystander CPR, witnessed cardiac arrest, and acute coronary angiography were independent predictors of lower 30-day mortality. Exclusion of patients with on-going resuscitation at admission resulted in HR=1.37 [1.14-1.65], p<0.001. A matched pair propensity score analysis of 574 patients confirmed the results of the proportional hazard analysis HR=1.35 (1.12-1.63), p=0.002.

Conclusion: Admission to tertiary centres with 24-hour cardiology service and invasive cardiac interventions is associated with lower mortality rates after OHCA compared with non-tertiary hospitals.

Women with heart failure and diabetes are at increased risk for mortality compared to men with and without diabetes

L. Johansson 1, M. Edner 1, P. Nasman 2, U. Dahlstrom 2, L. Ryden 1, A. Norhammar 1, 1Karolinska Institute, Department of Medicine, Cardiology Unit, Stockholm, Sweden; 2Royal Institute of Technology (KTH), Stockholm, Sweden; 3Linköping University, Department of Medical and Health Sciences, Div of Cardiovascular Medicine, Linkoping, Sweden

Purpose: Heart failure is reported as a common complication in women with DM, but information on long-term outcome in such patients from an all day practise population is sparse.

Methods: Patients included in the Swedish Heart Failure Registry (RiksSvikt) between the years 2004-2011 were followed for mortality until Sept 30, 2011 (median 22.5 months). Long-term prognosis, differences in background and heart failure characteristics were analysed in women and men with and without DM.

Results: Among 36397 patients 24% had type 2 DM and 39% were women. In patients with DM, women compared to men were older (77 vs. 73 yr) with more frequent hypertension (63 vs. 58%) and kidney dysfunction (clearance <30 ml/min/1.73m² vs. 20%) but more often an EF >50% (33 vs. 16%). Compared to men, women with DM received less of evidence based drug treatment (ACE-i; 64 vs. 55%, statins: 61 vs. 49%) and revascularisation (38 vs. 23%). Comparing women, those with DM more often had hypertension (63 vs. 48%) and ischemic heart disease (54 vs. 40%). The Figure shows Kaplan Meyer curves for mortality in the four groups. The unadjusted OR (95% CI) for mortality was 1.23 (1.13-1.34) in women compared to men with DM and 1.37 (1.27-1.48) in women with compared to men without DM. After adjustments for background characteristics these ORs were 0.89 (0.79-0.99) and 1.78 (1.60-1.98) respectively. In ages <65 yr, OR for women vs. men with DM was 0.92 (0.79-1.08) and for women with DM vs. men without DM 2.66 (1.99-3.57).

Conclusion: Women with heart failure and DM are at an especially high mortality risk partly due to higher age and co-morbidities such as renal dysfunction. However incomplete drug treatment and lack of revascularisation are important contributors that are possible to improve.
Conclusion: In a real-life chronic heart failure population renal function worsens in the early period of treatment optimization, however it remains stable on long term thereafter. In patients with severe renal dysfunction therapeutic changes may significantly improve renal function.

NURSING/ALLIED PROFESSIONAL INVESTIGATOR AWARD

1062 Does refusal of Chronic Heart Failure management equal to usual care? Results of the which intervention is most cost-effective and consumer friendly in reducing hospital care? (Which?) Trial

P.J. Newton1, P.M. Davidson1, P. Macdonald1, S. Stewart2 on behalf of Which? Trial Investigators. 1University of Technology Sydney, Centre for Cardiovascular & Chronic Care, Sydney, Australia; 2St. Vincent's Hospital Sydney, Australia; 3Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Purpose: Although chronic heart failure management programs (CHF-MPs) are the gold-standard for post discharge management of predominantly old and fragile patients with CHF, their cost-effectiveness and key components of intervention are still the subject of debate. This study examines the results of the WHICH? trial. The WHICH? trial looked at the effectiveness of a protocolized education program (in the waiting area) versus usual care (at the time of discharge) in patients who had been discharged from hospital for treatment of CHF. They compared the total cost and the patient satisfaction with the education program versus usual care. The study was completed over a 6 month period, adjusting for pre-existing differences between the groups.

Methods: The WHICH? trial randomized 280 patients with CHF to two forms of CHF-MP as part of a multicentre, head-to-head trial of home versus clinic-based (HBI and CBI) post-discharge management. All patients were subject to comprehensive baseline profiling and followed-up for a minimum of 18 months. The primary endpoint was event-free survival from all-cause mortality and hospitalization. Pre-specified secondary endpoints included rate and type of hospitalization, related hospital stay and an economic analysis of health care costs. In this analysis, we were specifically interested in the rate of refusal (post randomization) and the patients who refused management had worse outcomes (in essence mimicking ‘usual care’ in historical trials).

Results: Patients who refused management via a CHF-MP are at high risk for poor health outcomes.

Conclusions: Patients who refuse management via a CHF-MP are at high risk for poor health outcomes.

1063 Type D (distressed) personality predicts impaired health status in patients presenting with chest suggestive of an acute coronary syndrome

K. Siebens1, H. Miljøen2, S. De Geest3, B. Drew4, C. Vrints2, J. Denollet5. 1Catholic University of Leuven, Center for Health Services and Nursing Research, Leuven, Belgium; 2Antwerp University Hospital, Edegem, Belgium; 3University of Basel, Institute for Nursing Science, Basel, Switzerland; 4Department of Physiological Nursing, School of Nursing, University of California, San Francisco, United States of America; 5Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Objective: Improving health status is challenging in patients with chest pain. We examined the persistent effect of Type D (distressed) personality on health status was examined over a 6-month period, adjusting for intervention group, diagnosis type (cardiac vs. non-cardiac), age, sex and heart failure.

Methods: 241 patients with symptoms suggestive of an acute coronary syndrome admitted to a chest pain unit of a university hospital were included in a pre-post quasi-experimental study to evaluate the implementation of a critical pathway. They completed the 14-item Type D Scale (DS14), the EuroQol (EQ-5D), a Visual Analogue Scale (VAS) and the Hospital Anxiety and Depression Scale (HADS) during admission and at 1 and 6 months follow-up to assess Type D personality, quality of life, anxiety/depression, respectively. The effect of Type D personality on health status was examined over a 6-month period, adjusting for pre-existing differences between the groups.

Conclusion: Type D personality had a persistent, deleterious effect on quality of life, anxiety and depression in patients presenting with chest pain suggestive of an acute coronary syndrome. Future efforts could be directed to the modification of maladaptive coping strategies and emotional reactions in chest pain patients with a Type D personality.

1064 Quality of life and physical capacity alter long-term right ventricular pacing in young adults with congenital atrioventricular block

K.R. Silva1, R. Costa2, R.M. Oliveira Jr3, M. Martellini Filho2, M.S. Lacerda4, A. Huang5, M.B. Rossi3, W. Mathias Jr4, R. Pietrobon5, N.A.G. Stolf6. 1Duke University Medical Center, Durham, United States of America; 2Heart Institute (InCor)/University of Sao Paulo Medical School, Sao Paulo, Brazil

Background: Although several studies have demonstrated the deleterious consequences of chronic right ventricular (RV) pacing on ventricular function and synchronicity, its effects on health-related quality of life (HRQOL) and physical capacity remains uncertain.

Objective: To evaluate the effect of RV pacing on HRQOL and physical capacity of children and young adults with congenital complete atrioventricular (AV) block.

Methods: Fifty consecutive patients with permanent RV cardiac pacing due to congenital AV block and under clinical follow-up for more than one year were enrolled in this study. Right ventricular ejection fraction and right ventricular pacing were assessed with the Short Form-36 Health Survey (SF-36) and Child Health Questionnaire (CHQ-PF50). Physical capacity was tested by the 6-minute walk distance test (6MWD).

Results: The scores for each domain and the distance performed at the 6MWD test were compared with demographic and clinical characteristics of patients, using the Student’s t-test and Qui-square test.

Conclusions: The results of this analysis indicated that chronic RV pacing did not affect the HRQOL and physical capacity of young patients. Female gender, DDD pacing mode (0.008) and the presence of hypertension (0.031) were associated with worse quality of life scores. The average distance performed at the 6MWD test was 677.2 meters (454.5 to 852.6). The 6MWD showed significant association with age (p=0.004), normal ventricular function (p<0.001) and the absence of cardiovascular drugs use (p=0.018).

BEST ABSTRACTS FROM ESC AFFILIATED CARDIAC SOCIETIES

1136 Pressure points in primary care: a study of blood pressure in 532,050 primary care patients (2005 to 2010)

M.J. Carrington, S. Stewart. Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Purpose: As in many countries, the prevalence of elevated blood pressure (BP) levels in the Australian population has decreased between 1980 to 2000. However, as in other countries, there is a paucity of contemporary data in the primary care setting.

Methods: Data from a national longitudinal patient-based database of demographic (physician), clinical, pathology and prescription information was collected by 732 primary care physicians located in metropolitan and regional areas across Australia between 2005 to 2010. Results: A total of 532,050 patients (55% women) had a BP measurement recorded at least once. At first presentation, mean BP levels remained stable across the 6 years of study data at an average of 129±17/79±11 mmHg and 36% of patients had hypertension (>140/90 mmHg and/or taking antihypertensive medication). Overall, BP was higher in men than women (132±17/79±11 mmHg vs 127±18/77±11 mmHg) and there were 3-fold more young adult men
Clinical benefit of percutaneous coronary intervention in early latecomers with acute ST-elevation myocardial infarction

D.S. Sim1, M.H. Jeong1, Y.K. Ahn1, Y.J. Kim2, G.C. Chae3, C.J. Kim4, M.G. Cho1, S.W. Rha1, J.H. Baek1, K.B. Seung2, Chonnam National University Hospital, Gwangju, Korea; Republic of; 2Yeungnam University Hospital, Daegu, Korea, Republic of; 3Kyungpook National University Hospital, Daegu, Korea, Republic of; 4Kyung Hee University Hospital, Seoul, Korea, Republic of; 5Chungbuk National University Hospital, Cheongju, Korea, Republic of; 6Korea University Guro Hospital, Seoul, Korea, Republic of; 7Konyang University Hospital, Daejeon, Korea, Republic of; 8Catholic University Hospital, Seoul, Korea, Republic of

Objectives: We evaluated the efficacy and optimal timing of percutaneous coronary intervention (PCI) in early latecomers with acute ST-elevation myocardial infarction (STEMI).

Background: Clinical benefit of PCI is controversial in stable patients with STEMI presenting between 12 and 72 hours after the symptom onset.

Methods: Employing data from the Korea Acute Myocardial Infarction Registry, we analyzed 2,640 stable STEMI patients with symptom-to-door time between 12 and 72 hours. Patients with cardiac arrest, ventricular arrhythmia, cardiogenic shock, heart failure, (Killip class III or IV), fibrinolysis, or urgent PCI during initial conservative treatment were excluded. Patients were divided into PCI group (n=2,185) and medical treatment group (n=455). PCI group was further divided into two subgroups: early PCI (n=1,083; median door-to-balloon time=6.5 hours) and delayed PCI (n=1,102; median door-to-balloon time=42.6 hours). Twelve-month clinical outcome was compared, with composite of death and MI as the primary endpoint.

Results: Patients in the PCI group were more often male and smokers; and more likely to have anterior MI with higher cardiac troponin, and history of MI, PCI, heart failure, stroke, and peripheral vascular disease. Patients receiving medical treatment were older and more often had renal dysfunction. After adjustment for confounders by propensity score methods, PCI group had lower mortality (2.2% vs. 2.9%; 0.95 CI: 0.58-1.58; P=0.001) at 12-month follow-up.

Conclusion: In stable patients with STEMI presenting 12 to 72 hours after symptom-onset, PCI was associated with significant improvement in 12-month clinical outcome. The optimal timing of PCI remains to be determined.

The association between clinical symptomatic hypoglycemia with cardiovascular events in type 2 diabetes: A nested case control study in nation-wide representative population

H. Pai Feng1, S.H. Sung1, J.S. Yeh1, H.M. Cheng1, W.L. Chen1, S.Y. Chuang1, 2Taipei Veterans General Hospital, Taipei, Taiwan; 2Taipei Medical University Municipal Wang-Fang Hospital, Taipei, Taiwan; 3National Health Research Institutes, Taiwan, India; 4National Health Research Institutes, Taiwan, India

Background: Hypoglycemia was already known to be associated with serious health outcomes. Previous evidences were all derived from clinical trials or patient database with other specific admission cause. How is the consequence of those clinically treated type 2 diabetes patients who had hypoglycemia episode experiences is unknown?

Methods: The study population was comprised of 76,987 type 2 diabetic mellitus patients identified from the “National Health Insurance Research Database” released by the Taiwan National Health Research Institutes between 2000-2009. We designed a nested case control cohort, which was consistent of hypoglycemic type 2 diabetes patients with randomly selected and matched type 2 diabetes patients without hypoglycemia. We investigated the relationship between hypoglycemia and cardiovascular events including stroke, coronary heart disease, cardiovascular events, and all cause of hospitalization.

Results: There were total 2,641 hypoglycemic events (589 defined by inpatient and 2,052 defined by outpatient) from 76,986 type 2 diabetes mellitus patients. The incidence risk of hypoglycemia was 3.43% (2.641/76,986). Women had higher risk of hypoglycemia than men (1.98% vs. 1.45%). Both in the mild and severe hypoglycemia cases have higher percentage of co morbidity, including hypertension, renal diseases, cancer, stroke and heart disease. Hypertension (HR = 1.74; 95% confidence intervals: 1.58-1.92), renal disease (2.96; 2.57-3.40), cancer (2.37; 1.94-2.91), stroke (2.79; 2.35-3.29), and coronary heart disease (1.81; 1.52-2.15) were independently associated with hypoglycemia. Those diabetes patients with hypoglycemia had significantly higher risk of cardiovascular events in clinical treatment periods in multivariate models. Even after propensity score adjusted model, mild and severe hypoglycemia still have around 1.94 (1.71-2.19), 2.23 (2.00-2.49) higher relative risk for CVD and all cause hospitalization.
respectively. Around 70% of hypoglycemic subjects experienced admission of any cause in the following first year.

**Conclusion:** Symptomatic hypoglycemia, both clinically mild and severe, were associated with an increased risk for cardiovascular and all-cause hospitalization. The adverse events after hypoglycemia are most frequently occurred in the following first year. Clinically, we should aggressively treat those hypoglycemic episodes accompanied type 2 diabetes patients and prevent their immediate and further clinical adverse events.

---

**Glycosylated hemoglobin A1c (HbA1c) in non-diabetic patients: an independent predictor of coronary artery disease and its severity**

N. Garg, N. Mooarith, A. Kappor, S. Tewari, S. Kumar, P.K. Goel. Sanjay Gandhi PG Institute of Medical Sciences, Lucknow, India

**Purpose:** Elevated glycosylated hemoglobin A1c (HbA1c) is associated with increased risk of atherosclerosis and cardiovascular mortality in diabetic patients. The association between HbA1c and cardiovascular risk is inconsistent in non-diabetic subjects. In the present study, we examined the association between HbA1c and presence & severity of angiographically proven coronary artery disease (CAD) in non-diabetic subjects.

**Methods:** Consecutive 1997 non-diabetic patients undergoing coronary angiography over last one year were included. All patients underwent haemogram, biochemical and HbA1c measurements. Significant CAD was defined as ≥50% stenosis in one major vessel and complex CAD was assessed by SYNTAX score. The study population was divided in 4 quartiles on the basis of HbA1c levels (<5.5%, 5.5-5.7%, 5.8-6.1%, >6.1%). Statistical analysis was done to compare the differences among the four groups. Logistic regression analysis was done to determine the factors predicting the presence, severity and complexity of CAD.

**Results:** Mean age was 56.7±10.6 years and 82.7% were males. Overall 243 (21.3%) patients had normal coronaries or insignificant CAD. With increasing HbA1c levels, there was significant increase in the prevalence of CAD. Number of vessels involved, triple vessel disease, coronary calcium, chronic total occlusions, left main disease and left ventricular dysfunction. SYNTAX score had a strong positive correlation with rising HbA1c (mean SYNTAX score in four quartiles was 9.9±12.2, 11.6±11.8, 12.6±12.6 and 15.8±12.2 respectively). There was a linear correlation with HbA1c levels and prevalence of significant CAD. Compared to the patients with HbA1c <5.5%, the risk of significant CAD in other quartiles was 1.8 times (OR 1.8, 95% CI 1.2-2.7, p < 0.003), 2.7 times (OR 3.7, 95% CI 2.3-5.9, p < 0.001), and 5.2 times (OR 5.2, 95% CI 3.3-8.3, p < 0.001) higher respectively. On multivariable analysis, age, male gender, smoking, serum creatinine levels, left ventricular dysfunction, serum LDL levels and HbA1c levels emerged as independent predictors of significant CAD [OR 2.7 (95% CI 1.9-3.7), p < 0.001]. Patients with impaired glucose tolerance (HbA1c ≥5.7%) were at significantly higher risk of having CAD when compared with nondiabetics (HbA1c <5.5%).

**Conclusions:** In the non-diabetic subjects, HbA1c levels strongly correlate with significant CAD independent of conventional cardiovascular risk factors. It also strongly correlated with severity and higher SYNTAX score. HbA1c measurement can therefore be utilized as an independent predictor of CAD in non-diabetic subjects.

---

**Renal Denervation in Hypertension**

M. D. Esser1, H. Krum2, M. P. Schlaich3, R. E. Schmieder4, M. Boehm5, P. Sobotta5, 1Baker ID Heart and Diabetes Institute, Melbourne, Australia; 2Monash University, Melbourne, Australia; 3University of Erlangen-Nuremberg, Department of Nephrology and Hypertension, Erlangen, Germany; 4Saarland University Hospital, Homburg, Germany; 5Medtronic, Inc., Mountain View, California, United States of America

**Purpose:** Catheter-based renal sympathetic denervation (RDN) has been shown to reduce blood pressure (BP) in patients with resistant hypertension (systolic BP ≥160 mm Hg while receiving optimal doses of ≥3 antihypertensive medications).

**Methods:** Eligible patients were randomized 1:1 to receive RDN plus antihypertensive medications or antihypertensive medications alone. Exclusion criteria included an eGFR <45 mL/min and type 1 diabetes. Control patients were allowed to crossover to RDN at 6 months. Change in office BP from pre-procedure measurements (6 months post-randomization for the crossover group), renal function, and medication use were collected at 6 months intervals after the RDN procedure.

**Results:** At baseline, mean age of the RDN group was 59 years, 32.7% were female, and 42.9% had type 2 diabetes. Mean age of patients crossed over to RDN was 58 years, 60% were female, and 28.6% had type 2 diabetes. There was 1 renal artery dissection; no other adverse events occurred. Change in office BP at 6, 12 and 18 months are shown below.

**Conclusion:** Treatment of resistant hypertension with RDN was safe and effective in both treatment groups to 18 months post-procedure.

---

**Orthostatic function after renal sympathetic denervation in patients with resistant hypertension**

M. Lenski, F. Mahfoud, C. Barth, A. Razouk, C. Ukena, D. Fischer, U. Laufs, I. Kindermann, M. Boehm, Saarland University Hospital, Department of Internal Medicine III, Cardiology, Homburg, Germany

**Background:** Catheter-based renal sympathetic denervation (RDN) is a novel treatment option for patients with resistant hypertension, proved to reduce local and whole-body sympathetic activity and blood pressure (BP). The effect of RDN on orthostatic regulation has not been studied.

**Method:** In 27 patients (age 64±7 years, 77% male) with resistant hypertension (office blood pressure 167/91±22/12 mmHg) treated with 4.8±0.3 mmol/L antihypertensive drugs, tilt table test (TTT) was performed before and 3 months after RDN. Patients were placed on a motorized tilt table. After resting for at least 10 min the recording started. After 5 min in supine position, all subjects were tilted at 60°
for 20 min. Subsequently drug provocation with 400 mg nitro-glycerine sublingual was performed while tilt position was maintained for additional 10 min. A recovery period was performed in initial supine position. Antihypertensive drugs were maintained related to natriuresis, the patients with atrial fibrillation, pacemaker/ICD or history of syncope were excluded.

**Results:** After RDN systolic (SBP) and diastolic blood pressure (DBP) in supine position were reduced by 7.7±4.4 mmHg (p<0.005) and heart rate (HR) was reduced by 4.5 beats/min (p<0.01). After tilting the maximal reduction of BP compared to supine position was not altered (Δ max. SBP: –32±5.5 vs. –27.5±5.5 mmHg, Δ max. DBP: –30.3±4.9 vs. –33±3.5 mmHg; p<0.05). In addition, the minimal BP during 20 min tilting period was also not different after RDN (min. SBP: 135±6 vs. 132±6 mmHg, min. DBP: 77±3 vs. 73±3 mmHg; p=0.05) whereas mean HR during 20 min tilting period was significantly reduced by 4.9 beats/min (p<0.05).

Following drug provocation the maximal BP reduction compared to tilting period was unchanged after RDN (Δ max. SBP: –63±6 vs. –60±7 mmHg, Δ max. DBP: –30±3.3 vs. –36±4 mmHg; p<0.05). During 10 min drug provocation period minimal BP (Δ min. SBP: 98±7 vs. 99±7 mmHg, Δ min. DBP: 61±4 vs. 61±4 mmHg; p=0.05) and minimal HR (74±5 vs. 70±3 mm/min; p=0.05) were not significantly changed. The total number of pre-syncopes and syncopes were not different after RDN: Before and after RDN 6 pre-syncopes (p=0.670) as well as 3 vs. 4 syncopes (p=0.05) occurred during the TTT (p<0.05).

**Conclusion:** In patients with resistant hypertension catheter-based renal sympathetic denervation significantly reduced blood pressure and heart rate during tilting testing after 3 months without causing orthostatic dysfunction or (pre-)syncope.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Δ Relative UNa Excretion [%]</th>
<th>Δ FE Na (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100±32%</td>
<td>0.86±0.28</td>
</tr>
<tr>
<td>3 month</td>
<td>107±15%</td>
<td>0.56±0.26</td>
</tr>
<tr>
<td>6 month</td>
<td>90±17%</td>
<td>0.96±0.28</td>
</tr>
</tbody>
</table>

Mean ± SEM; *p<0.05 vs. baseline.

**Conclusion:** (i) Catheter-based renal denervation causes substantial and sustained blood-pressure reduction in patients with resistant hypertension. (ii) The blood pressure lowering effect of RDN may be in part related to enhanced but transient natriuresis, thereby leading to a new balance between salt intake and salt excretion. (iii) FEa as a predictor for tubular failure is not affected by RDN.

### Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Δ Relative UNa Excretion [%]</th>
<th>Δ FE Na (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>100±32%</td>
<td>0.86±0.28</td>
</tr>
<tr>
<td>3 month</td>
<td>107±15%</td>
<td>0.56±0.26</td>
</tr>
<tr>
<td>6 month</td>
<td>90±17%</td>
<td>0.96±0.28</td>
</tr>
</tbody>
</table>

Mean ± SEM; *p<0.05 vs. baseline.

**Conclusion:** Catheter-based renal sympathetic denervation (RD) offers a new approach to reduce renal activation of the sympathetic nervous system and blood pressure in resistant hypertension. The influence of RD on renal hemodynamics, renal function, and UAE has not been studied before.

**Methods and Results:** One hundred consecutive patients with resistant hypertension were included in the study: 88 underwent interventional RD and 12 served as controls. Systolic, diastolic and pulse pressure (SBP/DBP/PP) as well as RRI in interlobar arteries, renal function and UAE were measured prior to and at 3 and 6 months follow-up. RD reduced SBP, DBP and PP at 3 and 6 months by 22.7/9.6 mmHg, 7.9/7.7 mmHg, and 15.1/15.9 mmHg (p for all <0.001), respectively, without significant changes in the control group. SBP reduction after 6 months correlated to SBP baseline values (r = 0.46, p<0.001). There were no differences in renal arterial stiffness, dissections or aneurysms on follow-up. RRI decreased from 14±2.1 to 13±1.5 (p<0.05), whereas the number of patients with micro- or macroalbuminuria decreased.

**Conclusion:** Renal denervation reduced blood pressure, renal resistive index and incidence of albuminuria, without adversely affecting GFR or renal artery structure within 6 months. RD approaches to reduce blood pressure in patients with resistant hypertension and is associated with favorable effects on renal hemodynamics and urinary albumin excretion rate.
Methods: RDN was performed in 173 patients with resistant hypertension (BP 174/88 ±23/13 mmHg, 5 antihypertensive drugs in median) aged 63±10 years (53% male). Patients were instructed to rate their physical and mental state and arousal level on a 0-100% scale. Stress was induced by a multi-tasking situation (Determination Task). Total number of correct reactions and errors were registered. Furthermore depression and anxiety (Hospital Anxiety and Depression Scale (HADS); quality of life (Short Form-12 Health Survey (SF-12)) and insomnia and regeneration process of sleeping (0-100%) scale were assessed. Intensity of headache was measured by visual analogual scale (VAS). Results: Decreased by -17.7 mmHg 3 months after RDN (p<0.01). In addition patients showed more correct reactions (p<0.0001), and less errors (p<0.05) in the multi tasking situation. Patients felt improved in physical (from 55.6% to 67.2%, p<0.01) and mental (from 51.6% to 68.4%, p<0.01) state as well as in quality of life (p<0.05). Furthermore anxiety (p<0.0001) and depression (p<0.0001) scores decreased. The arousal level was reduced from 49.9% to 36.9% (p<0.0001). At baseline 32.2% of the patients suffered from sleeping disorders and 60% suffered from headache respectively. 3 months after RDN quality of sleeping (p<0.0001) and the intensity of headache (p<0.0001) improved.

Summary: In patients with resistant hypertension RDN leads to a positive development of physical and mental state and beyond this to an improvement in quality of life. In addition patients might react more effectiv and faster in any stress situation.

HEART DISEASE THROUGH THE PATIENTS’ EYES

1173 Self-care behaviors in heart failure patients: international similarities and differences

T. Strooyna, B. Riegelt, A. Stromberg, 1 Linkoping University, Department of Social and Welfare Studies, Linkoping, Sweden;
2 University of Pennsylvania School of Nursing, Philadelphia, United States of America; 3 Linkoping University, Department of Medical and Health Sciences, Division of Nursing Science, Linkoping, Sweden

Background: Clinicians worldwide seek to optimize self-care among heart failure (HF) patients to improve patient outcomes. Although health care systems and cultures differ, the specific self-care behaviors recommended for HF patients are similar internationally, such as advice regarding diet, exercise and symptom monitoring. In this study we describe similarities and differences in self-care behaviors across 21 countries representing 3 continents.

Method: Data on HF self-care were pooled from 21 samples of HF patients gathered from 3 different parts of the United States, 6 different European countries, 7 countries in Australasia and South America, totaling 5577 HF patients. None of the patients had received structured education on HF self-care behavior at the time of data collection. The mean age in the samples ranged from 62 to 67 years and data on self-care were collected with the Self-care of Heart Failure Index (SCHFI) or the European Heart Failure Self-care Behaviour Scale (EHSbS). Data were obtained from the primary investigators and analyzed using descriptive statistics.

Results: Across the 21 samples we found many similarities in self-care behaviors. In all the samples, most patients reported that they took their medications. The highest number of patients who reported not taking their medication on a regular basis was 25%, but most were far better (median 4% not taking medicines). In contrast, self-care with exercise and daily weighing were low in all most samples: 30% to 90% of patients in the samples reported low exercise levels. In 14 of the 21 samples, more than 50% of the patients reported low exercise levels (median 54%). Adherence to weight monitoring was irregular in most samples. In 15 samples, less than half of the patients weighed themselves regularly, with large differences between the countries. Self-care with regard to diet varied more across the countries than other self-care behaviors. Adhering to a sodium restricted diet varied between 8% and 82% (median 60%). Annual flu shot also varied immensely among the countries; 16% to 75% of patients reported not getting an annual flu shot (median 45%).

Conclusion: Most self-care behaviors need to be improved worldwide. The differences evident in reports of a low salt diet and the annual flu shot may also indicate local issues of food quality, health policies and access to care. Exercise, a self-care behavior with good evidence of effectiveness, needs much more focus from providers to increase the level of exercise among HF patients. Further research is needed on cultural differences in HF self-care.

1174 Depression, loneliness, parental support, perceived health and quality of life in adolescents with congenital heart disease: influences and reciprocal effects

S. Apers1, K. Luycx2, E. Goossens1, J. Rassart2, J. Vanhalslift, P. Moons1, 1 Catholic University of Leuven, Center for Health Services and Nursing Research, Leuven, Belgium; 2 Catholic University of Leuven, Leuven, Belgium

Purpose: The present study examined how depressive symptoms, loneliness, paternal and maternal support, perceived health and quality of life influenced one another over time in adolescents with congenital heart disease (CHD).

Methods: We conducted a 3-wave longitudinal study, spanning 18 months (9 month intervals). Patients were selected from the database of paediatric and congenital cardiology of a university hospital in Belgium. Inclusion criteria were: confirmed CHD, aged 14-18 years at the start of the study; last cardiac consult <5 years ago 0-100% scale; Stress to read and write Dutch; and availability of valid contact details. Exclusion criteria were: cognitive and/or physical limitations inhibiting filling out questionnaires; prior heart transplantation; and absence of informed consent. Of the 498 eligible patients, 429 participated (median age 16 years; 53% boys). We used a linear analogue scale (quality of life and perceived health status); the CES-D-20 (depressive symptoms); the 8-item version of the UCLA loneliness scale (loneliness); and the responsiveness subscale of the child report of parent behaviour inventory (parental support). Cross-lagged path analysis was applied to examine the direction of effects over time, controlled for age, sex and disease complexity.

Results: Figure 1 shows the significant relations and their coefficients. Depressive symptoms and loneliness mutually reinforced each other and led to relative decreases in quality of life. Parental support was influenced by previous levels of depressive symptoms, which in turn influenced quality of life. Paternal support predicted relative changes in all variables.

Conclusions: The observed temporal sequences provided information on the dynamics of psychosocial functioning of adolescents with CHD.

1175 Impact of cognitive impairment on the management of patients with atrial fibrillation

J. Ball, M.J. Carrington, S. Stewart on behalf of SAFETY Investigators.

Atrial Fibrillation: A Heart Disease through the Patients’ Eyes 183

Purpose: Atrial Fibrillation (AF) is an increasingly common condition that is often difficult to manage given that: a) patients are typically older with multiple co-morbidities and b) there is a fine line between treatment benefit and risk. Cognitive impairment (CI) is often associated with AF and potentially impacts a patient’s ability to self-care. We explored the prevalence and implications of CI in patients hospitalised with chronic AF.

Methods: The Standard versus Atrial Fibrillation-specific managementT study (SAFETY) is a multisite, randomised controlled trial comparing a nurse-led, home-based AF-specific management program to usual post-discharge care in patients hospitalised with AF. The Montreal Cognitive Assessment (MoCA) was used as an easy screening tool at baseline during index hospitalisation and on intervention patients during an initial home visit (7-14 days post-discharge); a score of ≤26 (maximal score 30) indicates mild CI. Self-care was also assessed in intervention patients during the home visit via the self-care index (range 0 to 70).

Results: Of 216 subject to baseline cognitive function screening, mean age was 71±11 years and 53% were male. Highest level of education attained was ≤13 years for 48% of patients and ≤7 years for 22%. Mean baseline MoCA score was 23±4 with mild CI identified in 70% of patients (n=136). As expected, those with mild CI were significantly older 73±10 versus 68±13 years. However, on an adjusted basis, of all demographic and clinical profiling data, an increasingly higher CHADS2-VASc score was the only independent predictor of mild CI (mild CI versus rest: 3.6±1.7 versus 2.7±1.6, adjusted OR 1.39 95% CI 1.03 to 1.80 per unit increase, p=0.032). The higher the clinical risk of thrombo-embolic events, therefore, the more likely the patient had CI (at index hospitalisation). At the home visit, (paired) MoCA scores in intervention patients had improved from 23±3.9 to 24±1.0, p=0.005 with a similar proportion (68%) still displaying mild CI. Ability to self-care was judged to be poor in nearly all patients (88%) with no significant differences between those with intact cognition and mild CI.

Conclusions: In this “real world”, cohort of high risk patients with chronic AF, mild CI was common (>2/3 affected). Although MoCA scores improved post-discharge, the majority of patients remained cognitively impaired. Older patients with more complex clinical profiles (requiring more aggressive treatment) were more likely to have CI. These data have important implications for safe and effective management of chronic AF.
ASTA—a new validated questionnaire for arrhythmia patients

U. Walfridsson, A. Stromberg, K. Arstedt. Division of Nursing Science, Department of Medicine and Health Sciences, Linköping University, Linköping, Sweden

The main purpose was to develop and validate a disease-specific questionnaire assessing symptoms and health-related quality of life (HRQOL) in patients with different forms of arrhythmias.

Method: Items were developed through a literature review and interviews. The items were evaluated by an expert panel. SF-36 and Symptoms Checklist (SCL) were used in the validation of the new Arrhythmia-Specific questionnaire in Tachycardia and Arrhythmia (ASTA). Homogeneity was evaluated using Spearman’s correlations and Cronbach’s alpha coefficient (α) for internal consistency. Construct validity was evaluated using item-total correlations. Convergent and discriminant validity was examined by comparisons between ASTA symptom scale, SCL and SF-36 and by comparisons between the HRQOL scales, the SF-36 physical component summary (PCS) and mental component summary (MCS). Construct validity for the HRQOL scales was further evaluated using confirmatory factor analyses (CFA).

Results: The correlations between the ASTA symptom scale items showed generally sufficient homogeneity and α was satisfactory (≥0.8). All items in the symptom scale were sufficiently correlated (≥0.3). Convergent and discriminant validity was supported by the higher correlations to the SCL compared to the SF-36. Concurrent validity demonstrated sufficient, but not extremely strong correlations between the ASTA symptom scale and the SF-36 PCS and SCL. The ASTA HRQOL items reached the expected level of item-total correlations, ≥0.30. The CFA demonstrated satisfactory factor loadings for the HRQOL scales. Once error variances had been allowed to correlate, a good fit was reached between model and data. Convergent validity was also supported by the internal consistency and lower bound confidence intervals were ≥0.70 for all of the ASTA HRQOL scales.

Conclusion: The scales in the validated ASTA questionnaire were all found to have good psychometric properties in the targeted patient population. Patients reported outcome measures are being increasingly emphasized in research as well as in quality of care evaluations. It is of great importance to evaluate the effect of arrhythmias on patients’ daily life as well as patient reported treatment effects. The new ASTA questionnaire could be a valuable contribution for health care interventions and for clinical research.

Cultural factors increase pre-hospital delay in myocardial infarction for Saudi women

H. Alshahri1, D. Fitzsimons1, R. Mooney1, J. Wilson1, M. Youssef2 . 1University of Ulster, Belfast, United Kingdom; 2King Fahad Medical City, Prince Salman Heart Center, Riyadh, Saudi Arabia

Many factors have been implicated in patients’ decisions to seek care in MI, but most research has a Western origin and it is possible that reasons for delay differ in Arab cultures. Our study aimed to explore the factors that contribute to pre-hospital delay among MI patients in Saudi Arabia. This cross sectional study comprised a convenience sample of research participants (n=311), who presented with a diagnosis of MI to three hospitals in Riyadh over a 20 month period from January 2011 to June 2013. Of these, 169 patients met the eligibility criteria. There was a statistically significant difference between pre-hospital delay time (onset of symptoms to hospital arrival) and patients’ gender. For males the median delay was 5 hours (M=5.78, SD=1.786) and for females it was 12.9 hours (M=6.79, SD=1.851; 187 = 3.097, p=0.002). This was despite similar intervals between the genders for symptom onset to decision to seek care (male= 2.5 hours, female=3 hours). In addition, only 12% of females versus 88% of male participants arrived at hospital in the first hour of symptom onset. The median transfer time for all participants was 45 minutes, (0.9hrs for men and 2.5 hours for women).

The gender differences in pre-hospital delay in Saudi are likely to be influenced by cultural factors, since the majority of females (97%), in this study cannot drive and it is culturally prohibited for them to go to hospital without a male relative escorting them. Only 11% of patients from both genders resided close to the hospital by ambulance. Moreover, symptom onset most commonly occurred at home for both males (65%) and females (78%) and the most popular response (41%) was to try a self-help remedy. Two factors fit the nature of females that delay significantly more than males when they are non-Saudi, have no dyspnea and when they are outside their home at symptom onset (< 0.05), perhaps due to language and cultural barriers.

This the first study conducted with MI patients in Saudi within the restrictions of an Arab culture. Overall the total pre-hospital delay time reported here is longer than in studies in other settings and there are significant gender differences. We postulate that cultural factors are implicated. Health promotion interventions for potential MI patients should consider offering culturally-sensitive, gender related messages.

Effects of a 6 months educational program for CPAP initiation in hypertensive patients with obstructive sleep apnea

A. Brostrom1, B. Fridlund2, M. Ulfsand1, O. Sunnergren2, E. Svartborg1, P. Nilsson3 on behalf of HypnoSleep. 1Department of Clinical Neuropsychology, Linköping University Hospital, Sweden, Linköping, Sweden; 2Linköping University, School of Health Sciences, Department of Nursing Science, Jönköping, Sweden; 3Department of ENT, Jönköping, Sweden; *Faculty of Health Sciences Linköping University, Sweden., Linköping, Sweden

Background: Continuous positive airway pressure (CPAP) treatment of obstructive sleep apnea (OSA) can reduce blood pressure, morbidity and mortality, but has low long-term adherence. Educational interventions are few and sparsely described regarding content, methodological approach and the participants’ perceptions.

Aim: To (1) describe adherence to CPAP treatment, (2) knowledge about OSA/CPAP, as well as (3) hypertensive OSA patients’ perceptions of participating in a group-based program using problem-based learning (PBL) for CPAP initiation.

The Educational program: The PBL program was based on theories and models concerning motivation and habits. Tutorial groups consisting of 4-6 patients met at 6 sessions during 6-months.

Method: A sequential explanatory mixed method design was used on 25 strategically selected patients (mean age 59.6 yrs, range 49-65 and mean BMI 30.5 kg/m², range 21.9-48.1). Quantitative data regarding clinical variables, OSA severity (apnea) history, objective CPAP use, and knowledge regarding OSA were collected at baseline, after 2 weeks and 6 months. Qualitative data regarding patients’ perceptions of participation were collected after 6 months by semi-structured interviews in a phenomenographic approach and data. Convergent validity was supported by the significant correlations and Cronbach’s alpha coefficient (α) for internal consistency. Convergent and discriminant validity was supported by the higher correlations to the SCL compared to the SF-36. Concurrent validity demonstrated sufficient, but not extremely strong correlations between the ASTA symptom scale and the SF-36 PCS and SCL. The ASTA HRQOL items reached the expected level of item-total correlations, ≥0.30. The CFA demonstrated satisfactory factor loadings for the HRQOL scales. Once error variances had been allowed to correlate, a good fit was reached between model and data.

Results: Mild, moderate and severe OSA was seen among 8%, 56% and 36% of the patients, respectively before treatment. The amount of patients indicating daytime sleepiness decreased from 81% (84%) at baseline to 9% (36%) and 6% (24%) after 2 weeks and 6 months, respectively (p<0.01). 72% were adherent to CPAP treatment (use ≥4 h/night) both after 2 weeks and 6 months. Out of those who suffered from daytime sleepiness at 2 weeks and 6 months, 56% and 60% were adherent. Nine patients (36%) decreased and 15 (60%) of the patients increased their CPAP use/night during the follow up. None terminated their treatment. All patients improved their baseline knowledge about OSA and CPAP after 2 weeks and sustained it after 6 months.

Anxiety and fear, as well as difficulties and needs were motivational factors for CPAP use.

Patients described: Difficulties of behavioural change; an awareness that improvements do not occur immediately; a realization of the importance of both technical and emotional support; and the need for a healthier lifestyle.

Conclusion: A group-based program using a PBL approach seems to facilitate both adaptive and developmental learning, but also result in decreased symptoms and acceptable adherence. Pedagogic personnel, using research-based knowledge regarding CPAP adherence, as well as knowledge regarding behavioural theories are of importance to carry out the program.

Myocardial infarction with normal coronary arteries is common and associated with normal findings on CMR - results from the Stockholm Myocardial Infarction with Normal Coronaries (SMINC) Study

O. Collste1, P. Sorensson2, M. Frick1, S. Ageval2, M. Daniel3, T. Jernberg3, C. Hofman-Bang1, K. Malmqvist1, H. Arendt1, P. Tornvall4, 1Karolinska Institute, Sodersjukhuset, Department of Cardiology, Stockholm, Sweden; 2Karolinska University Hospital, Department of Cardiology, Stockholm, Sweden; 3Oslo University Hospital & University of Oslo, Dept of Cardiology, Oslo, Norway; 4Capio St Goran’s Hospital, Department of Medicine, Stockholm, Sweden; 5Karolinska Institute, Danderyd Hospital, Department of Cardiology, Stockholm, Sweden; 6Lund University Hospital, Department of Clinical Physiology, Lund, Sweden

Objectives: Myocardial infarction with angiographically normal coronary arteries (MINCA) is a rare condition where the prevalence is currently unknown. Cardio Magnetic Resonance Imaging (CMR) has the potential to clarify the underlying pathology in these patients. Our objective was to investigate the diagnostic value of CMR in this group of patients.

Design: The Stockholm Myocardial Infarction with Normal Coronaries (SMINC) study is a prospective multicenter observational study.

Setting: Coronary Care Units in the Stockholm Metropolitan Area.

Subjects: MINCA patients between 35-70 years of age were consecutively included in the screening phase of the SMINC study. All patients had a typical clinical presentation, fulfilling the universal definition of myocardial infarction according to ESC/ACC/AHA and had a normal coronary angiography. Patients with known structural or coronary heart disease or other known causes of elevated troponins were excluded.
Results: All together, 176 MINCA patients were screened 2007-2011. Of them 152 were investigated with CMR. During the time period 277 patients were eligible for the study representing 6.3% of all patients with a diagnosis of myocardial infarction undergoing coronary angiography. The investigation was performed median 12 (IQR 6-28) and mean 20 days after the initial presentation to hospital. Sixty-seven percent of the examinations were completely normal whereas 19% of the patients had signs of myocardial necrosis. Only 7% had signs of myocarditis. The remaining patients (7%) had either unrecognized hypertrophic cardiomyopathy or could not be classified. The frequency of Takotsubo stress cardiomyopathy was 22% of all patients screened with CMR. The incidence of MINCA was higher than previously shown. Based on the results and assumptions, we propose that the incidence of MINCA is 7.8%. We also found a lower prevalence of myocarditis than in previous studies. After excluding myocarditis, MINCA consists of a larger group of patients with a normal CMR and a smaller group with myocardial necrosis. The etiologies of these different CMR findings need to be explored.

Conclusions: Elderly patients benefit significantly from invasive strategies and modern pharmacotherapy recommended by treatment guidelines. Nevertheless, this approach is associated with an increased incidence of major bleeding.

Methods: We analysed 78,422 patients with NSTE CMR enrolled in the PL-ACS registry from 10.2003 to 2009.

Results: The percentage of elderly patients with NSTE CMR was 17.5% (N=13,707). Invasive treatment received 24% of them. In-hospital complications were significantly less frequent in the invasive group, with the exception of major bleeding, which occurred almost three times more frequently in the invasive group. The 12-month was lower in the invasive group and remained so after matching patients by the propensity score method (23.2% vs. 30.5%, p<0.0001). From 2003 to 2009 the use of thienopyridines, beta-blockers and statins rose significantly. The frequency of invasive strategy increased significantly, from 10% to over 50% in 2009, which caused an increase in revascularisation procedures (table). The frequency of major bleeding increased twofold, however a significant reduction in the 12-month mortality was observed.

Conclusions: Elderly patients receiving clopidogrel plus aspirin and 6799 treated with aspirin only were included; mean age 75 years (SD±8.85) and 55.2% males. Mean follow-up for bleeding events was 432 days (SD±194) and 432 (SD±190) for recurrent MI or death, respectively. Among patients treated with clopidogrel and aspirin 563 (8.46%) experienced fatal or non-fatal bleedings whereas these events occurred in 472 (6.94%) of the patients treated with aspirin alone (Log rank p=0.051). Among patients treated with clopidogrel and aspirin 1975 (29.68%) died from or experienced a new MI whereas these events occurred in 2129 (31.31%) of the patients treated with aspirin alone (Log rank p=0.06). Hazard ratios are displayed in Fig. 1.

Conclusions: Clopidogrel treatment in elderly patients after myocardial infarction is associated with lower risk of recurrent myocardial infarction and death without increasing the risk of bleeding.

Myocardial infarction of Takotsubo cardiomyopathy behaves similarly to viable myocardium of patients with acute myocardial infarction

D. Perez De Arenaza, M. Falconi, M. Pietrani, L. De Stefano, J. Navarro-Estrada, L. Dragontetti, R. Garcia-Monaco, A. Cagide. Italian Hospital of Buenos Aires, Buenos Aires, Argentina

Introduction: Takotsubo cardiomyopathy (TC) is a reversible form of acute heart failure of unknown pathophysiology. Several mechanisms have been proposed; including catecholamine induced myocardial stunning, ischaemia stunning due to multivessel epicardial or microvascular spasm, aborted acute myocardial infarction (AMI), and local myocarditis. Cardiac magnetic resonance imaging (CMRI) identifies patients with TC by apical or mid-ventricular hypokinesia and absence of high-signal areas of late enhancement with gadolinium. Myocardial edema detected by high T2 signal on CMRI was associated with areas of hypokinesia in TC patients. The purpose of this study was to compare the correlation of regional motility (wall thickening) and myocardial edema in T2 weighted images in patients with TC and patients with myocardial infarction.

Methods: All patients underwent a CMR with gadolinium: 10 patients with TC, 10 patients with ST-elevation AMI, 10 patients with chronic myocardial infarction and 10 controls. Patients with TC were followed up at a mean time of 8 months. Thickening of left ventricular 17 segments were analyzed. Hypokinesia was defined as thickening <30%. For myocardial edema in T2- weighted images, the ratio of mean signal intensity (SI) of the myocardium compared with that of skeletal muscle was used. Pearson correlation coefficients were obtained.

Results: Patients with TC have mean age of 71 ±11, were all women, 50% had hypertension and 70% hypercholesterolemia and had normal coronary angiograms. In TC patients, the correlation coefficient of left ventricular segment thickening and edema was -0.52 (p<0.001) but the correlation was lost at follow-up (r=-0.9, p=0.55). The mean SI ratio in hipokinetic segments was 1.95 compared with normal segments 1.30 (p<0.001). In a receiving operator curve (ROC) analysis, T2 SI ratio of 1.82 identifies segments with hypoxia (area ROC 0.87, CI 0.95% 0.81-0.92). In patients with AMI, the correlation coefficient was 0.18 (p=0.31) in segments with late enhancement with gadolinium and -0.49 (p<0.001) in viable segments without late enhancement. In chronic myocardial infarction and control patients, there was a lack of correlation with correlation coefficients 0.05 (p=0.60) and 0.09 (p<0.043) respectively.

Conclusions: An inverse correlation was found between myocardial edema and wall thickening in patients with TC and viable segments of patients with AMI. This correlation was not seen in infarcted segments in patients with AMI, patients with chronic myocardial infarction and normal subjects. These findings support the concept that TC is a type of acute ischemic event.
Newly detected diabetes mellitus and impaired glucose tolerance adversely affects prognosis after myocardial infarction

A. George, G.L. Buchanan, A. Whiteside, R.S. Moisey, S.F. Beer, J. John, S. Chattopadhyay, Southrope General Hospital, Southrope, United Kingdom

Background: We investigate whether newly detected diabetes mellitus (NDM) and impaired glucose tolerance (IGT) using pre-discharge oral glucose tolerance test (OGTT) after myocardial infarction (MI), is related to long-term prognosis in the context of current practice.

Methods: 768 non-diabetic post-MI patients were categorised into normal glucose tolerance (NGT) (n=337), IGT (n=279) and NDM (n=152) groups based on pre-discharge OGTT and followed up for a primary end-point, the first occurrence of major cardiovascular adverse events (MACE) including cardiovascular (CVS) death, non-fatal MI, heart failure (HF) or non-haemorrhagic stroke. Secondary end-points were all cause mortality, cardiovascular mortality, non-fatal MI, severe heart failure or stroke.

Results: Except for age, the clinical characteristics of the groups were well matched. Prevalence of NGT, IGT, IGT and NDM changed from 90%, 6%, 0% and 4% on fasting plasma glucose (FPG) to 43%, 1%, 36% and 20% on OGTT respectively. 12% of patients with post-challenge hyperglycaemia, had normal FPG. 102 deaths from all causes (79 as the first event of which 46 were cardiovascu lar), 95 non fatal MI, 18 HF and 9 non haemorrhagic stroke totalling 168 MACE 102 deaths from all causes (79 as the first event of which 46 were cardiovascular), 95 non-fatal MI, 18 HF and 9 non-haemorrhagic stroke. 52% of the total deaths were due to cardiovascular disease. Using Cox proportional hazard modelling, IGT (HR 1.54, 95% CI: 1.06-2.24, p=0.024, NDM (HR 2.15, 95% CI: 1.42-3.24, p=0.002) predicted MACE. NDM also increased the risk for all cause death (HR 2.14, 95% CI: 1.17-3.7, p=0.014), CVS death (HR 2.83, 95% CI: 1.24-6.45, p=0.013) and non-fatal MI (HR 1.96, 95% CI: 1.16-3.29, p=0.012) but not IGT. Multivari at analysis confirmed this association, maintaining a clear significance, p value 0.00. Other factors that were significantly associated with the absence of ST elevation in the multivariate analysis were the localization of the culprit lesion at left circumflex (p=0.00), the BARI score for the culprit lesion was lower in the NSTEMI (p=0.00). With regards to the collateral blood flow, the univariate analysis showed no significant relationship between the presence of significant collateral blood supply and the absence of ST elevation. (p=0.00). The multivariate analysis confirmed this association, maintaining a clear significance, p value 0.00. Other factors that were significantly associated with the presence of ST elevation were: dilated ischemic or non-ischemic cardiomyopathy, moderate to severe mitral regurgitation pre-procedure was 3.54, p<0.05. Twenty five p, age 65±11 years. 100% with mechanical valves (22p with mitral leak) and 3p with mitral and aortic leaks. The mean number of previous surgeries was 2.2±0.93. The time from surgery to percutaneous intervention was 8±1.7 years. EuroScore Log 15±6±11.7. Clinical presentation: heart failure (60%), hemolytic anemia (3%) and both 75%. The NYHA functional class was 3±1.8, hematocrit 28.7±5.4%, LDH 1544±946 U/L. The mean degree of regurgitation pre-procedure was 3.5±0.6. Fifty two patients were attempted to close in 47 procedures. The devices were successful in 100% of the p but 6p required a second procedure and 2p a third one. A total of 64 devices were implanted (2.56/p). Paravalvular regurgitation decreased and averaged 1.3±0.65. Complications of the procedure: device embolization 1p (percutaneously captured and implanted in the same procedure), impingement prosthetic disc in 2p (1 solved by device repositioning and 1 referred for emergency surgery). One patient required a permanent pacemaker. Procedural success was 96%. Clinical events at 30 days: Percutaneous rein- tervention for residual regurgitation in 3p, mitral valve replacement surgery 1p, stroke 1p, hospitalization for heart failure 6p and death 2p. Clinical success in 85.1%.

Conclusion: Percutaneous repair of large and/or multiple leaks with AVPIII is a feasible and safe technique with high technical and clinical success at 30 days. We should be aware of potential complications during the procedure (device embolization, impingement of prosthetic disk). Long term clinical result of these p will depend on the success of the procedure and the general status post procedure.

Percutaneous closure of large and or multiple paravalvular lekas with multiple devices. Procedural and 30 days follow-up

J. Sandoval, M. Paulo, R. Hernandez-Antolin, C. Almeria, C. Rodas, J. Dutay, E. Garcia. Hospital Clinic San Carlos, Department of Cardiology, Madrid, Spain

Introduction: Percutaneous closure of paravalvular leak is a relatively recent technique. The result of large and/or multiple leaks bas barely been described.

Objective: To describe a population undergoing percutaneous closure of large and/or multiple leaks repaired with Amplazer Vascular Plug III(AVPIII) device, and to assess procedural and 30 day results.

Materials and methods: All Patients (p) with paravalvular leaks treated percuta- neously with more than the 1 AVPIII. Procedural success was defined when the device was successfully deployed and there was a significant decrease of regurgitation through a perivalvular leak. Device failure is defined: death at 30 days or new intervention on the same leaks at 30 days.

Result: Twenty five p, age 65±11 years. 100% with mechanical valves (22p with mitral leak) and 3p with mitral and aortic leaks. The mean number of previous surgeries was 2.2±0.93. The time from surgery to percutaneous intervention was 8±1.7 years. EuroScore Log 15±6±11.7. Clinical presentation: heart failure (60%), hemolytic anemia (3%) and both 75%. The NYHA functional class was 3±1.8, hematocrit 28.7±5.4%, LDH 1544±946 U/L. The mean degree of regurgitation pre-procedure was 3.5±0.6. Fifty two patients were attempted to close in 47 procedures. The devices were successful in 100% of the p but 6p required a second procedure and 2p a third one. A total of 64 devices were implanted (2.56/p). Paravalvular regurgitation decreased and averaged 1.3±0.65. Complications of the procedure: device embolization 1p (percutaneously captured and implanted in the same procedure), impingement prosthetic disc in 2p (1 solved by device repositioning and 1 referred for emergency surgery). One patient required a permanent pacemaker. Procedural success was 96%. Clinical events at 30 days: Percutaneous rein- tervention for residual regurgitation in 3p, mitral valve replacement surgery 1p, stroke 1p, hospitalization for heart failure 6p and death 2p. Clinical success in 85.1%.
associated with LV reverse remodeling and an increase in the systolic performance, that correlates with the reduction in mitral regurgitation.

**Impact of mitral regurgitation etiology and effective Transcatheter aortic valve implantation in patients with Predictive value of pre-procedural mitral regurgitation**

E. Lubos 1, V. Rudolph 1, D. Lubs 1, M. Schlueter 1, M. Knopf 1, H. Treede 2, J. Schirmer 1, H. Reichenspurner 2, S. Blankenberg 1, S. Baldus 1, 1University Heart Center Hamburg, Clinic for General & Intervventional Cardiology, Hamburg, Germany; 2University Heart Center Hamburg, Dept. of Cardiovascular Surgery, Hamburg, Germany

**Background and Objective:** MitraClip (MC) implantation is increasingly used to treat significant mitral regurgitation (MR) in patients deemed at high risk for surgical mortality and functional surgery. We sought to assess the impact of MR etiology and quantitative echocardiographic variables of MR severity on the acute procedural outcome.

**Methods and Results:** Between 09/2008 and 12/2011, 270 consecutive patients (74±9 years, 172 [64%] men, LV ejection fraction 44±16%, logistic EuroSCORE 29±15%) underwent MC therapy at our center. All patients were adjudicated as not amenable to surgery by heart team consensus. MR of grade 3±4 was present in 57 and 43% of patients, respectively. MR etiology was functional in 61%, degenerative in 25%, and were AS in 14% of patients. Three-five clip transeptal implantation was performed in 259 procedures (1 clip in 167, ≥1 clip in 92 procedures). Overall procedural success rate, defined as residual MR severity of grade 2+ or less, was 92% (n=249 procedures). Median age at time of intervention, i.e., time from septic puncture to withdrawal of the clip delivery system from the left atrium, amounted to 66 minutes (interquartile range, 42 to 105 minutes). In the 239 successful procedures, the regurgitation severity was significantly reduced from grade 3+ (60%) or 4+ (40%) at baseline to grade 1+ (41%) or 2+ (59%) at discharge (P<0.0001). When patients were dichotomized by MR etiology (purely functional [FMR] vs. degenerative/mixed [DMR]), a significantly lower procedural success rate was noted in DMR patients (72/88 [81.8%] vs. 167/182 [91.8%], P = 0.024) and successfully treated DMR patients were significantly less often discharged with MR grade 1+ (22.5%, 22.2% and 30% in groups 1, 2 and 3, respectively, p= 0.86). Functional mitral regurgitation (FMR) treated patients were significantly less often discharged with MR grade 1+ (41%) or 2+ (59%) at discharge (P<0.0001). In group 1 pa-

**Conclusion:** The incidence of AR was not influenced by any other clinical, echocardiographic or hemodynamic parameters and CT scan data. Pre-procedural AR was the only predictor of significant post-TAVI AR.

**Transcatheter aortic valve implantation in patients with high-risk severe aortic stenosis: analysis of 30-day mortality in low-gradient versus high-gradient subgroups**

M. Marwan, M. Abdel-Wahab, A. Mostafa, V. Geist, B. Stoecker, S. Bettina, R. Toelg, G. Richardt. Segeberger Clinics, Heart Center, Bad Segeberg, Germany

**Introduction:** Patients with low-flow, low-gradient severe aortic stenosis are considered at a more advanced disease stage compared to patients with high-gradient aortic stenosis (AS), with a poor prognosis if left untreated. Transcatheter aortic valve implantation (TAVI) is an emerging technique for treatment of patients with high-risk severe aortic stenosis. We prospectively assessed 30-day all-cause mortality and functional status in patients with high-gradient versus low-flow, low-gradient AS.

**Patients and Methods:** Between September 2007 and October 2011, transcatheter TAVI was performed in 184 consecutive high-risk patients with symptomatic severe aortic stenosis (aortic valve area ≤0.7±0.2 cm²) using both Medtronic CoreValve and Edwards SAPIEN prostheses. Three patient groups were identified; 155 patients with high-gradient severe AS [group 1], 18 patients with low-gradient severe AS who were ASIS with ≥1% of patients, one or more clips transeptal implantation in 259 procedures (1 clip in 167, >1 clip in 92 procedures). Overall procedural success rate, defined as residual AR severity of grade 2+ or less, was 92% (n=249 procedures). Median age at time of intervention, i.e., time from septic puncture to withdrawal of the clip delivery system from the left atrium, amounted to 66 minutes (interquartile range, 42 to 105 minutes). In the 239 successful procedures, the regurgitation severity was significantly reduced from grade 3+ (60%) or 4+ (40%) at baseline to grade 1+ (41%) or 2+ (59%) at discharge (P<0.0001). When patients were dichotomized by MR etiology (purely functional [FMR] vs. degenerative/mixed [DMR]), a significantly lower procedural success rate was noted in DMR patients (72/88 [81.8%] vs. 167/182 [91.8%], P = 0.024) and successfully treated DMR patients were significantly less often discharged with MR grade 1+ (22.5%, 22.2% and 30% in groups 1, 2 and 3, respectively, p= 0.86). Functional mitral regurgitation (FMR) treated patients were significantly less often discharged with MR grade 1+ (41%) or 2+ (59%) at discharge (P<0.0001). In group 1 pa-

**Conclusion:** The incidence of AR was not influenced by any other clinical, echocardiographic or hemodynamic parameters and CT scan data. Pre-procedural AR was the only predictor of significant post-TAVI AR.

**Transcatheter aortic valve implantation in patients with high-risk severe aortic stenosis: analysis of 30-day mortality in low-gradient versus high-gradient subgroups**

M. Marwan, M. Abdel-Wahab, A. Mostafa, V. Geist, B. Stoecker, S. Bettina, R. Toelg, G. Richardt. Segeberger Clinics, Heart Center, Bad Segeberg, Germany

**Introduction:** Patients with low-flow, low-gradient severe aortic stenosis are considered at a more advanced disease stage compared to patients with high-gradient aortic stenosis (AS), with a poor prognosis if left untreated. Transcatheter aortic valve implantation (TAVI) is an emerging technique for treatment of patients with high-risk severe aortic stenosis. We prospectively assessed 30-day all-cause mortality and functional status in patients with high-gradient versus low-flow, low-gradient AS. Patients and Methods: Between September 2007 and October 2011, transcatheter TAVI was performed in 184 consecutive high-risk patients with symptomatic severe aortic stenosis (aortic valve area ≤0.7±0.2 cm²) using both Medtronic CoreValve and Edwards SAPIEN prostheses. Three patient groups were identified; 155 patients with high-gradient severe AS [group 1], 18 patients with low-gradient severe AS who were ASIS with ≥1% of patients, one or more clips transeptal implantation in 259 procedures (1 clip in 167, >1 clip in 92 procedures). Overall procedural success rate, defined as residual AR severity of grade 2+ or less, was 92% (n=249 procedures). Median age at time of intervention, i.e., time from septic puncture to withdrawal of the clip delivery system from the left atrium, amounted to 66 minutes (interquartile range, 42 to 105 minutes). In the 239 successful procedures, the regurgitation severity was significantly reduced from grade 3+ (60%) or 4+ (40%) at baseline to grade 1+ (41%) or 2+ (59%) at discharge (P<0.0001). When patients were dichotomized by MR etiology (purely functional [FMR] vs. degenerative/mixed [DMR]), a significantly lower procedural success rate was noted in DMR patients (72/88 [81.8%] vs. 167/182 [91.8%], P = 0.024) and successfully treated DMR patients were significantly less often discharged with MR grade 1+ (22.5%, 22.2% and 30% in groups 1, 2 and 3, respectively, p= 0.86). Functional mitral regurgitation (FMR) treated patients were significantly less often discharged with MR grade 1+ (41%) or 2+ (59%) at discharge (P<0.0001). In group 1 pa-

**Conclusion:** The incidence of AR was not influenced by any other clinical, echocardiographic or hemodynamic parameters and CT scan data. Pre-procedural AR was the only predictor of significant post-TAVI AR.
Scar Dechanneling in patients with chronic myocardial infarction and ventricular tachycardia

Methods: 40 consecutive post-MI patients (34±12 LVEF) with ventricular tachycardia (VTs) episodes/patient were included. A high-density (551±251 sites mapped) voltage map was obtained to identify conducting channels (CCs). Electrograms with isolated delayed components (E-ICDs) inside/between scars were tagged and classified as entrance or inner CC points, depending on the delayed component polarity. The procedural endpoint was the elimination of all identified E-ICDs (by discrete RF ablation at CC entrance), and the abolition of residual inducible VTs afterwards.

Results: Mean procedure and fluoroscopy time were 239±84 min and 19±9 min, respectively. A mean of 14±9 entrance-CC points/patient were identified and targeted for RF application (24±15 discrete RF lesions/patient). Re-maps showed a dramatic reduction in the number of E-ICDs (61±24 vs. 9±8, p<0.01), that required 7±8 additional RF applications. After substrate ablation 68% of patients had no residual inducible VTs. Scar Dechanneling and residual VT ablation resulted in 98% non-inducibility of clinical VT, 93% of monomorphic VT and 80% of any VT recurrence. There was a single major bleeding. During a follow-up of 10 months, 36 (90%) patients remained without VT recurrences. Any VT/VF. There was a single major bleeding. During a follow-up of 10 months, 36 (90%) patients remained without VT recurrences.

Procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia. The procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia. The procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia. The procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia. The procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia. The procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia. The procedural endpoint was the elimination of all identified E-ICDs firstly and the abolition of residual inducible tachycardia.
Catheter ablation of ventricular tachycardia / Evaluation and outcome of syncope

1237 Single port subxiphoid epicardial ablation using snake robotic system

P. Neuzil1, V.V. Reddy2, R. Kuenzler3, O. Svarnad3, M. Zenati4, S. Cerryn2, 1.1. Homolce Hospital, Prague, Czech Republic; 2. Mount Sinai Medical Center, New York, United States of America; 3. CardioRobotics, Middletown, United States of America; 4. South Coast Radiological Group, Laguna Hills, United States of America; 1. University of Pittsburgh Medical Center, Pittsburgh, United States of America.

Objective: Minimally invasive techniques are being developed to treat lone atrial fibrillation (AF) since mid-90s. While performed via multiple bi-lateral access ports, these procedures required advanced thoroscopic skills and take long time to complete. The novel CardioARM robotic system is designed to access all outer surfaces of the heart confined within the pericardium providing multiple open device channels inside its highly articulated, multiple degrees of freedom arm which can accept flexible interventional tools along with an on-board visualization system or suitable tracking device. The CardioARM is controlled by the physician with one hand using joystick control pad attached to the OR table. The study evaluated feasibility of using CardioARM for single-port off-pump epicardial ablation in live animal model.

Methods: Six female pigs (42 - 78 kg) underwent the procedure under general anesthesia. Percardial access was gained through 3-4 cm midline skin incision over the xiphoid. The CardioARM probe was inserted into the pericardial space through 12 mm thorascopic cannula fixed to the skin. The navigation was done under fiberoptic camera guidance and periodically checked with fluoroscopy. All procedures were performed endoscopic using an RF ablation catheter with a deflectable tip and RF ablation catheters were used to create epicardial lesions. The vital physiologic parameters were continuously monitored during intracardiac manipulations and ablations. Gross pathology examination of the hearts and pericardium had been performed after completion of each experiment.

Results: Percardial access with the CardioARM probe was successfully achieved in all animals. The direct visualization guidance feature of the probe allowed successful identification of the anatomical structures and precise pericardial delivery to the target sites. Series of linear ablations were created on the surface of LV and LA to simulate potential clinical applications and confirmed on post-experimental cardiac dissection. No significant changes of the vital parameters were detected during probe manipulations and ablations (2-3 hrs in each animal).

Conclusions: The study device was shown to be safe and effective in performing intended navigation and ablation tasks in the porcine model. Therefore, the CardioARM is considered ready for a small, single-center feasibility trial in humans.

1239 Electrical storm: a strong mortality and morbidity risk factor. Is it possible to predict it?

F. Guerra, M. Shiokza, L. Scappini, M. Flori, A. Capucci. Marche Polytechnic University of Ancona, Department of Cardiology, Ancona, Italy.

Objective: The aim of the current meta-analysis was to evaluate ES as a risk factor for death and cardiovascular events, and determine whether ES can be predicted by clinical variables.

Methods: The meta-analysis has been conducted according to international PRISMA guidelines. Two big databases (PubMed and Web of Science) were scanned for all original articles using “electrical storm” or “arrhythmic storm” as keywords. 561 articles were found and entered selection process. Two independent investigators selected eligible studies in a blinded fashion. At the end of the selection process 32 articles entered the quantitative analysis.

Results: The current meta-analysis included 6979 total patients and 1782 patients with ES. Patients with ES have a 3-fold increased risk of death (RR 2.85; IC 95% 2.11-3.86). The increased risk of death is also significantly increased when ES patients are compared with subjects with a history of simple VTs/VFs (RR 3.23; IC 95% 2.9-3.74). Patients with ES also have a 3-fold increased risk of cardiovascular events, defined as stroke, myocardial infarction, or systemic embolism (RR 2.98; IC 95% 1.86-4.79). The increased risk of cardiovascular events related to ES was still significantly higher when patients with history of simple VTs/VFs were used as control group.

Regarding all factors studied as possible predictive factors for ES, ICD implant for ventricular arrhythmias and monomorphic VT as triggering arrhythmia were found as predictive for ES. Patients with ES also have lower EF and higher mean NYHA class.

Conclusions: ES is a strong risk factor for death and cardiovascular events, even when compared with not clustered VTs/VFs. Secondary prevention, low EF, high NYHA class and monomorphic VT as triggering arrhythmia are reliable predictive factors for ES.

EVALUATION AND OUTCOME OF SYNCOPE

1240 First admission for syncope in a healthy population predicts mortality and cardiovascular events

M. Ruwald1, M. Lock Hansen1, M. Lamberts1, G. Malta Hansen1, M.V. Hojgaard2, L. Kober3, C. Torp-Pedersen1, J. Hansen1, G. Gislason1. 1. Gentofte Hospital - Copenhagen University Hospital, Department of Cardiology, Hellerup, Denmark; 2. Rigshospitalet - Copenhagen University Hospital, Heart Centre, Copenhagen, Denmark.

Background: Syncope is a common clinical event, but knowledge of long-term outcome is not fully elucidated. We examined risk of major cardiac adverse events and death in a nationwide cohort of patients without previous comorbidity admitted for syncope.

Methods and results: Patients without prior comorbidity admitted for syncope in Denmark from 2001-2009 were identified in nationwide administrative registers and matched on sex and age with 5 controls from the Danish population. The risk of recurrent syncope, implantation of pacemaker or implantable cardioverter defibrillator and cardiovascular hospitalization was analyzed with multivariate Cox proportional-hazard models.

We identified 48,430 patients with a first diagnosis of syncope and 242,150 controls; median age was 53 years (IQR: 36.5-69.5) and 45.3% were males. At total of 5,579 (11.5%) and 24,772 (10.2%) deaths occurred in the syncope and control population (Fig) yielding an event rate of 26 and 19 deaths per 1000 person years, respectively.

There was significantly increased risk of all-cause mortality (HR=1.14 [CI: 1.11-1.17], cardiovascular hospitalization (HR=1.82 [CI: 1.77-1.87]), recurrent syncope (HR=103.85 [CI: 94.67-113.93]), stroke (HR=1.38 [CI: 1.31-1.45]) and pacemaker or implantable cardioverter defibrillator (HR=5.03 [CI: 4.62-5.47]) p<0.0001.

Conclusion: First admission for syncope significantly predicts risk of all-cause mortality, stroke, cardiovascular hospitalization, device implantation and recurrent syncope, in a population without prior comorbidity.
Syncope in Brugada syndrome patients: ventricular tachycardia or neurally mediated?

L.R.A. Oide Nordkamp, A.S. Vink, A.A.M. Wilde, F.J. De Lange, J.S. van der Pal, W. Wieling, N. Von Dittekam, Tan. Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands

Purpose: Syncope episodes in Brugada syndrome (BrS) patients are a class Ila indication for implantable defibrillator therapy because these episodes are generally ascribed to ventricular arrhythmias (VT/VF) and therefore considered a major risk factor for fatal cardiac events. However, syncope is not always caused by VT/VF. In the general population, benign neurally mediated syncope (NMS) is far more frequent than syncope caused by ventricular tachyarrhythmias. We therefore aimed to study the prevalence of NMS and cardiac syncope in BrS patients, and to establish the clinical characteristics of these syncope episodes.

Methods: We analyzed charts with all available long-term follow-up data of 346 consecutive BrS patients and conducted telephone interviews about triggers and prodromes with patients who experienced at least one syncope episode. With these data, an expert committee classified patients with syncope into one of 4 categories: (1) NMS, (2) documented cardiac syncope, (3) suspected cardiac syncope, (4) other/unknown. Clinical data, triggers and prodromes were compared between these categories.

Results: Before the diagnosis BrS was made, 41% of patients experienced at least one syncope episode. In 54% of these patients the cause was NMS, while 40% had documented or suspected cardiac syncope. Cardiac syncope was more likely to occur in men (RR 2.1) and at an older age at first occurrence (41 vs. 24 years) than NMS. NMS occurred more frequently during standing (RR 0.5) and was more often preceded by sweating (RR 0.4) or paleness (RR 0.6) than documented cardiac syncope.

Conclusion: Many BrS patients experience benign NMS prior to BrS diagnosis. NMS is more likely when syncope occurs during standing or is preceded by prodromes such as sweating or paleness. The high prevalence of NMS must be taken into account during risk stratification in patients with BrS.

Orthostatic instability is an important co-factor and trigger of reflex syncope

A. Fedorowski1, P. Buri2, S. Juul-Møller2, O. Melander1, Dept. of Clinical Sciences, Lund University, Malmö, Sweden, 2Skåne University Hospital, Malmö, Sweden

Purpose: Two main components of a classical non-cardiac syncope are heart rate inhibition and loss of vascular tonus. Orthostatic hypotension (OH) rarely constitutes the sole etiology of syncope attacks but is often disregarded as a co-factor and important syncope reflex trigger thus being largely unreported in syncope studies.

Methods: A total of 380 patients (166 men; mean age, 60 yrs; range 15 to 90 yrs) with unexplained syncope attacks were enrolled. Patients were classified into cardiac (OH, CSH) or non-cardiac (NMS) syncope. Non-cardiac syncope (NMS) was defined as a reflex syncope triggered according to the expanded head-up tilt test protocol incl. carotid sinus massage, nitroglycerin provocation, and active standing test. Vasovagal syncope (VVS), carotid sinus hypersensitivity (CSH), and OH were diagnosed according to the current ESC guidelines (2009). All parts of the test were performed in order to explore a potential overlap between diagnoses. Multivariate-adjusted (age, gender, and BMI) logistic regression was applied to identify independent predictors of OH within VVS and CSH.

Results: An average of eight syncopal attacks over a period of 9 yrs was reported by investigated patients. A total of 211 patients (56%) were diagnosed with VVS, 72 (19%) with CSH, and 113 (30%) with OH of these 58 (16%) with the delayed variant of OH. In addition, postural orthostatic tachycardia syndrome (POTS) was found in 21 (6%) patients. In 46 (22%) out of all VVS patients, and 31 (43%) of CSH patients there was an overlap with orthostatic instability. Delayed OH was slightly more prevalent as a concomitant disorder compared to classical OH (13 vs. 9% for VVS, and 24 vs. 19% for CSH, respectively). Independent predictors of OH occurrence with VVS included advancing age (OR per 10 yrs: 1.28, 1.08-1.48, p=0.005), history of coronary event (OR:7.25, 2.03-25.9, p=0.002), history of cancer (OR:3.29, 0.94-11.4, p=0.062), and use of long-acting nitrates (OR:10.3, 0.97-110.1, p=0.05), whereas for overlap between OH and CSH there was a trend for lower age (OR per 10 yrs: 0.61, 0.53-1.01, p=0.055) and history of coronary event (OR: 3.91, 0.83-18.4, p=0.085). Moreover, baseline norepinephrine and renin levels were significantly increased among CSH patients with OH (OR per one SD: 3.19, 1.27-8.03, p=0.014) and 2.09, 1.12-3.92, p=0.022, respectively.

Conclusion: Orthostatic hypotension is often underestimated as a co-factor and trigger of reflex syncope attacks. This underlying hemodynamic instability may be found in one of five VVS patients and in almost every second patient with CSH. Higher respectively lower age and history of coronary event are common predictors of OH co-occurrence in VVS and CSH.
Background: Adenosine A2A receptor is involved in the regulation of heart rate and blood pressure. Plasma levels of adenosine are increased in patients with positive head-up tilt test (HUT). The presence of CC genotype in the adenosine A2A receptor gene polymorphism (1976 C/T) was shown to predispose to the positive head-up tilt test (HUT) in a study of normal volunteers and permit an accurate prediction of cardiovascular response to HUT in one study. The goal of the present study was to investigate the possible role of another adenosine A2A receptor gene polymorphism (1976 C/T) in the predisposition to vasovagal syncope.

Methods: 377 consecutive patients (161 men, 216 women, mean age 64 ± 15 years) with unexplained syncope underwent a head-up tilt test with fluid challenge. CC genotype was associated with a high risk of syncope (P = 0.002). Conclusion: Our observations suggest that vasovagal syncope may be prevented by avoiding a head-up tilt test with fluid challenge in patients with a CC genotype.
Ambiguity in detection of necrosis in IVUS plaque characterization algorithms

A. Katozian1, A. Karamalis1, G.A. Konig2, S.G. Cartier1, N. Navab1.
1Technical University of Munich, Munich, Germany; 2Medical Polyclinic, University of Munich, Munich, Germany; 1University Hospital (UZ) Brussels, Department of Cardiology, Brussels, Belgium

Background: We previously developed an atherosclerotic tissue characterization algorithm independent of transducer frequency, which could be applied on both radiofrequency (RF) and grayscale IVUS images. We morphed IVUS-histology images through deformable registration. We evaluated tissue colormap result, coined as prognosis histology (PH) image, with in vitro histology (40MHz) and in vivo with virtual histology (VH, 20MHz).

Results: Compared with histology, PH results demonstrated classification accuracy of 99.60%, 87.75%, and 90.87% for calcified, fibrotic, and fibro-lipidic tissues, respectively in 83 in vitro frames (30 cadaver hearts). Due to unsupervised construction of PH images, we could not detect necrosis. We also found 93.1±6.1%, 87.5±9.5%, 78.4±7.6%, and 61.3±21.3% accuracy for calcified, necrosis, fibrotic, and fibro-lipidic tissues among PH and VH images in 155 in vivo frames (4 patients). Among a sub-sample of 892 histology images (12 arteries) only 156 (17.5%) of them contained necrosis whereas this rate was 155/155 (100%) for all in vivo VH images with average of 40% plaque burden. Histology showed 1.6±2.2% of necrosis tissues per artery, whereas, it was 10.1±21.8% in VH images.

Conclusions: Necrosis appears to be overestimated in VH image while histology shows that it is a rare tissue. The necrosis pattern in VH is sparse (along lateral direction and around calcified plaques) whereas histology shows it is confluent (toward vessel wall). Often, VH necrotic pattern is due to rapid attenuation of IVUS signals in calcified plaques and is not related to tissue characteristics as confirmed by PH-histology cross validation. Detection of necrosis requires more advanced method, combining textual and spectral features.

Sensitivity of quantification methods to tracer arrival time for myocardial perfusion estimation in DCE-MRI

N. Zarinabad Nooralipour1, A. Chiribiri1, G. Haugoii1, M. Breeuwer1, E. Nagel1, 1King's College London, Division of Imaging Sciences, London, United Kingdom; 2Philips Healthcare, Imaging Systems – MR, Best, Netherlands

A common technique for calculating myocardial blood flow (MBF) is to track a bolus of contrast agent using DCE-CMR and measure MBF using quantitative methods. However flow quantification have been shown to be sensitive to the delay between the arterial and myocardial tissue tracer arrival time (Onset). Thus an accurate estimation of MBF relies on the precise identification of Onset. The aim of this study is to examine the effect of Onset on flow estimates in pixel-wise analysis.

Perfusion data were obtained from a hardware perfusion phantom whilst clinical data from CMR images performed on patients during adenosine-induced hyperaemia. Data were analyzed by a software, which uses iterative deconvolution to identify the optimal Onset. 3 deconvolution methods Fast, exponential bases and ARMA method have been compared. Figure 1 shows the MBF absolute error vs. timing shifts for the perfusion phantom. The lowest absolute error has been obtained when the actual Onset has been used. Comparing the three methods accuracy, ARMA has shown to have the lowest absolute error. Figure 2 shows the voxels wise perfusion maps in a patient with occluded LAD and a significant coronary artery lesion on the LCx and symptoms of angina. Onset estimation has been used for the analysis in Figure 2b which resulted in the identification of perfusion abnormalities in both the LAD and LCx territories. The latter was missed in an analysis with fixed Onset (Figure 2a).

Towards regional IILT variation in abdominal aortic aneurysms: integration between experimental data and computational finite element analyses

S. Celli1, P. Losi1, S. Beri2, 1Institute of Clinical Physiology of CNR, G. Pasquini Hospital, Massa, Italy; 2Gabriele Monasterio Foundation/CNR, Heart Hospital, Massa, Italy

Purpose: The intimal/sub intimar thickness (IILT) is present in the majority of abdominal aortic aneurysms (AAA) and it plays an important role in aneurysm wall weakening. However, little is known about architecture and mechanical properties of IILT and its effect on wall stress distribution is controversial.

The aim of this study is to characterise IILT material by integrating data from mechanical test (MT) and histological investigations (HI), and to investigate the role of IILT on the aortic wall stress by means of Finite Element (FE) computational analysis.

Methods: IILT specimens were extracted from patients undergoing elective open AAA, histological (Masson's trichrome and haematoxylin and eosin staining) and mechanical test were performed from different regions of the IILT. Computational FE models were developed on the bases of the CT patient-specific images and FE simulations have been performed by means of a specific probabilistic approach where the material properties and the main geometrical features were used as input variable. The maximum peak stress (MPS) has been chosen as output variable.

Results: Our results confirm the different structure along the IILT thickness (THK) and, in particular, indicate that the microstructure of IILT differs between the ventral and dorsal region. The lateral posterior area was stiffer than the budge region. The sensitivity FE analysis shows that the MPS is primarily affected by the THK and that, in particular, an increase in the THK decreases the MPS of about 30%.
BURNING ISSUES ACROSS THE SPECTRUM OF VALVULAR DISEASES

**P1287** Epigenetic regulation of 5-lipoxygenase in the phenotypic plasticity of valvular interstitial cells in aortic stenosis

E. Nagy, M.B. Back. Department of Medicine, Karolinska Institutet and Dept. of Cardiology, Karolinska University Hospital, Stockholm, Sweden

**Purpose:** Development and hemodynamic progression of aortic valve stenosis have been associated with increased inflammatory activity promoting valvular calcification. In this process, differentiation of valvular interstitial cells (VICs) into proinflammatory and osteogenic phenotypes may play a key role. Within the inflammatory pathway, 5-lipoxygenase (5-LO) pathway leading to leukotriene production was recently implicated in the pathophysiology of aortic stenosis. Since epigenetic mechanisms such as altered DNA methylation pattern regulate 5-LO promoter- and transcriptional activity, we hypothesized that epigenetic modulations of DNA methylation status may be involved in the phenotypic differentiation of VICs.

Therefore the aim of the present study was to examine the DNA methylation status and the transcriptional profile for 5-LO in valvular tissue and in VICs.

**Methods:** Human aortic valves, obtained from 17 patients undergoing aortic valve replacement surgery, were used for mRNA and DNA extraction. Primary cultures of VICs were isolated from human non-calcified aortic valve samples. Expression levels of 5-LO were determined by quantitative real-time PCR. For DNA methylation analysis, restriction enzymatic digestion followed by SYBR green-based real-time PCR was performed. LTB4 concentrations were determined by ELISA.

**Results:** Calciﬁed human aortic valve tissue exhibited a significantly lower degree of DNA hypermethylation of the 5-LO promoter (0.36±0.28%) compared with non-calcified valve tissue (2.1±0.50%; p=0.028), whereas 5-LO mRNA levels were increased 2.1±0.41-fold (p=0.001). There was a signiﬁcant and inverse correlation between 5-LO promoter methylation and 5-LO mRNA levels in aortic stenosis. In an additional group of 17 patients, we found that the degree of DNA hypermethylation of the 5-LO promoter was perfectly correlated with the 5-LO mRNA levels (r=-0.28%, p=0.001), respectively. Renal function was compared in patients who were not on dialysis when admitted or discharged from hospitalization (n=17) and in patients who had similar eGFR 70 ml/min vs. 76 ml/min (p=0.012).

**Conclusion:** Reducing gentamicin treatment in enterococcal IE to two weeks does not have a negative impact on relapse of IE or on mortality. Renal function however, is preserved only during the shorter treatment period.

**P1288** Two weeks of gentamicin treatment is adequate in enterococcal endocarditis

A. Dahl¹, R.V. Rasmussen¹, H. Bundgaard², C. Hassager², L.E. Bruun¹, P. Soegaard², N.E. Bruun¹

¹Department of Cardiology, Copenhagen University Hospital, Gentofte, Copenhagen, Denmark; ²Department of Cardiology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark; ³Department of Clinical Microbiology, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark

**Purpose:** Due to the nephrotoxic effects of aminoglycosides the Danish guidelines on infectious endocarditis (IE) were changed in January 2007 reducing gentamicin treatment in enterococcal IE from 4-6 weeks to only 2 weeks. In this study we have compared the outcome in patients with enterococcal IE treated in the years before and after endorsement of these new recommendations.

**Methods:** From October 2002 to October 2011, data has been prospectively collected, from consecutive IE patients at two tertiary centers in Denmark. Mortality, relapse of IE and changes of renal function were compared in patients with enterococcal IE admitted before and after January 2007. Renal function was assessed by the estimated glomerular filtration rate (eGFR). Information on hospital admissions and information on death were drawn from the Central Patient Registry and the Civil Registration Number Registry, respectively using each patient's civil registration number.

**Results:** A total of 122 patients were included, 58 were treated before, and 64 after January 2007, respectively. No significant differences were found between the two groups in baseline characteristics including co-morbidities. The number of patients undergoing surgery was also similar. The primary outcome, 3 months relapse free survival, did not differ between the groups: 72% vs. 81% (p=0.25). One year mortality from also identical: 33% vs. 27% (p=0.51). Patients treated before and after January 2007 received gentamicin for a mean of 27.5±16 days vs. 11±6 days (p=0.001), respectively. Renal function was compared in patients who were not on dialysis when admitted or discharged from hospitalization (n=17) and in patients who had similar eGFR 70 ml/min vs. 76 ml/min (p=0.21). However, at discharge the patients treated before 2007 had a lower eGFR 53±ml/min vs. 72±ml/min (p=0.004), and a significantly greater decrease in eGFR, 16±ml/min vs. 4±ml/min (p=0.012).

**Conclusion:** Reducing gentamicin treatment in enterococcal IE to two weeks does not have a negative impact on relapse of IE or on mortality. Renal function however, is preserved only during the shorter treatment period.

**Image processing for complex cardiovascular disease / Burning issues across the spectrum of valvular diseases**

**P1289** Prophylaxis for bacterial endocarditis: new guidelines did not improve the safety of patients during dental work

C. Piper, M. Ritschel, T. Kottmann, D. Horstkotte. Heart and Diabetes Center NRW, Ruhr-University of Bochum, Department of Cardiology, Bad Oeynhausen, Germany

**Purpose:** Since the 2007 revision of the guidelines to prevent bacterial endocarditis, only patients at a very high risk for infective endocarditis (IE) are considered candidates for antibiotic prophylaxis. It is unknown how this revision has influenced the management of IE prophylaxis by dentists.

**Methods:** Questionnaires containing 18 questions regarding indications for IE prophylaxis, patient-related and intervention-related risks, timing, dosage and choice of antibiotics have been answered by 430 randomly selected dentists in 2008. A slightly modified animal questionnaire was returned by 415 also randomly selected dentists in 2009/2010.

**Results:** Indication for IE prophylaxis after heart valve replacement was correctly reported most frequently during both surveys (results 2003 vs. 2009: 96.7%).
Results: TAVI was technically successful in all patients with overall mortality rates of 9% and 20% at 30 days and 1 year, respectively. PAR was observed in 113 patients (67%). 89 (53.3%) showing mild, 21 (12.6%) moderate and 3 (1.8%) severe PAR. Cardiovascular mortality at 30 days and 1 year was significantly increased in patients with moderate/more-severe PAR compared to those with no/mild PAR (46 vs. 4% and 73 vs. 7%, respectively, p<0.05). Analysis of intra-procedural invasive hemodynamics suggested a ΔP DAP-LVEDP of 18 mmHg and DPTI:SPTI of 0.7 as new predictors of mortality (figure 2).

Conclusions: At least moderate PAR after TAVI was observed in 14.4% of patients and associated with increased cardiovascular mortality. Hemodynamic evaluation using ΔP DAP-LVEDP and DPTI:SPTI as quantitative parameters provide excellent cut-off values of ≤ 18 mmHg and ≤ 0.7 for prediction of associated mortality.
Long-term efficacy of percutaneous mitral valve repair using the MitraClip® system may depend on acute MR reduction: insight in the Mitra-SWISS registry

D. Suerder1, G.B. Pedrazzini1, T. Moccetti1, P. Erne2, M. Zuber2, R. Jeger2, M. Moccetti1, P. Billag6, J. Gruenenfelder5, R. Cori4, 1Foundation Cardiocentro Ticino, Lugano, Switzerland; 2Luzern Cantonal Hospital, Department of Cardiology, Luzern, Switzerland; 3University Hospital Basel, Department of Cardiology, Basel, Switzerland; 4University Hospital Zurich, Cardiovascular Center, Department of Cardiology, Zurich, Switzerland; 5University Hospital Zurich, Zurich, Switzerland; 6University Hospital, Department of Cardiology, Lucerne, Switzerland

Introduction: Percutaneous mitral valve repair (MVR) utilizing the MitraClip® system has become a valid alternative for patients with severe mitral regurgitation (MR) and high operative risk. However, factors predisposing for long term clinical success are still unknown. Presenting the 12-months results of the first 100 consecutive patients treated with MVR in Switzerland, we aim to learn more about this.

Methods: Clinical, echocardiographic and procedural data are prospectively collected and centrally stored in an online database. After assessment of all parameters, survival time has been associated to different variables using log-rank test and Cox regression and a Kaplan-Meier curve estimate has been provided.

Results: Acute procedural success (APS), defined as a successful Clip-implantation with a residual MR grade of <3+, was achieved in 85%. MR grade remained stable for most of the patients over follow up and NYHA class decreased from class 3 to 2. Mortality at 30 days and 12 months was 5% and 16% respectively. Cox regression analysis indicated an association between the following parameters and overall survival:

- discharge MR grade - p<0.0002 (see figure).
- occurrence of congestive heart failure after the procedure - p<0.0005
- APS - p<0.0018

There was no association with survival depending on whether patients had functional MR or degenerative MR.

Discussion: In this series of 100 high-risk patients with severe MR, treated with percutaneous MVR, MR reduction appears to be stable in most patients with initially good results. Strong predictors of survival were absence of heart failure after also after percutaneous MVR.

ADVANCES IN DIAGNOSIS AND PROGNOSTIC EVALUATION OF CARDIOMYOPATHIES

The etiology of amyloidosis influences pathophysiology and outcome of heart failure in amyloidotic cardiomyopathy

C. Quarta, S. Longhi, C. Gagliardi, M. Lorenzini, A. Milandri, F. Del Corso, F. Grigioni, L. Potena, I. Gallelli, C. Rapezzi. Institute of Cardiology, Bologna, Italy

Purpose: In amyloidotic cardiomyopathy (AC) heart failure (HF) has traditionally been attributed to diastolic dysfunction, but little is known on the features of HF in relation to the specific etiology of amyloidosis. We present data for the three main etiologies of AC: light-chain (AL), hereditary (ATTR) and non-mutant (SSA) transthyretin-related.

Methods: Among the 260 patients diagnosed with AC at our Centre in 1990-2011, we analyzed clinical, ECG, echocardiographic, hemodynamic and survival profiles of those with advanced HF (NYHA III-IV) all diagnosis.

Results: Ninety-nine (38%) had HF at diagnosis (Table). Survival curves are shown in the figure.

Table 1

<table>
<thead>
<tr>
<th>Etiology</th>
<th>NYHA III-IV (% at diagnosis)</th>
<th>NYHA III-IV (% at follow-up)</th>
<th>Cause of death</th>
<th>SCD %</th>
<th>30-day mortality</th>
<th>12-month mortality</th>
<th>5-year mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>AL</td>
<td>38</td>
<td>16</td>
<td>54.5%</td>
<td>31.4</td>
<td>5.3%</td>
<td>16%</td>
<td>16%</td>
</tr>
<tr>
<td>ATTR</td>
<td>37</td>
<td>15</td>
<td>43.1%</td>
<td>29.4</td>
<td>6%</td>
<td>18%</td>
<td>18%</td>
</tr>
<tr>
<td>SSA</td>
<td>36</td>
<td>14</td>
<td>53.6%</td>
<td>31.6</td>
<td>5.3%</td>
<td>16%</td>
<td>16%</td>
</tr>
</tbody>
</table>

Conclusion: In AC, both pathophysiology and outcome of HF are profoundly influenced by the etiology of amyloidosis. Despite shorter disease duration and lesser left ventricular wall thickness, AL etiology shows the worst outcome due to a combination of chronic interstitial infiltration and acute toxic effect of circulating light chains.

Validation of the 2003 ACC/ESC guidelines on the risk stratification of sudden cardiac death in hypertrophic cardiomyopathy

C. O’Mahony1, M. Tome-Estebaranz2, A. Pantazis2, S. Dickie3, W. McKenna1, P. Elliott1. 1University College London, London, United Kingdom; 2University College Hospitals London NHS Trust, University College London (UCL), London, United Kingdom

Purpose: The ACC/ESC 2003 guidelines on hypertrophic cardiomyopathy (HCM) recommend identifying patients at high risk of sudden cardiac death (SCD) by assessing non-sustained ventricular tachycardia, syncope, abnormal blood pressure response, family history of SCD and ventricular hypertrophy. The aim was to examine whether the accumulation of risk factors reflects increased SCD risk and quantify the predictive accuracy of different risk factor profiles.

Methods: A retrospective cohort study of 1635 consecutively evaluated HCM patients. The effect of accumulating risk factors on SCD was examined using Cox proportional hazards method. The performance of the guidelines in discriminating patients who would suffer SCD in the future was examined using time-dependent receiver operating characteristic curves, and calculating time-dependent positive (PPV) and negative (NPV) predictive values for each threshold.

Results: During follow-up (12175 patient years), 93 patients (6%) suffered SCD or equivalent with an annual rate of 0.8% and 5-year cumulative incidence of 4%. Compared with patients without any risk factors, those with multiple risk factors had an increased risk of SCD (in the presence of 2 risk factors HR 2.6, p=0.002; 3 risk factors HR 6.2, p<0.0001; 4 or more risk factors HR 8.3,p=0.0001). A single risk factor was not associated with increased risk of SCD (HR 1.6, p=0.131). The area under the curve was 0.57 at 1 year, 0.58 at 5 years and 0.55 at 10 years. The NPV and PPV are shown in the figure.

Figure 1. Predictive value of risk factor profiles

Table 1

<table>
<thead>
<tr>
<th>Risk factor profile</th>
<th>PPV</th>
<th>NPV</th>
<th>PPV</th>
<th>NPV</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>0 risk factors</td>
<td>5.7</td>
<td>9.6</td>
<td>9.6</td>
<td>9.6</td>
<td>9.6</td>
<td>9.6</td>
</tr>
<tr>
<td>2 risk factors</td>
<td>82%</td>
<td>14%</td>
<td>14%</td>
<td>14%</td>
<td>14%</td>
<td>14%</td>
</tr>
<tr>
<td>3 risk factors</td>
<td>41%</td>
<td>31%</td>
<td>31%</td>
<td>31%</td>
<td>31%</td>
<td>31%</td>
</tr>
<tr>
<td>4 risk factors</td>
<td>63%</td>
<td>72%</td>
<td>72%</td>
<td>72%</td>
<td>72%</td>
<td>72%</td>
</tr>
</tbody>
</table>

Conclusion: The aggregation of risk factors in a particular patient is associated with increased risk of SCD. Even though the current strategy can identify patients at high risk, the PPV remains low even in the presence of multiple risk factors. The NPV of the absence of risk factors is excellent.
Prognostic value of N-terminal pro-brain natriuretic peptide in outpatients with hypertrophic cardiomyopathy

R. D’Amato1, B. Tomberli2, E. Servettini2, R. Spoladore2, F. Cecchi3, F.G. Camici3, I. Gliotti3, H. San Raffaele Hospital (IRCCS), Department of Cardio-Thoracic-Vascular, Milan, Italy; 2Careggi University Hospital, Referral Center for Cardiomyopathies, Florence, Italy

Background: N-terminal pro-brain natriuretic peptide (NT-proBNP) predicts adverse outcomes in patients with chronic heart failure. In patients with hypertrophic cardiomyopathy (HCM), NT-proBNP levels are known to be elevated and correlate with NYHA class and left ventricular outflow tract obstruction; however the value of NT-proBNP as an independent predictor of outcome in HCM remains undefined.

Methods: We evaluated serum levels of NT-proBNP in 286 HCM outpatients attending the Referral Center for Myocardial Diseases. Patients with known coronary artery disease (n=15) and systolic dysfunction (LV ejection fraction <50%); n=20) or incomplete follow-up (n=69) were excluded; the remaining 183 patients (mean age 49.7±17.3 years, 64.4% male, 36%obstructive) were followed for 47±34 months. The primary endpoint (PE) was a composite of cardiovascular death, heart transplantation and resuscitated cardiac arrest. Secondary endpoint (SE) was a composite of acute heart failure requiring hospitalization, progression to end-stage disease and septostomy or alcohol septal ablation.

Results: Median NT-proBNP for the 183 patients was 615.1 pg/ml (range 21.8-16031 pg/ml). The occurrence of PE during follow-up was significantly different across tertiles of NT-proBNP: the highest tertile with NT-proBNP value >1025 pg/ml had 5 PE occurred in the lowest tertile (<310 pg/ml), 6% in the mid (310-1025 pg/ml), and 15% in the highest tertile (>1025 pg/ml; overall p<0.01). Furthermore, patients in the highest NT-proBNP tertile had higher rate of SE (55.7%) than those in the lowest (19.6%; p=0.001). Among non-obstructive patients, a NT-proBNP value >1025 pg/ml identified patients at increased risk of cardiac events (HR 2.1, 95%CI 1.1-3.8, p=0.01). Patients in the highest NT-proBNP tertile had higher rate of SE (55.7%) than those in the lowest (19.6%; p=0.001). Among non-obstructive patients, a NT-proBNP value >1025 pg/ml identified patients at increased risk of cardiac events (HR 2.1, 95%CI 1.1-3.8, p=0.01). Non-obstructive patients in the highest NT-proBNP tertile had higher rate of SE (55.7%) than those in the lowest (19.6%; p=0.001). Among non-obstructive patients, a NT-proBNP value >1025 pg/ml identified patients at increased risk of cardiac events (HR 2.1, 95%CI 1.1-3.8, p=0.01). Non-obstructive patients in the highest NT-proBNP tertile had higher rate of SE (55.7%) than those in the lowest (19.6%; p=0.001).

Conclusions: In outpatients with HCM, NT-proBNP is an independent predictor of heart-failure related events, but not of overall cardiovascular mortality. Such limitation is likely due to the confounding effect of arrhythmic events unrelated to heart failure.

Gender-specific differences in cardiac disease penetrance and mortality in lamin A/C mutation carriers

I.A.W. Van Rijssingen1, E. Arbustini2, P.M. Elliott3, J. Mogensen4, I.P. Van Tintelen1, A. Perrotti2, S. Panukiewitz4, P. Charron4, L. Bortolotti1, Y.M. Pitt4, 1Academic Medical Center, Amsterdam, Netherlands; 2Foundation IRCCS Polyclinic San Matteo - University of Pavia, Pavia, Italy; 3The Heart Hospital, University College London Hospital Trust, London, United Kingdom; 4Aarhus University Hospital, Skejby, Aarhus, Denmark

Purpose: Mutations in Lamin A/C (LMNA) cause a variety of clinical phenotypes, including dilated cardiomyopathy. LMNA is one of the most prevalent mutated genes in dilated cardiomyopathy, which is associated with a high risk of arrhythmias, sudden cardiac death, and heart failure. However, it is unclear whether there are gender-specific differences in cardiac disease penetrance and mortality in LMNA mutation carriers.

Methods: In an multicenter cohort of 269 LMNA mutation carriers, we evaluated gender-specific penetrance of cardiac involvement and major cardiac events. Furthermore, we determined all cause mortality of the mutation carriers (main outcome measure: Standardized Mortality Ratio (SMR)).

Results: Cardiovascular penetrance was age-dependent and almost complete at the age of 70years. The presence of a left ventricular ejection fraction <45% was similarly high in men (p=0.001). However, there was no difference between genders regarding atrioventricular-block, atrial tacharrhythmias and non-sustainedventricular tachycardia. The major events malignant ventricular arrhythmias (24%), 8% and end-stage heart failure (8 vs. 14%), were also significantly more prevalent in men than in women (p=0.001 and p=0.006, respectively). All-cause mortality of mutation carriers was significantly increased (SMR 4.0, 95%CI: 2.8-5.2) between the age of 15 until 75 years. Mortality in men was even higher than in women (HR 2.2, 95% CI 1.2-4.3).

Conclusions: This large cohort of LMNA mutation carriers does confirm high cardiovascular disease penetrance and mortality and a high mortality in mutation carriers.Besides, our study demonstrates that male mutation carriers have a worse prognosis due to a high prevalence of malignant ventricular arrhythmias and end-stage heart failure.

High level of physical activity may impair myocardial function in patients with arrhythmogenic right ventricular cardiomyopathy

J. Sabbernig1, N.E. Hasselberg1, A.G. Holst1, T. Edvardsen1, K.H. Haugaa2, P.K.H. Haugaa2, 1University of Oslo, Rikshospitalet University Hospital, Department of Cardiology, Oslo, Norway; 2Rigshospitalet - Copenhagen University Hospital, Heart Centre, Department of Cardiology, Copenhagen, Denmark

Purpose: Exercise is supposed to increase the risk of ventricular arrhythmias in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC). However, the impact of exercise on myocardial function in ARVC has not been fully described.

Methods: In all, 98 Norwegian ARVC patients and mutation positive family members from the Nordic ARVC registry were studied (age 44±17years, 55% male). Patients with activity >750 MET-min/week were defined as athletes. LV ejection fraction (EF), right ventricular outflow tract (RVOT) diameter and RV diastolic di-ameter (RVDD) were assessed by echocardiography. Exercise induced VT was defined as VT or VF occurring during significant exercise.

Results: Of the 98 ARVC patients, 26 (27%) were defined as athletes (69% male). Athletes were younger than non-athletes (39±15 vs 46±17years, p=0.04). Athletes were not more frequently probands than non-athletes (p=0.26) and occurrence of total VT did not differ (p=0.33). However, exercise induced VT occurred in 31 patients (34%) and was more frequent in athletes (54%) compared to non-athletes (24%) (p=0.01). Athletes had lower LVEF compared to non-athletes (54±7 vs 59±3, p=0.03). RVOT diameter (36±7 vs 30±7mm, p=0.01) and RVDD (46±7 vs 39±8mm, p=0.01) were increased in those with exercise induced VT (p=0.01).

Conclusions: LV EF was reduced in athletic ARVC patients. Reduced EF was related to increased RV dimensions in athletes, but not in non-athletes. RV dimension differences related to exercise induced VT. These findings indicate that history of vigorous exercise may reduce LV function in ARVC patients in addition to be a risk factor for VT during ongoing exercise.

Influence of genetics in sudden death risk in hypertrophic cardiomyopathy

A.J. Romero Puche1, I. Perez Sanchez2, M.J. Oliva3, F. Ruiz Espejo2, I. Gomez Milanes2, E. Garcia Molina2, M. Sabater2, J. Lacunza3, J.R. Gimeno3, M. Valdes4, 1University Hospital Reina Sofia, Department of Cardiology, Murcia, Spain; 2University Hospital Virgen de la Arrixaca, Murcia, Spain; 3University Hospital Virgen de la Arrixaca, Department of Cardiology, Murcia, Spain; 4University of Murcia, School of Medicine, Department of Cardiology, Murcia, Spain

Purpose: Characterization of patients at risk for sudden death (SD) is one of the challenges in hypertrophic cardiomyopathy (HCM). Our purpose is to determine the risk of SD according to the causal mutations identified in our clinical experience.

Methods: We included all patients with diagnosis of HCM with known responsible mutation. Familial history was reviewed in search of SD among their relatives. We analyzed prevalence of SD and performed time-to-event analysis to determine risk profile in the most prevalent mutations.

Results: We had positive genetic results in 139 affected patients with HCM (69% males, age 50±16 yrs.). Most prevalent mutations were, in order of prevalence, MYBPC3-IVS23+1G-A with non-IVS23+1G-A 25%; MYBPC3-Arg891fs 4.3%; MYBPC3-A107fsX116 10.0%; MYH7-T1377M 6.3%; MYBPC3-A216T 14.3% (Chi square p=0.1; when comparing IVS23+1G-A with non-IVS23+1G-A, p=0.007). Time-to-event analysis showed a trend towards increased risk in..
Definition of clinical relevant Fabry disease by the biomarker lyso-Gb3 in patients with alpha-galactosidase A mutations

M. Niemann 1, A. Rollf 2, F. Breuning 1, M. Beer 1, S. Herrmann 3, G. Enti 1, C. Wanner 2, F. Weidemann 2, 1Medicalinische Klinik I, Wuerzburg, Germany; 2Abbrecht-Kassel Institute for Neuroregeneration, Rostock, Germany; 3Radiologische Klinik, Wuerzburg, Germany.

Background: Fabry disease is a very heterogeneous and heterophenotypic disease caused by private mutations in the alpha-galactosidase A (α-galA) gene. The aim of this study was to define clinical relevant Fabry cardiomyopathy in patients with α-galA mutations by the biomarker lyso-Gb3.

Methods and Results: 124 Fabry patients were investigated with a comprehensive clinical work up, genetic analysis and laboratory testing, including α-galA activity and lyso-Gb3 measurement. An extensive family screening was carried out including clinical work up of relatives. The study consisted of two parts: Previously described mutations were included in the evaluation study (n=72), new mutations in a validation study (n=52).

Evaluation study: First patients were subdivided in two groups: 1) "classical cardiomyopathy mutations" = mutations with clinical relevant Fabry cardiomyopathy (n=55) and 2) "atypical mutations" = comprising patients with questionable Fabry cardiac involvement and patients without organ involvement (n=17). Afterwards the lyso-Gb3 was determined. All patients with atypical mutations had lower lyso-Gb3 levels than any of the patients with classical Fabry cardiomyopathy. A cut off of 2.6 ng/ml separated the two groups.

Validation study: Six out of the 52 patients with new mutations showed a lyso-Gb3 below the cut-off of 2.6 ng/ml. Clinical investigation, blinded to the results of lyso-Gb3, revealed that none of these patients or their relatives showed classical cardiac involvement. In contrast, clinical characterisation of the patients with new α-galA mutations and lyso-Gb3 above 2.6 ng/ml suggested classical Fabry cardiomyopathy mutations, without exception. Moreover, 25 female patients from the complete cohort had an agalA activity around the normal threshold (0.3-0.5 nmol/min/mg protein). Out of these 25 female patients with atypical mutations, without exception.

Conclusion: Our data show that the definition of clinical relevant Fabry cardiac mutations can be done by the biomarker lyso-Gb3. This is especially helpful in new mutations and women with agalA activity around the normal threshold.

Echocardiographic predictors of hard events in patients with tako-tsubo cardiomyopathy

R. Citro 1, F. Rigo 1, G. Provenza 1, D. Bovelli 1, A. D'Arenta 1, M. Mira 1, R. Guicciardi 1, F. Piccione 1, E. Bossonne 1, J. Salerno 1, Uriarte 1 on behalf of Tako Tsubo Italian Network. 1University Hospital San Giovanni di Dio Ruggi d'Aragona, Department of Cardiology, Salerno, Italy; 2Umberto I Hospital, Department of Cardiology, Mestre-Venice, Italy; 3Santa Maria Hospital of Terni, Department of Cardiology, Terni, Italy; 4Second University of Naples, Department of Cardiovascular, Naples, Italy; 5University of Insubria, Hospital of Circolo and Foundation Macchi, Department of Cardiology, Varese, Italy.

Aim: To investigate the echocardiographic features and their prognostic implication of tako-tsubo cardiomyopathy (TTC).

Methods: 227 consecutive pts (66.2±12.2 years; 90.3% females) enrolled in Tako-tsubo Italian Network underwent comprehensive transthoracic echocardiography at admission and at 6 weeks follow-up. Patients with and without hard events (acute heart failure, cardiogenic shock, VT/VF, stroke and death) have been compared.

Results: In the overall study population LVEDV (from 91.9±22.7 to 66.4±26.4 ml, p = 0.015), LVEF (from 37.5±5.3 to 35.5±7.6%, p<0.001), WMIs (from 1.83±0.25 to 1.20±0.21, p<0.001), EF (from 11.05-4 to 71.5±2.26, p<0.001), LV area change (from 37.3±8.8 to 41.1±8.5%, p<0.001) and PASP (from 40.5±10.9 to 28.6±7.12 mmHg, p<0.003) significantly improved from admission to discharge. LVOT obstruction (28 pts; 12.3%), = moderate MR (43 pts; 18.9%) and RV involvement (33 pts; 15%), were reported. Hard events occurred in 66 pts (28.6%). LVEDV (97.3±21.3 vs 89.4±23 ml; p =0.03), LVEF (63.3±14.8 vs 54.4±14.5 ml; p <0.001), EF (35.6±1.4 vs 36.6±4.4%, p =0.01), WMIs (1.94±0.26 vs 1.78±0.24, p <0.001), E/e' (13.8±4.3 vs 9.7±3.3, p<0.001), PAP (47.1±12.1 vs 37.6±9.2 mmHg, p <0.001), RV area change (32.8±10.5 vs 39.5±6.9%, p <0.001), RV involvement (15 vs 18%, p <0.003), severe MR (24 vs 19, p =0.003) were significantly different in pts with vs without hard events. Univariate and multivariate analysis of predictors of hard events are listed in the table.

Endothelial progenitor cells to the ischemic heart. Involvement of the micro-RNA-150-3pCXCR4-SDF-1α pathway

E. Gorelli 1, M. Boutouyrie 1, M. Rolland-Turner 1, C. Nicolas 1, F. Maskalí 2, P.Y. Marie 3, Y. Devaux 2, J.R. Wagner 1, Centre de Recherche Public- Santé Luxembourg. Luxembourg; 2University Hospital of Nancy - Hospital Brabois, Vandoeuvre les Nancy, France; 3Hospital Centre, Luxembourg, Luxembourg.

Purpose: Endothelial progenitor cells (EPC) represent a promising option to regenerate the infarcted myocardium. This therapy is limited by the number of cells recruited to the injured sites. Mobilization of EPC from the bone marrow and migration are mainly under the control of the chemokine stromal cell-derived factor 1α (SDF-1α), which binds to the cell surface receptor CXCR4. Adenosine is pro-angiogenic because of its effects on CXCR4 is unknown. Therefore, we determined whether adenosine affects the CXCR4-SDF-1α pathway.

Methods: EPC were obtained from peripheral blood mononuclear cells of healthy volunteers. Expression of chemokines and their receptors was evaluated using microarrays and quantitative PCR. Cell surface expression of CXCR4 was assessed by flow cytometry. A modified Boyden chamber assay was used to measure the migration of EPC. Recruitment of EPC to the infarcted heart was investigated in rats after permanent occlusion of the left anterior descending coronary artery (n=18). Rats received twice daily injections of NaCl (control group, n=6), or the stable analog of adenosine 2-chloroadenosine (CADO, n=6), or CADO with the non selective antagonist of adenosine receptors 6 (s-puflfenyl)thephyline (8-SPT, n=6). Treatments were given for 2 months, starting 7 days after coronary ligation. 6 rats were sham-operated. EPC recruitment was evaluated by immunohistochemistry.

Results: Microarrays and PCR experiments showed that adenosine increased CXCR4 mRNA expression (3-fold; P <0.001). Cell surface expression of CXCR4 was also increased by adenosine. Expression of miR-150, a microRNA known to regulate CXCR4 expression, was decreased (2-fold; P <0.001). We determined that EPC express A3, A2A and A2B adenosine receptors. Using pharmacological inhibitors of signaling pathways and RNA interference, we identified the A2B receptor as mediator of the effect of adenosine on CXCR4. EPC migration towards recombinant SDF-1α or conditioned medium from human primary cardiac fibroblasts was enhanced by pre-incubation of the cells with 10μM adenosine. This effect was abolished by pre-incubation with anti-CXCR4 blocking antibodies. Administration of CADO to rats after induction of myocardial infarction stimulated EPC recruitment to the border zone. This effect was prevented by administration of 8-SPT.

Conclusion: We have shown that adenosine increases the expression of CXCR4 in EPC and stimulates their recruitment to the heart after myocardial infarction. These results suggest that adenosine may be used to enhance the capacity of EPC to revascularize the ischemic heart.
Sitagliptin therapy enhances the number of circulating endothelial progenitor cells and angiogenesis: evaluations in vitro and in the rat critical limb ischemia model. 

S. Chua 1, J.J. Sheu 2, Y.L. Chen 1, H.K. Yip 1, Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Kaohsiung, Taiwan; 2Kaohsiung Chang Gung Memorial Hospital Chang Gung Univ, College of Medicine, Cardiovascular Surgery, Kaohsiung, Taiwan

Purpose: We propose the hypothesis that sitagliptin is capable of increasing blood flow in the rat critical limb ischemia (CLI) model by enhancing angiogenesis.

Methods: Adipose tissue from adult-male Fischer 344 rats (n=6) were cultured in endothelial progenitor cell (EPC) culture medium for 14 days with (25 μM) or without sitagliptin. CLI was induced by ligation of the left femoral artery. Rats (n=32) were equally separated into four groups: untreated controls (group 1), sitagliptin (4 mg/kg/day, group 2), CLI (group 3), and CLI with sitagliptin (group 4).

Results: In vitro, 7 and 14 days after cell culture, EPC biomarkers assessed by flow cytometry (Sca-1+/CD31+, CXCR4+, CXCR4+/CXCR4+ and CXCR4-+CXCR4-) and Western blot (VEGF, CXCR4, SDF-1α) were remarkably higher in group 4 than in the other groups (all p<0.01). In vivo, 2 and 14 days after the CLI procedure, circulating EPC (Sca-1+/CD31+, Sca-1+, CD31+ numbers were significantly higher in group 4 than in the other groups (all p<0.001). Additionally, the mRNA and protein expression of angiogenic biomarkers (CXCR4, SDF-1α, and VEGF), immunofluorescent staining of angiogenic cells (CXCR4+/SDF-1α+, CXCR4+/VEGF+) and immunohistochemical staining of small (<15 μm) vessel numbers in the ischemic area were significantly higher in group 4 than in the other groups (all p<0.001). Furthermore, laser Doppler showed that the ratio of ischemic/normal blood flow was remarkably higher group 4 than in group 3 by day 14 after the CLI procedure (all p<0.001).

Conclusions: Sitagliptin therapy enhances circulating EPC numbers, angiogenesis, and blood flow in the CLI area.

Methods and Results: Wild-type C57/Bl6 mice and ApoE−/− mice were used for these studies. Aleglitazar was administered at 10 mg/kg/day ip versus vehicle for 3 weeks. ApoE−/− mice were fed a western-type diet (21% fat, 19.5% casein and 1.5% cholesterol) for 6 weeks, with and without aleglitazar, to induce vascular dysfunction and atherogenesis. Body weight, blood pressure, heart rate, plasma cholesterol, triglycerides, glucose and electrolytes were monitored during the study. Plasma adiponectin, indicating activation of PPAR receptors, was up-regulated by aleglitazar (>5-fold in both strains. Sca-1/VEGFR-2-positive EPC were quantified by FACS analysis. In C57/Bl6 mice, aleglitazar increased the number of circulating blood EPC to 153±8.6%, and bone marrow-derived EPC to 197±21% compared with vehicle controls. Spleen-derived cultured EPC (DiDL/Dlectin-positive) were also increased by aleglitazar to 182±8.4%. Stromal cell-derived factor-1α-dependent progenitor capacity of cultured EPC, assessed ex vivo using a modified Boyden chamber assay, was also increased by aleglitazar to 176±5.5% compared with controls. Neangiogenesis increased by 2-fold after aleglitazar treatment. The effects of aleglitazar on EPC and atherogenesis in an environment of endothelial dysfunction were studied in ApoE−/− mice. In aleglitazar-treated ApoE−/− mice, DiDL/Dlectin-double positive EPC increased to 256±14% of controls. Aleglitazar increased EPC migratory capacity to 149±13.9%. Endothelial-dependent vasodilation, assessed in isolated aortic ring preparations, was significantly improved by aleglitazar. Atherosclerotic lesion area in the aortic sinus, as assessed by quantitative histomorphometry, showed a reduction of 22.8±7.8% of control ApoE−/− mice (all experiments, n=6 per group, p<0.05).

Conclusions: Our data show that dual PPAR-α/γ activation exerts protective vascular mechanisms in mice, including improvement of endothelial function and up-regulation of both number and functionality of endothelial progenitor cells. Clinical studies to investigate the effects of aleglitazar on EPC and vascular function in patients with cardiovascular disease appear warranted.

The balanced dual PPAR-alpha/gamma agonist aleglitazar up-regulates endothelial progenitor cells, enhances endothelial vasodilation and reduces atherogenesis in mice.

C. Gerisch, J. Poess, V. Pavlickova, M. Boehm, U. Laufs, Saarland University Hospital, Dept. of Internal Medicine III, Cardiology, Angiology & Intensive Care, Homburg/Saar, Germany

Purpose: Bone marrow-derived endothelial progenitor cells (EPC) improve endothelial function, promote vascular repair and enhance angiogenesis. The vascular effects of combined activation of PPAR-α and γ receptors are not known. We therefore studied the effects of aleglitazar, a balanced dual PPAR-α/γ agonist, on EPC, endothelial function and atherosclerosis in mice.

Methods: Aleglitazar increased EPC migratory capacity to 149±13.9%. Endothelial-dependent vasodilation, assessed in isolated aortic ring preparations, was significantly improved by aleglitazar. Atherosclerotic lesion area in the aortic sinus, as assessed by quantitative histomorphometry, showed a reduction of 22.8±7.8% of control ApoE−/− mice (all experiments, n=6 per group, p<0.05).

Conclusions: Our data show that dual PPAR-α/γ activation exerts protective vascular mechanisms in mice, including improvement of endothelial function and up-regulation of both number and functionality of endothelial progenitor cells. Clinical studies to investigate the effects of aleglitazar on EPC and vascular function in patients with cardiovascular disease appear warranted.

Kinin-mediated recruitment of circulating progenitor cells promotes endothelial healing: alterations in patients with coronary disease.

N. Krasnek1, K. Kuschnerus2, M. Mueller3, T. Speer4, S. Briand5, M. Bader4, P. Mageddu5, T.F. Luescher2, U. Landmesser2. 1University of Zurich-Irchel, Department of Anatomy and Physiology, Cardiovascular Research, Zurich, Switzerland; 2University Hospital Zurich, Cardiovascular Center, Department of Cardiology, University of Zurich-Irchel, Department of Anatomy and Physiology, Cardiovascular Research, Zurich, Switzerland; 3University Hospital Zurich, Cardiovascular Center, Department of Cardiology, University of Zurich-Irchel, Department of Anatomy and Physiology, Cardiovascular Research, Zurich, Switzerland; 4Max Delbruck Center for Molecular Medicine, Berlin, Germany; 5University of Bristol, Bristol, United Kingdom.

Background: Kinins derived from the vascular wall may not only impact on resident endothelial cells, but may also have the potential to promote recruitment of distinct circulating cell types which bear the B2 kinin receptor (B2R). We therefore investigated the role of this mechanism for endothelial healing in healthy subjects (HS) and in patients with coronary artery disease (CAD).

Methods: Expression of the B2R on peripheral blood mononuclear cell subsets of CAD patients and age-matched HS was assessed by flow cytometry. Adhesion to an endothelial monolayer and subsequent closure of a scratch endothelial gap, supported by paracrine effects of the adhering cells were studied in vitro. In vivo, recruitment of systemically injected cells to injured carotid endothelium, and endothelialization of the injured artery were assessed in B2R blockade by icatibant, transplantation of B2R-deficient bone marrow cells (B2R−/− BM), as well as adenoviral B2R overexpression were used to verify the relevance of the B2R.

Results: In HS, B2R was low expressed (~1000MFI) on CD141+ monocytes and on lymphocytes, but high in angiogenic Tie2+ or KDR+ monocytes and in KDR+ or CXCR4+ angiogenic progenitor cells (PC) (2517 ± 7516MFI; P < 0.05 vs. CD141+). Recruitment of healthy CXCR4+ PC to endothelial cells or to the injured murine vascular wall was blocked by B2R inhibition in vitro (-67% vs. vehicle, P < 0.05) and in vivo (-56% vs. vehicle; P < 0.05), while adhesion of CD141hi monocytes was unchanged, indicating a critical role of B2R for vascular homing of CXCR4+ PCs, but not of CD141+ monocytes. In vivo endothelial healing was lower in mice receiving B2R−/− BM than in mice receiving B2R+/+ BM (21% vs. 36.1%; P < 0.05). Kinin receptor expression on Tie2+ or KDR+ PC (175% vs. H; P < 0.05) and on angiogenic “early outgrowth cells” (EOC) (68% vs. HS; P < 0.05) was reduced in CAD patients. Adhesion of CXCR4+ PC from CAD patients to endothelial cells was markedly reduced versus CXCR4+ PC of HS and not regulated by the B2R. Adenoviral B2R overexpression rescued the capacity of CAD EOCs to support re-endothelialization in vivo, associated with enhanced vascular recruitment of CAD EOC after B2R overexpression.

Conclusions: We newly describe that vascular kinins do not only act via the endothelial B2R, but can also recruit endothelial-supportive circulating cells to the vessel wall via B2R on these circulating cells. The loss of B2R expression on circulating endothelial repair-promoting cells might jeopardize the healing of endothelial injuries and thus contribute to the pathophysiology of endothelial dysfunction in CAD.
Intranasal instillation of diesel exhaust particles impairs endothelial progenitor cells and increases atherosclerosis in mice

J. Poess, D. Lorenz, C. Gensch, V. Pavlickova, C. Werner, U. Laufs, S. van der Meer, J. Boehringer, U. Laufs, Saarland University, School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; 2Kansai Medical University, Moriguchi, Japan; 3Kyoto Medical Center, National Hospital Organization, Kyoto, Japan; 4Kyoto University Graduate School of Medicine, Department of Cardiovascular Medicine, Kyoto, Japan; 5Rak肥 Oasis Medical Center General Hospital, Hyogo, Japan.

Background and aims: Exposition to fine particulate matter is associated with increased cardiovascular morbidity and mortality. However, the underlying patho-physiological mechanisms of vascular damage are incompletely understood. Number and function of endothelial progenitor cells (EPC) predict outcome of patients with vascular disease. The aim of the present study was to examine the effects of diesel exhaust particles (DEP) on EPC and atherosclerosis in C57Bl/6 and ApoE−/− mice.

Methods and results: C57Bl/6 mice were exposed to diesel exhaust particles (DEP, standard reference material 1655b, National Institute of Standards in Technology, USA) or solvent (PBS) for three weeks. DEP were applied intranasally on 5 days per week in a dosage of 2 μg/application. EPC were quantified by counting the number of spleen-derived, DilDLD and lectin positive cells. Exposure to DEP reduced DilDLD/lectin positive cells to 58.37±5.63% (n = 6, p < 0.005). Mitotitary capacity as key parameter of EPC function was determined in a modified Boyden chamber using SDF-1 as chemotraactant. Treatment with DEP reduced migratory capacity of EPC to 25.6±5.84% (n = 6, p < 0.005). Atherosclerotic plaque area was quantified by histomorphometric analysis of cryostat sections of the aortic sinus. In mice treated with DEP, atherosclerosis was significantly increased to 157.74±18.09% (n = 6, p < 0.05). In vivo neangiogenesis was assessed with subcutaneously implanted discs quantifying the area of the disc invaded by fibrovascular growth. In mice treated with DEP, neangiogenesis was reduced to 75.62±3.85% (n = 6, p < 0.005). Cultured human EPC were treated with DEP (0.1 μg/ml to 100 μg/ml) or solvent (PBS). Treatment with DEP concentration-dependently reduced migratory capacity to 25.2.6% (p = 0.0001). Clonal expansion capacity determined by quantifying the number of colony forming units (CFU) was reduced by DEP treatment to 8.82±0.9% of control (p < 0.0001).

Conclusion: Intranasal instillation of diesel exhaust particles reduced the number and function of endothelial progenitor cells in C57Bl/6 and ApoE−/− mice. This finding was confirmed in cultured human EPC. In ApoE−/− mice, the reduction in EPC was associated with a reduction in neangiogenesis and an increase of atherosclerotic lesion formation.
fold (p<0.01). Furthermore, the migration activity of IL-1Ra/- macrophages was 4.2-fold higher than that of WT macrophages (p<0.01).

**Conclusion:** IL-1Ra in IM-derived cells caused suppression of arterial inflammation and promotion of re-endothelialization, resulting in a decrease of neointimal formation after arterial injury. These novel findings may provide new insights into the mechanisms underlying atherosclerosis and restenosis after angioplasty.

**AUTONOMIC NERVOUS SYSTEM AND HUMORAL REGULATIONS**

**362 Investigation of the thiazolidinedione’s pleiotropic effects to automatic function in patients with diabetic mellitus and acute myocardial infarction**

H. Yokoe, K. Murakawa, G. Yoshida, R. Yuyama, A. Kawamura, F. Yasu, T. Sugiuza, T. Iwashka, Kansai Medical University; Osaka, Japan; *Kochi University, Kochi, Japan

**Background:** Pioglitazone has been shown to reduce the occurrence of fatal and non-fatal MI in patients with type 2 diabetes mellitus (DM) and acute myocardial infarction (MI). However, the mechanisms of such favorable effects remain speculative. The aim of this study was to investigate the pleiotropic effects on automatic function in patients with type 2 DM and MI.

**Methods:** 30 patients with type 2 DM and MI were randomly assigned to those taking pioglitazone (n=15, group I) and those not taking pioglitazone (n=15, group II) at 4 weeks after the onset of MI. Pressure acutely applied and mean arterial baro pathetic nerve activity (MSNA) were continuously recorded at rest. Baroreceptor modulation of MSNA and arterial baroreflex sensitivity were evaluated by phenylephrine and nitroprusside infusion. Serum adiponectin, insulin, high sensitive C reactive protein (hsCRP) were measured by fasting blood sampling. These measurements were performed at baseline and after 12 weeks.

**Result:** Pioglitazone increased markedly plasma adiponectin (from 9.3±3.0 to 12.2±2.7 μg/ml; p<0.003) and reduced significantly the homeostasis model assessment of insulin resistance index (HOMA-IR) (from 4.0±2.2 to 1.0±0.8; p<0.019). HsCRP decreased in both groups. However, the increase in atherogenic plaque (MDA) was significantly larger in group I compared with those in group II. Not only resting MSNA significantly reduce (from 37.1±7.2 to 25.1±9.4; p<0.003, from 60.1±30.4±21.1 burst/100 heartbeats; p=0.017) but arterial baroreflex sensitivity (BRS) improved strikingly (phenylephrine method; from 6.7±3.0±9.9±3.2 msec/mmHg; p=0.027, nitroprusside method; from 6.0±1.8±8.6±2.1 msec/mmHg; p=0.003) in group I. The percentage changes of MSNA response to vasoactive drugs were significantly greater in group I (phenylephrine infusion; from -26.3±13.4±45.1%; p=0.011, nitroprusside infusion; from 115.1±140.1±23.2%; p=0.037). Moreover, a significant the tight relationship was found between the change in MSNA and adiponectin, HOMA-IR in group I (MSNA and adiponectin: r=0.6; p=0.028, MSNA and HOMA-IR: r=0.7; p=0.031).

**Conclusion:** The administration of pioglitazone augmented arterial baroreflex control of sympathetic nerve activity in patients with DM and MI. The pleotropic effects of pioglitazone may have favorable effects to the automatic function in patients with DM and MI through the increase in adiponectin.

**363 Baroreflex and cardiac dysfunctions evaluated by tranespassogephal echocardiography, baroreflex sensitivity, autonomic control and invasive measurements in rats submitted to sinoaortic denervation**

R.A. Sventeke, M.C. Iriogeny, L. Souza, C. Mostarda, R. La Fuente, G. Candido, R. Souza, A. Medeiros, C. Mady, V.M.C. Saleni. Heart Institute (InCor), Hospital das Clinicas da Faculdade de Medicina da Universidade de Sao Paulo, Sao Paulo, Brazil

**Purpose:** Sympathetic hyperactivity commonly seems to be related to cardiac dysfunction, and baroreflex and chemoreflex impairment in hypertension. However, myocardial dysfunction has not been evaluated regarding the association of hyper tension and baroreflex dysfunction using tranespassogephal echocardiography.

**Methods:** Exercise test (ET), baroreflex sensitivity, cardiovascular autonomic control, transthoracic and tranespassogo echocardiography using intracardiac echocardiographic catheter (AcuNav, Siemens, Mountain View, CA, USA), and invasively biventricular end-diastolic pressures were evaluated in rats 10 weeks after sinoaortic denervation (SAD). The rats (n=32) were divided in 4 groups: 16 Wistar (W) with (n=8) or without SAD (n=8) and 16 spontaneously hypertensive rats (SHR) with (n=8) or without SAD (n=8).

**Results:** Blood pressure (BP) and heart rate (HR) did not show any change between the groups SAD and without SAD, although, SHR showed higher BP levels in comparison to W. SHR variance in BP was increased in SHR groups compared to W. After SAD, BP variation increased in all groups compared to W (W: 15 mmHg2; DSA: 49 mmHg2; SHR: 60 mmHg2; SHR-SAD: 137 mmHg2; p<0.05 vs. W). Exercise tests results showed that SHR had better functional capacity compared to SAD and SHR-SAD (W: 1.16 mmHg2; DSA: 0.9 mmHg2; SHR: 1.46, SHR: DSA: 1.02; p<0.05 vs. SAD and SHR-SAD). Left ventricular concentric hypertrophy, segmental systolic dysfunction and global diastolic LV dysfunction, segmental and global systolic dysfunction, and global diastolic RV dysfunction, indi-
Maximal exercise capacity is significantly decreased in essential hypertensive erectile dysfunction patients with low total testosterone and high CRP level

A. Aggelis1, C. Vlachopoulos1, N. Ioakeimidis1, A. Synodinos1, D. Terentes-Printzios2, A. Sameritakis3, E. Christoforatou1, A. Aggelakas1, D. Kardara1, C. Stefanadis1,1 Hipppokration General Hospital, Athens, Greece; 2Elpis General Hospital, Athens, Greece

Purpose: Erectile dysfunction (ED) is a very common problem in hypertensive men. Exercise workload (measured in metabolic equivalents, METs) is an important prognostic variable derived from the exercise stress test (EST). Subclinical inflammation and low androgen levels are involved in the pathophysiology of ED. In this study, we investigated the combined effect of increased C-reactive protein (CRP) levels and low androgen total testosterone (TT) concentration on exercise capacity in hypertensive ED patients undergoing EST.

Methods: 197 asymptomatic non diabetic hypertensive ED patients (56±8 years) underwent maximal EST under the standard Bruce protocol. Blood specimens were analyzed for CRP and TT levels.

Results: In univariate analysis, maximal exercise capacity was negatively correlated with CRP (r=-0.225, P<0.001) and positively correlated with TT (r=0.325, P<0.001). Stepwise regression analysis revealed that age, CRP (b=-0.171, P=0.011) and TT (b=0.207, P=0.001) were independent predictors of exercise intensity (adjusted R2=0.322). The distributions of CRP and TT were split by the median (1.36 mg/l and 4.45 ng/ml, respectively) and accordingly subjects were stratified into those with high and low levels. ED patients were then categorized by CRP level and further subdivided according to TT concentration. The subgroup of hypertensive ED patients with high CRP/low TT exhibited significantly lower age-adjusted maximum workload (figure) as compared to the subgroups of high CRP/low TT, low CRP/low TT and low CRP/low TT (overall P<0.001).

Conclusions: In essential hypertensive men with ED, pronounced subclinical inflammation and low androgen level exert an additive unfavourable effect on maximum workload.

Vitamin D deficiency is associated with decreased systolic blood pressure reduction after renal sympathetic denervation

J. Pees, F. Mahloud, C. Ukena, B. Cremers, U. Laufs, M. Boehm, Saarland university hospital, Internal Medicine III, Cardiology, Angiology and Intensive Care Medicine, Homburg/Saar, Germany

Background: Vitamin D deficiency is associated with hypertension. However, it is unclear if vitamin D status influences therapeutic blood pressure reduction. Renal sympathetic denervation (RDN) reduces blood pressure in patients with therapy resistant hypertension. We hypothesized that vitamin D status might influence blood pressure response to RDN.

Patients and methods: Plasma vitamin D concentration was measured in 100 patients (mean age: 62±1.2 years; 59% male) with therapy resistant hypertension who underwent RDN. The association between vitamin D status and systolic blood pressure (SBP) reduction six months after RDN was analyzed. Non-response was defined as reduction in SBP of <10 mmHg after 6 months.

Results: Median vitamin D concentration was 11.2 ng/ml (normal: 20-90 ng/ml). Mean office SBP at baseline was 171.5±2 mmHg despite an intake of 5.3±0.2 antihypertensive drugs. Six months after RDN, mean office SBP was reduced by 28.4±2.3 mmHg (p<0.001). Out of the 100 enrolled patients, 84 patients (82%) were responders. In the group of non-responders (n=16, 18%), significantly more patients had a vitamin D concentration below the median compared to the group of responders (81 vs. 46%, p=0.013). The percentage of patients with normal vitamin D concentration gradually increased with increasing tertiles of SBP reduction (tertile 1 (<18 mmHg): 6%, tertile 2 (18-34 mmHg): 19%; tertile 3 (>34 mmHg): 29%; Np for trend = 0.02). Conversely, in patients with a vitamin D concentration below the median, SBP reduction was lower compared to patients with a vitamin D concentration above the median (23.46±2.3 mmHg vs. 33.71±1.3 mmHg, p = 0.026). Vitamin D concentration was lower in non-responders compared to responders (8.95±4.5 ng/ml vs. 13.71±7.3 ng/ml, p<0.001).

Conclusion: In patients with therapy resistant hypertension undergoing RDN, baseline vitamin D concentration below the median was associated with a decreased SBP reduction after six months and a higher rate of non-response compared to a vitamin D concentration above the median.
occurred. The difference in hypogonadism (TT<3.4 ng/ml) prevalence between patients with and those without CV events was significant (35% vs. 19%; P <0.01). Kaplan-Meier survival analysis by tertiles of TT levels revealed that the subjects with the lowest TT tertile were more likely to develop CV events than those with the highest tertile (P<0.012 by log-rank test, figure). A Cox proportional hazard model showed that hypertensive patients with the lowest tertile of serum TT (<4.0 ng/ml) had an approximately 2.5 fold higher CV event risk compared to those with the highest TT tertile after adjustment for age, blood pressure, metabolic profile, antihypertensive therapy and statins (multivariate-adjusted hazard ratio, 2.6; 95% CI, 1.01–8.38, P=0.030). Multivariate analysis did not show any significant association of C-reactive protein with CV events.

Conclusions: Low serum testosterone concentration is associated with CV events in middle-aged hypertensive patients with ED, independent of risk factors and low grade inflammation.

**Tobacco: From Early Damage to Late Impact**

1372

Cardiovascular risk profile and impact of adolescent smoking

J. Draha1, N. Kuerss1, A. Schmidt-Trucksass2, E. De Groot1, B. Bettchar Th Rothe1, D. Stolz1, A. Turk1, J.M. Gasp Poch Rochat1, N. Probst-Hensch3, E. Zemp1, 1Swiss Tropical and Public Health Institute, Basel, Switzerland; 3University of Basel, Institute of Exercise and Health Sciences, Division of Sports Medicine, Basel, Switzerland; 2Vascular Medicine, AMC, Amsterdam and Imagingonline, Eindhoven, Netherlands; 1University Hospital Basel, Basel, Switzerland; 2Zürcher Höhenklinik, Wald, Switzerland; 4University Hospital of Geneva, Geneva, Switzerland

Background: Early exposure to tobacco smoke is associated with various adverse health outcomes in children and adolescents, however little is known on the impact of tobacco smoke exposure on cardiovascular health (CVH) in adolescence, although tobacco smoke is considered to be highly atherogenic in adults and remains prevalent in childhood and adolescence. We investigated the cardiovascular risk profile and the association between active smoking and carotid artery intima media thickness (CIMT) in the SAPALDIA Youth study.

Methods: The SAPALDIA Youth Study is a nested study in the Swiss SAPALDIA cohort, including 361 offspring aged 8–20 yrs. 293 of these offspring underwent a clinical examination following a standardized protocol: anthropometry, blood pressure measurement, echocardiography and vascular compliance of large (C1) and small (C2) arteries using an HDI/Pulse Wave™ CR-2000 Research Cardiovascular Profiling Instrument. Results: There were no significant differences between smokers and non-smokers in age (54.2±7.7 yrs vs 55.3±8.6 yrs, p=0.3999), BMI (21.5±0.4 kg/m² vs 21.2±0.3 kg/m², p=0.5534), SBP (127.0±0.7 mmHg vs 126.4±0.6 mmHg, p=0.2341), elasticity of the large artery (C1) in smokers group (p=0.6350). Total cholesterol (5.6±0.1 mmol/l vs 5.5±0.1 mmol/l, p=0.1759) and LDL-cholesterol (3.8±0.1 mmol/l vs 3.9±0.1 mmol/l, p=0.0001) were highest in smokers group compared to non-smokers. There were no significant differences between smokers and non-smokers in HDL-cholesterol (1.0±0.3 mmol/l vs 1.0±0.3 mmol/l, p=0.867), triglycerides (1.0±0.3 mmol/l vs 1.0±0.3 mmol/l, p=0.685), and fasting glucose levels (94.8±3.9 mmol/l vs 94.8±3.9 mmol/l, p=0.9694) and dancing values (94.8±3.9 mmol/l vs 94.8±3.9 mmol/l, p=0.9694). Coronary artery disease was more common in smokers compared to non-smokers (p=0.0414). Myocardial infarction was also more common in smokers compared to non-smokers (p=0.0435). The multiple linear regression analysis revealed a relationship between smoking and small artery elasticity index (C2) independently of BMI, SBP and elasticity of the large artery (C1) (p=0.0001). The negative correlation between smoking and elasticity of the small artery wall (C2) was showed (r=-0.1506, p=0.0062).

Conclusions: Smoking decreases elasticity of the small artery wall (C2) in smokers compared to non-smokers (p=0.0001). Elasticity of the large artery (C1) in smokers group was lower compared to non-smokers men (2.74±0.1 mm/m²/100 vs 3.92±0.1 mm/m²/100, p=0.0001). T otal cholesterol (5.64±1.5 mmol/l vs 4.85±1.3 mmol/l, p=0.0001) and LDL-cholesterol (3.80±1.36 mmol/l vs 2.97±1.14 mmol/l, p=0.0001) values were highest in smokers group compared to non-smokers.

1. Smoking decreases elasticity of the small artery wall (C2) in smokers compared to non-smokers (p=0.0001).

1373

The acute effect of passive smoking on platelet activity in healthy volunteers

M.G. Kaya, M. Yarlioglu1, I. Ardic, O. Dogdu, M. Akpek, C. Zencir, S. Keseoglu, H.A. Kasapkina, I. Ozdogru, A. Ozguziran, Eryos, University of Medicine and Health Sciences, Department of Cardiology, Kapsali, Turkey

Objective: Mean platelet volume (MPV) is one of the well established indicators of platelet activation that is increased in acute thrombotic events. Carbonmonox-

Meador is suspected to play a major role in cigarette smoke-induced cardiovascular diseases. Lactate accumulation occurs when the supply of oxygen to the cells is limited. We aimed to determine whether MPV levels are elevated after pas-

sive smoking in healthy volunteers. In addition, we tried to find out if carbohy-

HDL, lactate and MPV levels were taken at baseline and after spending one an hour in the smoking room in all the subjects.

Results: There was no significant difference in heart rate, respiratory rate and both systolic and diastolic blood pressure after acute exposure. HDL, lactate and MPV levels of the subjects were statistically higher after passive smoking (0.8±0.3 vs. 1.2±0.4; p=0.001, 0.70±0.2 vs. 2.2±0.9; p=0.001, 7.8±0.4 fl vs. 8.5±0.6 fl; p=0.001, respectively). A significant correlations were determined between MPV and COHb levels (r= 0.55, p=0.001), MPV and lactate levels (r= 0.65, p=0.0001) after smoking. There was also a remarkable relation between COHb and lactate levels(r=0.78, p=0.0001).

Conclusions: Our results suggest that passive smoking has acute effect on platelet activity demonstrating by MPV levels that is notably correlated with COHb and lactate levels. Prolonged exposure to passive smoking could contribute to increase the risk of acute thrombotic events in healthy population.

1374

Effect of cigarette smoking on arterial wall elasticity indices

E. Podoleck1, M. Tomaszewski2, G. Wyrzychowska1, W. Grzeszczak3, E. Zukowska-Szczechowska1, 1Medical University of Silesia, Department of Internal Medicine/Diabetes & Nephrology, Zabrze, Poland; 2University, Department of Cardiovascular Sciences, Leicester, United Kingdom

Cigarette smoking is a well-known risk factor for the development of cardiovascular disease. The aim of the study was to evaluate if smoking can negatively effect on arterial wall elasticity indices.

Methods: The study group comprised of 218 men (mean age 54.7±11.8 yrs), 118 men were current smokers and 100 men were non-smokers. Fasting serum glucose, TC-cholesterol, HDL-cholesterol, triglycerides and LDL-cholesterol were determined. All subjects underwent blood pressure measurement, echocardiography and vascular compliance of large (C1) and small (C2) arteries using an HDI/Pulse Wave™ CR-2000 Research Cardiovascular Profiling Instrument.

Results: There were no significant differences between smokers and non-smokers in age (54.2±7.7 yrs vs 55.3±8.5 yrs, p=0.3999), BMI (21.5±0.4 kg/m² vs 21.2±0.3 kg/m², p=0.5534), SBP (127.0±0.7 mmHg vs 126.4±0.6 mmHg, p=0.2341), elasticity of the large artery (C1) in smokers group (p=0.6350). Total cholesterol (5.64±1.5 mmol/l vs 4.85±1.3 mmol/l, p=0.0001) and LDL-cholesterol (3.80±1.36 mmol/l vs 2.97±1.14 mmol/l, p=0.0001) values were highest in smokers group compared to non-smokers.

There were no significant differences between smokers and non-smokers in HDL-cholesterol (1.0±0.3 mmol/l vs 1.0±0.3 mmol/l, p=0.867), triglycerides (1.0±0.3 mmol/l vs 1.0±0.3 mmol/l, p=0.867), and fasting glucose levels (94.8±23.95 mmol/l vs 101.00±29.42 mmol/l, p=0.2499). Coronary artery disease was more common in smokers compared to non-smokers (p=0.0414). Myocardial infarction was also more common in smokers compared to non-smokers (p=0.0435). The multiple linear regression analysis revealed a relationship between smoking and small artery elasticity index (C2) independently of BMI, SBP and elasticity of the large artery (C1) (p=0.0001). The negative correlation between smoking and elasticity of the small artery wall (C2) was showed (r=-0.1506, p=0.0062).

Conclusions: 1. Smoking decreases elasticity of the small artery wall (C2) in men in middle age.

2. Smoking negatively effect on elasticity of the small artery wall independently of BMI, SBP and elasticity of the large artery (C1).

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790/19394792/11 March 2019
Acute effects of using an electronic nicotine-delivery device (e-cigarette) on myocardial function: comparison with the effects of regular cigarettes

K. Frasalinos, T. Tsiapras, S. Kyrzopoulos, M. Savvopoulou, D. Vasilopoulou, V. Voudris, Onassis Cardiac Surgery Center, 2nd Department of Cardiology, Athens, Greece

Purpose: The addictive properties and devastating consequences of cigarette smoke on human health, including cardiac function, are well known. In recent years, the electronic cigarette (e-cigarette), a battery-powered nicotine-delivery device, has been marketed as a safer habit. Despite the global debate about its use, no studies have examined the device’s consequences on cardiac function. The purpose of our study was to evaluate the acute effects of using the e-cigarette on left ventricular myocardial function and to compare them with the effects of regular cigarettes.

Methods: Participants were 42 healthy volunteers (age 25-45 years): ex-smokers who were using the e-cigarette (group E, n=22), and regular cigarette smokers (group SM, n=20). A complete echocardiographic exam was performed in both groups after 3-hours abstinence from alcohol, coffee and e-cigarette use or smoking (eCIG-1 and SM-1, respectively). A repeat echocardiogram was performed in eCIG subjects after using an e-cigarette with nicotine concentration of 11mg/ml for 7 minutes (eCIG-2). In smokers, the repeat echocardiogram was done after smoking one cigarette (SM-2). A Brinkman index (number of daily cigarettes x smoking years) of 533 ± 150 was characterized by higher levels of hs-CRP (3.25 ± 0.84 mg/l, p = 0.001) and 24-h diastolic BP (97 ± 7 mmHg, p = 0.001), whereas did not differ regarding age, sex, body mass index and waist to hip ratio (r = 0.345, p = 0.05) and daytime pulse pressure (r = 0.185, p = 0.005).

Conclusions: Smoking in essential hypertension is accompanied by increased pressure (r = 0.185, p < 0.005) and 24-h diastolic BP (r = 0.220, p = 0.006). Regarding OPG, it was associated with pack-years index (r = 0.248, p < 0.005) and higher levels of hs-CRP (r = 0.175, p < 0.05), whereas PAI-1 exhibited a correlation with pack-years index (r = 0.248, p < 0.005) and 24-h diastolic BP (r = 0.005). A significant decrease in E velocity (p = 0.005) and Am/Em (p = 0.001) was observed in eCIG-2 compared to baseline.

Smoking is related to subclinical inflammation, impairment of thrombosis/ fibrinolyis system and increased osteoprotegerin levels in essential hypertensive subjects

K. Dimitriadis, C. Tsiofu, V. Tzamou, A. Kasiakogias, C. Thomopoulos, T. Katsimichas, A. Milkas, A. Kordalis, C. Stefanadis. 1st Cardiology Clinic, University of Athens.Hippokration Hospital, Athens, Greece

Purpose: Despite the fact that smoking has numerous effects that promote atherothrombosis, the data regarding its association with biological markers of risk in the setting of untreated essential hypertension are rather scarce. In the present study we investigated the interrelationships between smoking, high-sensitivity C-reactive protein (hs-CRP), osteoprotegerin (OPG), fibrinogen and plasmogen-activator inhibitor type 1 (PAI-1) levels in essential hypertensives. Methods: 245 newly diagnosed untreated non-diabetics with stage I to II essential hypertension (172 men, mean age 51 years, office blood pressure (BP) = 148/95 mmHg) were classified according to their smoking habits as current smokers (> =1 cigarette/day, n=115) and the remaining subjects as non-smokers (n=130). All subjects underwent ambulatory BP monitoring and venous blood sampling was performed for estimation of metabolic profile, hs-CRP, OPG, fibrinogen and PAI-1 concentrations.

Results: Hypertensive current smokers compared to non-smokers had increased hs-CRP (8.7 ± 3.2 mmol/l, p = 0.001) and 24-h diastolic BP (85 ± 10 vs 80.8 ± 7 mmol/l, p = 0.001), whereas did not differ regarding age, sex, body mass index and left ventricular mass index (p = NS). Although groups exhibited no difference regarding metabolic profile (p = NS), smokers compared to non-smokers were characterized by higher levels of hs-CRP (3.25 ± 1.1 vs 2.33 ± 0.84 mg/l, p = 0.001), OPG (5.8 ± 0.7 vs 4 ± 0.5 pmol/l, p = 0.005), fibrinogen (318.5 ± 66 vs 289.3 ± 67.3 mg/l, p = 0.005) and PAI-1 (40.02 ± 7.56 vs 24.5 ± 22.7 mg/l, p = 0.004), independently of confounding factors. In the entire population, hs-CRP was associated with pack-years index (r = 0.175, p = 0.05) and 24-h systolic BP (r = 0.188, p = 0.05). PAI-1 exhibited a correlation with pack-years index (r = 0.248, p < 0.005) and 24-h diastolic BP (r = 0.220, p = 0.006). Regarding OPG, it was associated with age (r = 0.228, p = 0.05), waist to hip ratio (r = 0.345, p = 0.05), 24-h systolic BP (r = 0.286, p = 0.001) and pack-years index (r = 0.348, p = 0.05), while fibrinogen was related to pack-years index (r = 0.176, p = 0.05) and daytime pulse pressure (r = 0.185, p = 0.005).

Conclusion: Smoking in essential hypertension is accompanied by increased inflammatory processes, atherosclerosis progression and impairment of thrombo-
between qualifying ECG and coronary angiography for PCI in STEMI patients. Not following the ESC guidelines was associated with a three-fold increase in hospital mortality. A similar trend was observed for lytic-treated patients. When meeting the ESC guidelines for PCI seems unlikely, timely administration of fibrinolysis should be considered.

### In-hospital complications in relation with use and timing of prehospital antithrombotic medications in STEMI patients. The FAST-MI 2010 registry

P. Goldstein1, D. Carlier1, Y. Cottin1, S. Charpentier1, P. Motreff2, G. Leurent1, Y. Valy1, V. Probst3, T. Simon4, N. Danchin5 on behalf of the FAST-MI 2010 investigators. 1Hospital Regional University of Lille, Department of Emergency, Lille, France; 2University Hospital of Toulouse-Rangueil, Hospital Opt, Cardiology/Cardiovascular & metabolic pole, Toulouse, France; 3University Hospital Center - Hospital of Bocage, Dijon, France; 4University Hospital of Clermont-Ferrand, Department of Cardiology, Clermont-Ferrand, France; 5University Hospital of Rennes - Hospital Pontchaillou, Department of Cardiology and Vascular Disease, Rennes, France; 6Hospital of La Rochelle, Department of Cardiology, La Rochelle, France; 7University Hospital of Nantes, Nantes, France; 8AP-HP - Hospital Saint-Antoine, Faculty of Medicine Pierre & Marie Curie Paris 6, Paris, France; 9AP-HP - European Hospital Georges Pompidou, Paris, France

**Background:** France has a highly developed MICU system with emergency physicians on board the ambulances (SAMU), who have the ability to administer recommended medications at a very early stage of AMI.

**Aim:** To assess in-hospital outcomes in patients transported by the SAMU, in relation to the pre-hospital administration of antithrombotic medications and time from symptom onset to first call.

**Methods:** FAST-MI 2010 is a nationwide French registry that included 4169 patients with AMI at the end of 2010 in 213 centres. Of those, 2364 had STEMI, of whom 1868 (79%) were transported by the SAMU and 1836 had the time from symptom onset to first call.

**Results:** From time from onset to first call was ≤ 60 min in 923 pts (50%), 1172 pts (64%) received an antplatelet agent, with 101 receiving dual oral antplatelet therapy (DAPT, 55%) in the admission. In addition, 27% received enoxaparin and 29% received unfractionated heparin. Patients calling within 60 min of onset had significantly lower in-hospital mortality (7% vs 6.5%, 40% vs 39% vs 24% for any antplatelet therapy, DAPT, and enoxaparin, respectively. Younger age, male sex, short time from onset to call, absence of diabetes and lower GRACE score were independent predictors of the use of pre-hospital antithrombotic medications. Fibrinolysis treatment was administered prehospital in 11% (5% when onset to call ≤ 60 min vs 7% when onset to call > 60 min). When time from onset to call was ≤ 60 min, in-hospital mortality was lower with prehospital antithrombotic therapy: any antplatelet 2.3% vs 5.9% (P<0.001), DAPT 1.8% vs 6.0% (P<0.001), any heparin 1.9 vs 5.7% (P=0.002), prehospital heparin 2.9 vs 3.4% (P=NS). In contrast, prehospital antithrombotic therapy was not associated with lower in-hospital mortality when time from symptom onset to call was > 60 minutes: 2.7 vs 2.8%, 2.5 vs 3.0%, 2.4 vs 3.0%, 4.8 vs 2.6% respectively (all P = NS).

**Conclusion:** The use of prehospital antithrombotic therapy remains suboptimal in patients managed by physician-staffed ambulances. In patients calling early after symptom onset, the use of prehospital antithrombotic therapy was associated with lower in-hospital mortality. In contrast, in patients calling beyond one hour of symptom onset, the association with hospital mortality was neutral.

### Comparative validation of three contemporary bleeding risk scores in acute coronary syndromes


**Background:** Hemorrhagic complications are strongly linked with subsequent adverse outcomes in acute coronary syndrome (ACS) patients. Various risk scores (RS) are available to estimate the bleeding risk in these patients.

**Aims:** To compare the predictive accuracy of the three contemporary bleeding RS in ACS.

**Methods:** We studied 4500 consecutive patients with ACS. For each patient, the ACTION, CRUSADE, and Mehran et al bleeding RS were calculated. We assessed their performance either for the prediction of their own major bleeding events (c-statistic=0.8), or to predict the TIMI serious bleeding (c-statistic=0.745). We compared the prediction of new major bleeding events (c-statistic<0.80, 0.791, and 0.81 for the entire sample, for STEMI, and for NSTEACS patients, respectively) or to predict the TIMI serious bleed occurrence (c-statistic=0.745). We also evaluated the bleeding risk in STEMI patients, and NSTEACS patients, respectively. The lowest bleeding rates observed in patients classified as low risk corresponded to the CRUSADE RS. All scores performed moderately in patients who did undergo percoronary angiography (c-statistic=0.70). The CRUSADE score was significantly superior to the ACTION model in predicting the TIMI serious bleeding occurrence in terms of NRI overall and by ACS subgroups (p<0.05). Overall, the CRUSADE RS exhibited better calibration of the TIMI bleeding compared to the ACTION and Mehran et al scores (Hosmer-Lemeshow χ² p-values of 0.26, 0.13, and 0.07, respectively).

**Conclusion:** The CRUSADE RS represents, among the more contemporary bleeding RS, the most accurate and reliable quantitative clinical tool in STEACS and STEMI patients. We encourage the utilization of the CRUSADE index for bleeding risk stratification purposes in daily clinical practice and in ACS outcome studies. The performance of the three more contemporary bleeding RS is modest in those patients who received conservative management.

### Switch and non switch in P2Y12 inhibition: the real life use of clopidogrel and prasugrel in patients with acute myocardial infarction. Insights from the FAST MI 2010 registry

F. Schiele1, E. Puyimirt2, L. Logis3, G. Dent4, E. Faure5, G. Rouault5, F. Lecerq5, E. Drouet5, T. Simon5, N. Danchin6 on behalf of FAST-MI 2010. 1University Hospital of Besancon, Besancon, France; 2AP-HP - European Hospital Georges Pompidou, Paris, France; 3University Hospital Center, Department of Cardiology, Dijon, France; 4Clinic Fontaine, Fontaine les Dijon, France; 5Hospital Center of Hospital Quimper, Department of Cardiology, Quimper, France; 6University Arnaud de Villeneuve, Montpellier, France; 7French Society of Cardiology, Paris, France; 8AP-HP - Hospital Saint-Antoine, Paris, France

**Background:** In patients with AMI, the choice between clopidogrel and prasugrel requires information that is not always available at the early phase, such as indication for PCI or assessment of bleeding and thrombosis risk. When initial clopidogrel treatment seems suboptimal, switching to prasugrel seems attractive, but is not yet recommended. We assessed baseline characteristics and in-hospital outcomes in prasugrel-treated patients, according to the initial use of clopidogrel before prasugrel initiation.

**Aims:** FAST-MI 2010 is a nationwide French registry including 4169 patients with AMI in 213 centres. In total, 4115 received thienoopyridines, of whom 1259 received prasugrel (31%). Among these, 391 received "de novo" prasugrel (G1), 807 (64%) were treated with clopidogrel first and then switched to prasugrel (G2), of whom 11% had a 60mg loading dose of prasugrel. We excluded 61 pts who received prasugrel initially and subsequently switched to clopidogrel. We compared baseline characteristics, bleeding and ischemic complications between G1 and G2, and then used propensity-score matching (propensity to be treated with prasugrel) to compare outcomes in 2 cohorts with similar baseline characteristics.

**Results:** Age and sex were similar in G1 and G2: more G2 pts had a history of AMI (13% vs 8%, P=0.01), PCI (14% vs 9.5%, P=0.02), underwent PCI during the hospital stay (36% vs 83%, P=0.047) or received lytic therapy for STEMI (21% vs 5%, P<0.001). With the exception of major bleeding, which was less frequent in G2 (0 vs 1.0%, P=0.004), none of the other complications differed significantly (Table). The 2 propensity-score matched cohorts (316 patients each) had comparable baseline characteristics and 96% (switch clopidogrel to prasugrel) vs 5% (vs 5%, P=0.01). With the exception of major bleeding, which was less frequent in G2 (0 vs 1.0%, P=0.004), none of the other complications differed significantly (Table). The 2 propensity-score matched cohorts (316 patients each) had comparable baseline characteristics and 96% (switch clopidogrel to prasugrel) vs 5% (vs 5%, P=0.01). With the exception of major bleeding, which was less frequent in G2 (0 vs 1.0%, P=0.004), none of the other complications differed significantly (Table).

**Conclusion:** In this real-world registry, a high proportion of patients treated with prasugrel were switched from clopidogrel therapy (64%). There was no evidence of excess risk of bleeding or in-hospital complications in the patients who were switched, compared with those who received prasugrel treatment only. Further randomized studies are mandatory to determine the safety and efficacy of this strategy.

### Major improvement in early mortality of AMI over the past 15 years in relation to management changes: data from 4 nationwide French surveys

E. Puyimirt1, G. Sieg1, D. Blanchard1, P. Goldstein1, M. Hanssen1, E. Durand1, P. Guerin1, J.P. Cambau1, T. Simon2, N. Danchin2 on behalf of the FAST-MI 2010 investigators. 1AP-HP - European Hospital Georges Pompidou, Paris, France; 2AP-HP - Hospital Bichat-Claude Bernard, Department of Cardiology, Paris, France; 3Clinic Saint Gallien, Tours, France; 4Hospital Regional University of Lille, Department of Emergency, Lille, France; 5General Hospital of Haguenau, Department of Cardiology, Haguenau, France; 6AP-HP - University Hospital Henri Mondor, Department of Cardiology, Creteil, France; 7University Hospital of Toulouse, Department of Epidemiology, Inserm U558, Toulouse, France; 8AP-HP - Hospital Saint-Antoine, Faculty of Medicine Pierre & Marie Curie Paris 6, Paris, France

**Background and aim:** The management of AMI has undergone profound changes in the past 2 decades. We assessed early mortality in 4 surveys of AMI
Impact of immediate multivessel intervention on outcome of patients with multivessel disease undergoing primary PCI for cardiogenic shock

U. Zeymer1, M. Hochadel1, A. Gitt2, U. Tebbe1, H. Mudra1, A. Elsasser1, R. Zahn3,1, Institut für Herzinfarktforschung, Ludwigshafen am Rhein, Germany;2Clinical Center of Ludwigshafen, Medical Clinic B/Department of Cardiology, Ludwigshafen am Rhein, Germany;3Heart Center Ludwigshafen, Department of Cardiology, Ludwigshafen am Rhein, Germany.

Background: There is still uncertainty about the optimal strategy in patients with multivessel disease undergoing primary PCI for cardiogenic shock. Therefore we compared outcome of patients with culprit lesion only PCI and immediate multivessel PCI for cardiogenic shock in real life.

Methods: We used the data of the prospective ALKK-PCI registry and included patients with primary PCI for cardiogenic shock with 2-3 vessel disease. We excluded patients with left main PCI and patients with prior coronary artery bypass surgery.

Results: Between 2008 and 2010 a total of 742 patients 2-3 vessel disease were treated with primary PCI for cardiogenic shock. Of these 176 (24%) received immediate multivessel PCI while in the remaining 566 the culprit vessel was treated.

Baseline characteristics, procedural features and outcomes are given in the table.

Table 1. Presenting symptoms of patients with type I and type II MI (numbers indicate percent of patients in each group)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type I</th>
<th>Type II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical angina</td>
<td>84.5%</td>
<td>54.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Apical chest pain</td>
<td>75.5%</td>
<td>20.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>23.5%</td>
<td>59.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Syncope</td>
<td>4.1%</td>
<td>5.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>4.7%</td>
<td>14.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>3.9%</td>
<td>11.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>11.7%</td>
<td>26%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Immediate multivessel PCI for cardiogenic shock used in about 25% of patients is associated with similar success rates as culprit lesion PCI, but with a higher mortality. Therefore a randomized trial seems warranted to evaluate the optimal interventional strategy in these patients.

BIOMARKERS AND CLINICAL SCORES IN PREDICTING THE OUTCOME OF ACUTE CORONARY SYNDROMES

Incidence, clinical characteristics, management and outcomes of patients with type-II myocardial infarction: results from the Acute Coronary Syndrome Israeli Surveys (ACSIS) 2008-2010

S. Fuchs1, G. Hershco civ1, R. Korenfeld1, S. Matezky2, G.Y. Stein1

1Rabin Medical Center, Beilinson Hospital, Petah Tikva, Israel; 2Sheba Medical Center, Heart Institute, Ramat Gan, Israel.

Background: Although almost 5 years have elapsed since a consensus document classified type-II myocardial infarction (MI) as MI secondary to ischemia due to either increased oxygen demand or decreased supply, little is known regarding patient characteristics, causes, management and outcomes.

Methods: We performed a comparative analysis between patients with type-I and type-II MI who participated in two national Acute Coronary Syndrome Israeli Surveys (ACSIS) in the years 2008 and 2010.

Results: The survey included 2916 consecutive patients with acute MI of whom 127 (4.5%) had type-II MI. The main causes for type-II MI were: anemia (36%), sepsis (28%), arrhythmia (20%) and post-surgical procedures (16%). Compared to type-I MI, patients with type-II MI tended to be older (75.6±12 vs. 63.8±13 years, p<0.0001), more frequently females (43.3% vs. 22.3%, p<0.0001) and have more comorbidities (p<0.0001). Patients with type-II MI were less likely to have STEMI (19.7% vs. 52.5%, p<0.0001) and more often had atypical clinical presentation (Table 1). Coronary angiography was not as frequently performed in patients with type-II MI (36% vs. 88%, p<0.0001) including those who presented with STEMI (68% vs. 94%, p<0.0001). Patients with type-II MI had substantially higher 30-day mortality rates (13.6% vs. 4.9%, p<0.0001).

Table 1. Presenting symptoms of patients with type I and type II MI (numbers indicate percent of patients in each group)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Type I</th>
<th>Type II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical angina</td>
<td>84.5%</td>
<td>54.3%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Apical chest pain</td>
<td>75.5%</td>
<td>20.5%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>23.5%</td>
<td>59.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Syncope</td>
<td>4.1%</td>
<td>5.5%</td>
<td>NS</td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>4.7%</td>
<td>14.2%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>3.9%</td>
<td>11.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Other</td>
<td>11.7%</td>
<td>26%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Patients with type-II compared to those with type-I MI are older, have more comorbidities and undergo less frequently coronary angiography. These distinctions may explain, at least in part, their higher early mortality rates despite having lower rates of STEMI.

Diagnostic and prognostic value of copeptin in patients with acute chest pain and diabetes

C. Zellweger1, K. Wildl1, T. Reichlin1, P. Hafl1, R. Hoeller1, M. Rubini Gimenex1, B. Moehring1, R. Twerenbold1, C. Mueller1

1University Hospital Basel, Department of Cardiology, Basel, Switzerland; 2University Hospital Basel, Department of Internal Medicine, Basel, Switzerland.

Purpose: Patients with Diabetes are at high risk for acute myocardial infarction (AMI) therefore need a careful diagnostic evaluation and risk stratification.
Copeptin is released in case of relevant endogenous stress such as AMI. We evaluated diagnostic and prognostic value of copeptin in combination of high sensitive cardiac Troponin T (hs-cTnT) in diabetic patients.

Methods: In a prospective observational international multicenter study, we enrolled 1837 consecutive patients presenting to the emergency department with symptoms suggestive of AMI. Final diagnoses were adjudicated by two independent cardiologists using all available information including hs-cTnT (Roche). Levels of copeptin at presentation were measured in a blinded fashion.

Results: 322 patients had diabetes. AMI was the adjudicated final diagnosis in 111 (35%). Copeptin was significantly higher (p < 0.001) in patients with AMI (median 21.7, SD 33.9) compared to patients without AMI (median 8.0, SD 33.9). Diagnostic accuracy as quantified by the area under the curve showed that the combination of copeptin with hs-cTnT (AUC 0.91, CI 95% 0.88-0.94) was comparable with hs-TnT for rule-out AMI in patient with diabetes and further allows identification of patients at high risk of death within two years.

Conclusion: The additional use of copeptin in conjunction with hs-cTnT is comparable with hs-TnT for rule-out AMI in patient with diabetes and further allows identification of patients at high risk of death within two years.

BIOMARKERS AND CLINICAL SCORES IN PREDICTING THE OUTCOME OF ACUTE CORONARY SYNDROMES

1395

Prospective evaluation of the safety of the 2011 ESC guidelines for rapid rule-out of NSTEMI using a novel high sensitive assay for troponin I

B. Moehring, R. Twerenbold, K. Willi, P. Haaf, R. Hoeller, M. Rubirini Gimenez, N. Artenja, M. Reiter, T. Rechlin, C. Mueller. University Hospital Basel, Department of Cardiology, Basel, Switzerland

Purpose: High-sensitive cardiac troponin (hs-cTn) assays have been shown to significantly improve the early diagnosis of acute myocardial infarction. The novel 2011 ESC guidelines for the management of acute coronary syndromes in patients with persistent ST-elevation contain for the first time a novel fast track rule-out protocol including hs-cTn. We intended to verify the safety of this fast track protocol in our prospective study setting.

Methods: In a randomized prospective observational multicenter study 1127 consecutive patients who presented with symptoms suggestive of acute myocardial infarction and absence of significant ST-elevations in the ECG were included. The final diagnosis was adjudicated by two independent cardiologists using all available informations including high sensitive cardiac Troponin T (Roche). We examined the diagnostic accuracy of the novel ESC rapid rule-out protocol using the pre-commercial Siemens high sensitive cardiac troponin I assay (hs-cTnI, 99th percentile defined as 9.0 ng/L) performed on blood samples obtained in the emergency department at presentation and after 3 hours according to the novel guidelines. All patients were divided in line with the ESC algorithm into the subgroups of late presenters with chest pain onset/maximum (CPM) > 6 hours and early presenters with CPM < 6 hours. In the former group rule-out was based on a single measurement using hs-cTnI, and in the latter group on two hs-cTnI values, at presentation and at 3 hours.

Results: Of all late presenters (n=396), 17% (n=69) received the final diagnosis of NSTEMI compared to 15% (n=107) of early presenters (n=731). Two late presenters and two early presenters with the final diagnosis of NSTEMI had hs-cTnI levels below the cutoff of 9 ng/L. The overall negative predictive value (NPV) applying only the hs-cTn I criteria was for CPM ≥ 6 h 99.1% (95% CI 96.8 to 99.9%) and for CPM < 6h 99.2% (95% CI 97.6 to 99.9%). As one of the late presenters had a GRACE Score > 140 and the second late presenter and the two early presenters were not free of symptoms at the point of time when the decisive troponin became available, the NPV increased to 100% in the both subgroups.

Conclusions: Using a novel high sensitive prototype assay for troponin I, the 2011 ESC guidelines provide an effective way of rapid rule-out of NSTEMI with a perfect negative predictive value (ClinicalTrials.gov number, NCT00470587).

1396

ACHTUNG - An improved model for prognostic assessment in Myocardial Infarction

S. Barra, R. Providencia, L. Pava, P. Gomes, F. Caetano, I. Almeida, A. Leitao Marques. Coimbra’s Hospital Center and University, Coimbra, Portugal

Purpose: The TIMI, PURSUIT and GRACE scores have been developed for risk stratification in Myocardial Infarction (MI). The latter is the most validated one, yet active research is ongoing for improving prognostication in MI. The purpose of this research is to test the efficacy of a new model for inhospital and 2-year all-cause mortality prediction – ACHTUNG score – and to compare it with GRACE.

Methods: 846 patients admitted for MI (age 68.6±13.4, 63.2% males, 43.7% STEMI) and followed for 2 years. Two versions of the ACHTUNG score were developed for inhospital (ACHTUNG-IH) and 2-year (ACHTUNG-2) all-cause mortality prediction. ACHTUNG-IH included: Age, Creatinine clearance < 68mL/min, Haemoglobin, maximum Troponin-I, maximum Urea > 9.85mg/dL, Glicemia > 7.45mmol/L, Glicemia (analytic parameters at admission). ACHTUNG-2 included: Age, Admission Creatinine clearance < 68mL/min, admission Haemoglobin, maximum Troponin-I, maximum Urea > 9.85mg/dL, Glicemia > 7.45mmol/L. Comparison through area under the curve (AUC) on ROC curve analysis and the net recategorization improvement index (NI) was performed between ACHTUNG-IH and GRACE score for inhospital mortality (GRACE-IH), and between ACHTUNG-2 and GRACE score for 6-month mortality (GRACE-6).

Results: ACHTUNG-IH displayed better performance than GRACE-IH in predicting inhospital mortality. Although the AUC was not significantly different (AUC ACHTUNG-IH 0.860, CI95% 0.834-0.883; vs. AUC GRACE-IH 0.828, CI95% 0.800-0.854, p=0.354), ACHTUNG-IH correctly reclassified 21.5% of patients in different risk subgroups (NRI 0.216, CI 95% 0.121-0.266, p < 0.001). ACHTUNG-2 was superior to GRACE-6 in predicting 2-year mortality (AUC 0.845, CI95% 0.814-0.872; vs. 0.798, CI95% 0.765-0.828, p=0.021). A significant net improvement in risk classification was shown by an NRI value of 0.134 (CI 95% 0.076-0.192, p<0.001).

Conclusions: This study suggested superior prognostic performance of the ACHTUNG score in inhospital and 2-year mortality prediction when compared to the current gold-standard in MI prognostication (the GRACE algorithm). These results should be reproduced and validated in wider multi-centre registries in order to further validate the ACHTUNG score as a new, practical and improved score for inhospital and 2-year all-cause mortality prediction following a MI.

Hospital composite performance indicator adherence is associated with reduced mortality in survivors of acute Myocardial Infarction

A.D. Simms1, P.D. Baxter1, P.B. Batim2, J.J. Wilson3, I.R. Pearson3, A.S. Hall1, C.F. Weston4, C.P. Gale1. 1University of Leeds, Leeds, United Kingdom; 2Pinderfields General Hospital, Wakefield, United Kingdom; 3Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom; 4Regional Cardiac Centre Morriston Hospital, Swansea, United Kingdom

Purpose: Composite performance indicators (CPI) have been proposed to assess hospital performance. We evaluate an opportunity based composite score (OBCS) in survivors of hospitalization for ST elevation and non-ST elevation myocardial infarction (AMI) using data from the Myocardial Ischaemia National Audit Project (MINAP) in 2008 and 2009.

Methods: For each hospital (n=165), we expressed an OBCS (as a percent), where the numerator was the number of times a care process (aspirin, thienopyridine, β blocker, statin, ACE inhibitor and referral for cardiac rehabilitation on discharge) was delivered and the denominator was the sum of all opportunities to give this care. Association between hospital OBCS and 30-day and 30-6-month mortality was studied using hierarchical models.

Results: There were 59115 complete cases suitable for analysis. In total 93.6% of care was delivered, 100% of all opportunities to provide care were NDI. Lowest hospital quartile median OBCS was 88.9% (IQR 83.8-94.0%) compared with 97.5% (95.9-99.1%) in the highest quartile. Unadjusted mortality decreased with increased OBCS, 30-day mortality: lowest quartile (95% CI) 2.34% (2.09-2.59%), highest quartile 1.42% (1.23-1.61%); 6-month mortality: 8.81% (8.34-9.28%) and 6.08% (5.69-6.46%), respectively. Following adjustment for GRACE risk score variables, with a random intercept for hospitals, this relationship persisted - 30-day mortality: 2.37% (2.33-2.41%) versus 1.71% (1.69-1.74%); 6-month mortality: 8.66% (8.89-9.2%) versus 6.53% (6.6-6.8%), respectively. Hospitals in the highest quartile (39 hospital) that treated 6806 patients had higher rates of referral for coronary intervention than those in the lowest quartile (47 hospitals, 14386 patients). 70.4% vs 58.2%. Hospital baseline characteristics were otherwise similar.

Increasing hospital performance profile was associated with decreased 30-day mortality (OR 95% CI): 0.90, 0.82-0.98; and 6-month mortality: 0.91, 0.87-0.96. After adjustment for referral for coronary intervention, 30-day mortality was (OR 95% CI): 0.91, 0.82-0.99; 6-month mortality was 0.93, 0.89-0.97.
Conclusion: There is an association with improving hospital CPI adherence and lower hospital mortality following discharge from hospital with AMI in England and Wales. The use of such measures in assessment of hospital ACS quality of care might be more appropriate than current measures. However, consideration of other variables associated with outcome, not included in the CPI, is also important in interpreting hospital performance and relation to hospital outcomes.

LEARNING MORE ON HEART TRANSPLANTATION AND BEYOND

Development of anti-HLA donor specific antibodies after heart transplantation and rejection: importance of a new method to detect the first component of the complement cascade


Purpose: The development of anti-HLA donor specific antibodies (DSAs) after cardiac transplantation has been linked to rejection with mixed results. Our aim is to define whether de novo DSAs are associated with the development of antibody mediated rejection (AMR) or acute cellular rejection (ACR), and to determine if complement fixing capability of the DSAs influences this association.

Methods: Diagnosis of DSAs was assayed quarterly in 145 consecutive patients following heart transplantation, between January 2006 and July 2011. Patients received induction therapy as per protocol, and a calcineurin antagonist based regimen with tapering doses of corticosteroids during the first year after transplant.

A new analytical method developed at our institution was used to differentiate DSAs capable of fixing the first component of the complement cascade (C1q+) from non-complement fixing antibodies (IgG+ C1q-). The frequency of either class of DSA was compared in patients with ACR, defined as a biopsy grade 3A/2R or higher using the ISHLT classification system, and in AMR, defined as a positive biopsy staining for C4d, C3d or CD68.

Results: 29 patients with DSAs prior to transplantation were excluded from analysis. Among the 116 patients studied (mean age 49 years; min19 max 72; 71% males), 88 patients (76%) did not develop any DSA during follow-up, 31 patients (27%) developed IgG+ DSAs and 19 patients (16%) C1q+ (both types coexisted in 17 patients).

Overall, patients with de novo DSAs (IgG+ or C1q+) experienced rejection more frequently than patients without DSAs, both AMR (30% vs. 6%, OR 7.0, p = 0.002) and ACR (44% vs. 19%, OR 3.6, p = 0.003).

With respect to DSA subtypes, patients with IgG+ DSAs more frequently experienced AMR (23% vs. 8%, OR 3.43, p = 0.03) and ACR (50% vs. 15%, OR 4.37, p = 0.001). In contrast, patients with C1q+ DSAs had a higher odds of AMR (39% vs. 9%, OR 6.36, p = 0.001) but showed no predisposition to ACR (33% vs. 28%, OR 1.2, p = 0.73).

Conclusion: The development of de novo DSAs after heart transplantation was clearly associated with the presence of both AMR and ACR in our population. While IgG+ DSAs were associated with both types of rejection, C1q+ DSAs showed a strong relationship with AMR only.

These results suggest the importance of monitoring DSAs post-transplant. Early detection of DSAs can specifically identify a subgroup of patients at risk of AMR who could potentially benefit from preventive therapies.

Impact of sildenafil treatment on pulmonary hemodynamics and outcomes in patients with severe pulmonary hypertension receiving heart transplantation

M. Senechal, J. Pons, M. Bernier, B. Cantin, S. Bergeron, G. Proulx, C. Nalli, N. Chateauvert, M.H. LeBlanc. Quebec Heart Institute, Laval Hospital, Quebec, Canada

Purpose: Pulmonary vascular resistance (PVR) in heart transplant candidates is associated with poorer post-transplant survival. The aim of this study is to assess the impact of preoperative sildenafil administration on pulmonary hemodynamics and clinical outcomes in patients with advanced heart failure who were considered high-risk patients for heart transplantation (HT) because of elevated PVR and transpulmonary gradient (TPG).

Methods: 119 consecutive patients receiving HT between 2004-2011 were included. Fifteen patients (group A) had severe pulmonary hypertension (PH) defined as PAPm >25mmHg and/or PVR >2.5 Wood units (WU) and/or TPG >12mmHg after vasodilator test or continuous administration of inotropic drugs compared to 104 patients (group B) without severe PH. Group A received sildenafil therapy. Pulmonary hemodynamics were evaluated before HT with and without sildenafil therapy. Right catheterization was also analyzed early after HT with sildenafil therapy and late after HT without sildenafil.

Post-transplant survival was compared between two groups.

Results: Sildenafil dosage was 109±42mg/day during 163±116 days before HT. After sildenafil therapy PAPm, PVR and TPG decreased from 43.9±12.5mmHg to 33.4±5.8mmHg, 5.0±1.1 WU to 3.0±1.6 and 17.3±3.2mmHg to 10.2±2.4mmHg respectively (p<0.01). All patients underwent successful HT. Sildenafil dosage was 140±70mg/day during 43±45 days after HT. There were no differences in PVR and TPG on sildenafil therapy early after HT and without sildenafil 6 months after HT. Post-transplant survival was similar between groups.

Conclusion: Sildenafil therapy successfully decreases PVR and TPG in patients with severe pulmonary hypertension allowing successful HT without increased post-transplant mortality.

Evelorimus after heart transplantation: 4 years’ single center follow-up in calcineurin inhibitor-free immunosuppression

M.A. Engelen1, S. Gunia1, P. Klamer1, D. Schlab2, S. Amier2, J.R. Sindersmann2, J. Stymann1, 1University Hospital of Muenster, Department of Cardiology and Angiology, Muenster, Germany; 2University Hospital of Muenster, Department of Thoracic and Cardiovascular Surgery, Muenster, Germany; 3University of Muenster, Department of Medical Informatics and Biomatics, Muenster, Germany

Purpose: Everolimus is a proliferation signal inhibitor introduced for orthotopic heart transplantation (oHTx) in Germany in 2004. This study reports the 4 years’ results of CNI-free immunosuppression using everolimus after oHTx in maintenance patients (pats) longer than 1 year after transplantation. To the best of our knowledge, our group is world-wide the first group reporting long-term data of a large collective of pats on this issue.

Methods: Pats after oHTx being switched to everolimus mostly due to CNI-induced adverse drug effects as deterioration of kidney function, arterial hypertension or recurrent rejections were continuously enrolled. 60 pats underwent standardized switching protocols, 39 pats completed full 48-months follow-up. Physical and laboratory examination ± echocardiography were performed regularly. Biopsies were carried out at switch, before deep surgical wound operations and in clinical suspicion of rejection. Coronary angiogram and myocardial scintigraphy were performed before and yearly after switching to CNI-free immunosuppression based on everolimus.

Results: After switching to everolimus, most pats recovered from the side effects associated with CNI’s. Renal function improved significantly after 12 months and was stable until the end of this study (creatinine at baseline (BL) mean 1.79 (IQR25/75: 1.49-2.51), at 48 months 1.14 (37). p<not significant (ns) for BL vs 48 months). Systolic and diastolic blood pressure was not elevated and stable over all 48 months (p=ns for all comparisons). LV ejection fraction was stable over 48 months in echocardiographic and scintigraphic

Biomarkers and clinical scores in predicting the outcome of ACS / Learning more on heart transplantation and beyond 207

Characterization of a specific mechanism for late loss of cardiac allograft: the antibody mediated rejection (AMR) as a major factor of cardiac allograft vasculopathy (CAV)

C. Touquet1, A. Loupy2, P.H. Rouver2, S. Varnous3, A. Cazes5, M. Tible3, T. Beaucar2, X. Jouven6, P. Brunere2, J.P. Duong Van Huyen2, 1University Hospital of Nanterre, Nanterre, France; 2AP-HP - European Hospital Georges Pompidou, Dept. Pathology, Paris Descartes University, Inserm U970, Paris, France; 3AP-HP - Hospital Pitie-Salpetriere, Paris, France

In heart transplantation CAV is the main cause for the late cardiac graft loss. The pathogenesis of CAV remains unclear and complex involving immune and non-immune factors. The rational of this study was to investigate expanded failing cardiac allograft biopsies (11/21) as shown by intravascular macrophages and/or C4d deposits and by positive DSA (10/14) versus nil in pure atherosclerosis pattern (p=0.05 and p=0.05, respectively).

In failing cardiac grafts CAV lesions are associated with makers of AMR. CAV and patheries of DSA were retrospectively assessed in stored sera using Luminex SA technique.

A pure classical coronary atherosclerosis pattern was observed in 6/31 (19%). A pure pattern of CAV was present in 12/31 (38%) and a mixed pattern associating CAV and atherosclerosis features in 9/31 (29%). The coronary arteries were devoid of significant lesions in 4/31 (13%). Interestingly the CAV pure and mixed patterns were associated with vascular endothelial growth factors and/or the microcirculation with C4d deposits and macrophages (15/21) in the explanted grafts versus nil (0/6) in pure atherosclerosis pattern (p=0.002). Furthermore they were associated with previous AMR episodes in endomyocardial biopsies (11/21) as shown by intravascular macrophages and/or C4d deposits and by positive DSA (10/14) versus nil in pure atherosclerosis pattern (p=0.05 and p=0.05, respectively).

In failing cardiac grafts CAV lesions are associated with makers of AMR. CAV should be the consequence in coronary arteries of an ongoing AMR process.
Is contemporary medication regimen after heart transplantation more myelotoxic?  
M. Pauderini, I. Malek, E. Kouteckova, J. Sochman, J. Kautzner  
Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic

Purpose: To evaluate the incidence of bone marrow suppression and associated consequences in patients within the first year after the heart transplantation.

Patients and Methods: The patient cohort was divided in two subgroups. Group I (n=47, period between 2008-2009) was treated with anti-infective and antiproliferative regimen which is currently used in patients after heart transplantation (mycophenolate mofetil-MMF, atazanavir-prim/sulfamethoxazole). Group II (n=47, period between 2004-2007) had only MMF among the potentially myelotoxic medication, as the use of valganciclovir and trimethoprim/sulfamethoxazole began in our center in 2008. The myelotoxic dose and need for dose adjustment or complete withdrawal of the MMF was assessed. Moreover the incidence of reactions associated with MMF adjustment was analyzed during the first 12 months after the index procedure in Group I.

Results: Significant difference in number of patients with lymphopenia (lymphocytes: 0.8×10^9/L) was observed between both patient groups at three months (38.3% vs. 6.4% in Group II; p<0.0002) and at one year (19.1% vs. 4.3% in Group II; p=0.03) Group I patients had a significantly higher proportion of patients with leucopenia (leucocytes: 4×10^9/L) in Group I as compared with Group II (19.1% vs. 2.1%; p=0.02) at three months after heart transplantation. No major difference in number of other blood elements (erythrocytes, neutrophils, thrombocytes) was observed in both study groups in the reference periods (1 month, 3 months, 6 months and 12 months after heart transplantation). MMF was reduced or discontinued due to bone marrow suppression in 63.8% patients in Group I, while only in 8.5% patients in Group II (p<0.001). Interestingly, at least 1 episode of higher degree cellular or humoral rejection occurred in 35% of patients with the standard MMF dosage as compared with only 26% occurrence rate in patients with dose reduction or complete withdrawal of MMF.

Conclusion: Addition of valganciclovir and trimethoprim/sulfamethoxazole to current medication regimen results in significant lymphopenia and leucopenia. Modification of immunosuppressive prophylaxis (reducing or stopping MMF) is associated with normalization of blood count without increased incidence of rejection.

Long-term follow-up of heart transplant recipients initially disqualified from the waiting list because of pulmonary artery hypertension: the pivotal role of PDE5 inhibition

L.S. De Santo1, A. Della Corte2, M. Buonocore2, C. Bancone2, N. Gaiden2, G.P. Romano3, G.A. Nappi3, C. Maelio3, A. Amarelli1, 1University of Foggia, Foggia, Italy; 2Second University of Naples, Naples, Italy; 3Dept. Cardiovascular Surgery and Transplant V Monaldi Hospital, Naples, Italy

Purpose: Unresponsive pulmonary hypertension (PH) may contra-indicate heart transplantation since it implies poor early outcomes. Present study reports the effectiveness of oral perioperative sildenafil in allowing heart transplant candidacy and surgery as well as long term survival in a selected group of patients initially deemed ineligible because of PH.

Methods: Between May 2005 and December 2009, 31 consecutive patients (5 females, 9 with an history of idiopatic cardiomyopathy and 16 with an history of pulmonary hypertension) were included and DAPT regimens were used irrespective of disease presentation.

Results: Two-year major bleeding rates were assessed prospectively and compared as secondary endpoints between the BASKET (B) and BASKET-PROVE (BP) trials using the Bleeding Academic Research Consortium (BARC) and Thrombolysis In Myocardial Infarction (TIMI) classifications. DAPT with clopidogrel was prescribed in B for 6 months (loading dose 300mg, maintenance dose 75mg) and in BP for 12 months (loading dose 600mg, maintenance dose 75mg). In both studies acute consecutive patients with significant comorbidities, chronic coronary disease were included and DAPT regimens were used irrespective of disease presentation or stent type. Multivariate Cox proportional hazard regression models for time to bleeding after orthotopic heart transplantation, including the effect of different dual antiplatelet therapies, adjusting for baseline differences between the two trials. Results: A total of 3,140 patients were studied (B=826, BP=2,314). Since oral anticoagulation used in B was administered either as an fixed dosage of vitamin K antagonists or as an individual dosage, ratios of vitamin K antagonists were higher in B than in BP (6 vs. 4%, p=0.004) as was the use of glycoprotein IIb/IIIa inhibitors (36 vs. 23%, p=0.001) despite less STE-elevation myocardial infarctions (21 vs. 32%, p=0.001). Compared with BP, BARC 3/5 bleeding events were more frequent in B during the first 3 days (1.0 vs. 0.3%, p=0.020) and 6 months (1.7 vs. 0.7%, p=0.019) but numerically less frequent during months 7 to 12 (0.1 vs. 0.6%, p=0.151) and similar during months 13 to 24 (0.5 vs. 0.4%, p=1.00). Results were similar with regard to TIMI major bleedings. After adjustment for baseline differences, enrollment in BP (hazard ratio (HR) 0.38, 95% confidence interval (CI) 0.18-0.83, age (HR 1.05, 95%CI 1.01-1.09) and female sex (HR 0.68, 95%CI 0.23-1.35) were independent predictors for BARC 3/5 bleeding during the first 6 months.

Conclusion: Major bleeding events up to 6 months were more frequent in B than in BP but most likely due to a higher use of vitamin K antagonists and glycoprotein IIb/IIIa inhibitors in B at baseline. Late major bleeding rates were generally low but numerically higher with residual DAPT in BP than without DAPT in BP during months 7 to 12. This signal raises a word of caution against prolonged DAPT after stent implantation.
curved in only 2 pts (0.1%), and BARC type 5 bleeding (lateral) occurred in 3 (0.2%) pts. As the BARC bleeding severity worsened, there was a gradient of increasing rates of 1-year death and reinfection (Table). The 1-year mortality rate increased from 12.1% with BARC 0+ type to 43.5% with BARC type 3b bleeding. After exclusion of pts with intracranial hemorrhage (BARC 3c bleeding) and multivariable adjustment for demographic and clinical characteristics of pts, the independent predictors of death were BARC type 3a (OR 2.97; 95% CI 1.16-6.94; p=0.017) and BARC type 3b bleeding (OR 4.62; 95% CI 1.75-12.16; p=0.002).

Conclusion: The BARC type 3 bleeding complicating STEMI occurs frequently and is associated with high mortality. Pts with BARC type 3a bleeding are at 2-fold higher risk of 1-year death, but those with BARC type 3b bleeding are at more than 4-fold higher risk.

**1422 Longitudinal stability of five contemporary coronary stent platform designs**

G. Leibundgut1, M. Gick1, A. Torna1, K. Harkopf2, G. Hummel2, H.-J. Buettner3, F.-J. Neumann1, 1Heart Centre Bad Krozingen, Bad Krozingen, Germany; 2Allurs GmbH, Freiburg, Germany

Objectives: The Promus Element stent platform features a unique design with beneficial physical and biological properties. The struts responsible for longitudinal strength of the open cell design are reduced in number, diagonally aligned, and thinner in diameter. Conceptually, this may reduce longitudinal stability which recently became clinically apparent and might have implications on future treatment. The aim of this study was to evaluate longitudinal compression behavior of five contemporary coronary stents.

Methods: We performed a new bench test to measure longitudinal strength properties of five contemporary stent platforms. Three individual 3.5 mm stents of each design and comparable length were tested consecutively being longitudinally compressed and force-strain curves (figure) were recorded.

Results: Mechanical testing of five different stent scaffold designs revealed a significant reduction of the longitudinal strength of the Element platform design compared to all other stents. Yields force (10.0 N) as well as ultimate strength (0.149 N) were significantly lower for the Promus Element stent (p<0.001) compared to all other stents. Yield force (0.100 N) as well as ultimate strength (0.360 N, 0.385 N; Xience Prime: 0.480 N, 0.668 N; Cypher: 0.500 N, 0.851 N). Spring constant derived from the force-strain curves also revealed differing elastic behavior, such as soft (Promus Element: 0.041 N/mm), intermediate (Resolute Integrity: 0.300 N, 0.520 N; Taxus Liberté: 0.360 N, 0.385 N; Xience Prime: 0.480 N, 0.668 N; Cypher: 0.500 N, 0.851 N). Significance was characterized into two groups according to whether FPA developed or not. All the parameters were compared between FPA and non-FPA groups.

Results: The incidence of FPA after primary PCI was determined to be 23.3%. The mean age was higher in the FPA group compared to the non-FPA group (mean age: 60.6±11.6 vs. 56.5±11.8, respectively, p<0.007). Furthermore, the FPA developing group experienced prolonged hospitalizations compared to the non-FPA group, but no differences in in-hospital or long term mortality were noticed. In the multivariable analysis of this study, female gender and age (>75 years) after primary PCI, were found to be independent predictors of FPA.

Conclusions: High incidence of FPA was noticed in STEMI patients undergoing primary percutaneous coronary intervention for ST-elevation myocardial infarction.
primary PCI, which prolonged in-hospital stay. Extra care must be given, especially to women and those who are >75 years of age, for this complication.

Age, glomerular filtration rate, ejection fraction, and the AGEF score predict contrast-induced nephropathy in patients with acute myocardial infarction undergoing primary PCI

G. Ando, G. Morabito, C. De Gregorio, O. Tro, F. Saporito, G. Oreo. University of Messina, Department of Medicine and Pharmacology, Messina, Italy

Background: In patients undergoing primary percutaneous coronary interventions (PCI) for ST-segment elevation myocardial infarction (STEMI), the occurrence of Contrast-Induced Nephropathy (CIN) has a pronounced impact both on morbidity and mortality. We investigated the variables associated with CIN development in the setting of primary PCI and evaluated the predictive value of a 3-variable clinical risk score (the AGEF score) based on age, left ventricular ejection fraction (LVEF) and estimated glomerular filtration rate (eGFR).

Methods: 481 consecutive patients with STEMI who were undergoing primary PCI were prospectively enrolled. CIN was defined as an absolute increase in serum creatinine ≥0.5mg/dL or an increase ≥25% from baseline within 72 hours after the administration of contrast medium. AGEF score was calculated by adding 1 point to the Age (EF%) ratio if the eGFR was <60 mL/min per 1.73 m². Results: Overall, the incidence of CIN was 5.2%. As expected, in-hospital mortality was higher in patients with CIN than in those without (16% vs 1.3%, p<0.001). At multivariate analysis age (OR 1.08, p=0.038, AUC 0.78), eGFR (OR 0.95, p=0.002, AUC 0.88), LVEF (OR 0.94, p=0.033, AUC 0.69) and post-procedural TIMI flow grade (OR 0.30, p=0.01, AUC 0.57) were independent predictors of CIN. AGEF score was an accurate (OR 5.19, p<0.001, AUC 0.88) and calibrated ( Hosmer-Lemeshow y’=6.24, p=0.62) predictor of CIN (Figure).

Figure 1. Scatter plot of ROC curve analysis

Conclusions: Advanced age, depressed LVEF and reduced eGFR are independent predictors of CIN development after primary PCI for STEMI. In our model, the pre-procedural individual patient risk can be assessed by calculating the AGEF score by solving this exponential equation: Risk = e^[AGEF score * (1.65 - 6.26)] (1 + e^[AGEF score * (1.65 - 6.26)]).

CHANELLOPATHIES: WHAT’S NEW IN GENETICS AND BEYOND

Early repolarization and increased risk of ventricular fibrillation in during acute myocardial infarction

T. Suzuki1, H. Watanabe1, N. Yaghari2, M. Oda1, A. Satou1, T. Oizawa1, M. Satou2, Y. Alcza2, Nigata University, Nigata, Japan; 1Tachikawa General Hospital, Cardiovascular Center, Nagaoka, Japan

Purpose: Early repolarization or J wave is a common finding on the 12-lead electrocardiogram and has generally been considered benign for decades. However, since we and others reported that early repolarization is associated with an increased risk of ventricular fibrillation and sudden cardiac death related to idopathic ventricular fibrillation, there is an increasing interest in early repolarization. Although early repolarization has been associated with the risk of arrhythmias in Brugada Syndrome, this is the incidence of abnormal ventricular repolarization in acute myocardial infarction. Methods: This study included 310 consecutive patients with acute ST-segment elevation myocardial infarction (70±12 years, 84 females) who underwent successful percutaneous coronary intervention in our institutions. Early repolarization was defined as an elevation of the QRS-ST junction >0.1 mV from the baseline manifested as QRS slurring or notching in at least 2 inferior or lateral leads of 12-lead electrocardiogram. Results: Among the 310 patients, 24 patients (7.7%) experienced one or more episodes of ventricular fibrillation within 48 hours after the onset of acute myocardial infarction. All of the patients who had ventricular fibrillation were successfully resuscitated. Early repolarization was present in 34 patients (11%). The frequency of early repolarization was higher patients with ventricular fibrillation (29%) than in those without ventricular fibrillation (10%; P<0.01). In multivariate models, early repolarization was associated with the increased risk of ventricular fibrillation (Odds ratio, 3.10; 95% confidence interval, 1.13-8.47; P=0.03). The heart rate, QT interval or conduction disease were not associated with ventricular fibrillation. There was no association of age, gender, family history of sudden cardiac death, body mass index, hypertension, dyslipidemia, diabetes, or metabolic syndrome with the risk of ventricular fibrillation. Severity of myocardial infarction including the maximum creatine phosphokinase level, culprit artery, ejection fraction, or heart failure were not associated with the risk of ventricular fibrillation.

Conclusion: Early repolarization increased the risk of developing ventricular fibrillation during acute myocardial infarction. Our data may be useful for risk stratification for arrhythmia events during acute phase of myocardial infarction.

Frequency of Brugada type ECG pattern in patients with fever

B. Hunuk, O. Erdogang, Marmara University, Faculty of Medicine, Department of Cardiology, Istanbul, Turkey

Purpose: It is well known that fever might induce Brugada Type ECG Pattern (BTEP) and be responsible for ventricular arrhythmias and sudden death in certain subjects. However, it is not known whether fever is always an underlying cause of BTEP in normal subjects who present with fever. Although there are many case reports about BTEP observed in some subjects with fever, there is a lack of prospective data investigating the true prevalence of BTEP associated with fever. Hence, our aim was to determine the true frequency of BTEP in normal subjects with fever by recording ECGs from routine and higher intercostal spaces.

Methods: A total of 103 male subjects (mean±SD age, 37.1±10.8 years) who came in with increased fever due to any reason and without any known cardiac disorder were prospectively enrolled in the study. After the standard ECG recording, two other recordings were obtained by carrying the V1-V3 leads to the 3rd and 2nd intercostal spaces (ICS). ECG recordings were repeated with the same technique after the body temperature of the patients with fever went down to normal values.

Results: The frequencies of BTEPs at the 4th, 3rd and 2nd ICS were 2.9% (3 type 3), 6.8% (7 type 3) and 10% (2 type 2 and 8 type 3), respectively (no type 1 BTEP detected). If 4th ICS compared to 3rd or 2nd ICS, the frequency of BTEPs increased. The frequencies of BTEPs compared to 2nd ICS for detecting BTEPs, 2nd ICS was much more sensitive and significant compared to 4th ICS (p = 0.016). BTEP was detected from higher ICS in only one subject with fever (1%) whose BTEP during afebrile status completely resolved. There were no statistically significant differences between the frequencies of BTEPs obtained in febrile and afebrile states in subjects with fever (p = 0.9).

Conclusion: The present study showed for the first time that BTEP recorded in normal subjects with fever did not resolve when the subjects were afebrile. Fever seems to play no specific role for BTEP in healthy subjects. Because of this, if it is solely seen (especially type 1) in a subject with fever, it may be considered as a unique finding for unmasking and diagnosing Brugada syndrome.

Mutations in the alpha-subunit of the cardiac L-type calcium channel in Brugada syndrome: implications for genotyping strategies

V. Novelli1, M. Memmi2, M. Cerone1, R. Yanlei1, C. Song1, S. Crespo-Carbone1, R. Blösser2, C. Napoliardo2, S.G. Priori3, New York University School of Medicine, New York, United States of America; 1IRCCS Salvatore Maugeri Foundation, Pavia, Italy

Brugada Syndrome (BrS) is an inherited arrhythmogenic disorder leading to juvenile sudden cardiac death (SCD) in the absence of structural heart disease. The typical ECG pattern shows ST segment elevation in leads V1-V3 with or without right bundle branch block. So far only a few genes have been associated with BrS and overall they account for about 25-30% of cases. Recently, mutations in the CACNA1C gene encoding the alpha-subunit of the cardiac L-type calcium channel have been identified in BrS patients (pts) and their prevalence is currently estimated around 5.5% of cases. It has been suggested that these pts show an overlapping phenotype encompassing BrS and Short QT Syndrome (SQTS). We screened a series of 194 BrS pts on the CACNA1C gene by direct sequencing. All were negative for mutations on the SCNS5A and OPLD-1 BrS genes. In this group, 26 pts showed BrS phenotype associated with short QT interval (OCT~360 msec), while the remaining 168 BrS pts had normal QT values. We discovered 7 non-synonymous mutations and one splice error mutation, not reported in the literature. None of these variants were found in the following
 databases of healthy controls: dbSNP_135; 1000 Genome Project database, NHLBI Grand Opportunity Exome Sequencing Project (ESP). All mutations had a minor allele frequency (MAF) less than 0.1%. Sequence homology tool (SIFT) was employed to predict the damaging effect of each variation identified.

Four of these occurred in the 15% of patients with BrS/SQTS (mean QTc 362±14 ms) and the remaining 4 mutations have been identified in the 12.38% of BrS pts with a QTc >360 ms at rest.

Functional expression studies performed on the two mutations with predictive damage effects with a score<0.01 led to loss of function on calcium channel current.

Our data suggest that the global yield of CACNA1c genetic screening in BrS/QTcBrS is approximately of 4%; the presence of QTc of CACNA1c mutations, comparable to the presence of SCN5A mutations. In a tiered approach to BrS genotyping, the presence of QTc+BrS is approximately of 4%; the presence of a short QT (QTc <360 ms at peak exercise, p not significant). Mean QT interval values were lower in the SQTS group in respect to controls, both at rest (271±6 ms vs 353±26 ms, p<0.0001) and at peak exercise (228±27 ms vs 246±25 ms, p=0.03). SQTS patients had a lower adaptation of the QTc interval at higher heart rates, with a mean variation from rest to peak effort of 48.1±14 ms vs 107±21 ms of the controls (p<0.0001). As a result, the regression analysis of the QT/HR relationship revealed a less steep slope for SQTS patients as compared to control group, never exceeding the value of −0.90 ms/beat/min (mean value −0.54±0.17 ms/beat/min vs −1.30±0.31 ms/beat/min, p<0.0001). Multilevel analysis revealed that the QT/HR relationship was not influenced by age.

Conclusion: SQTS patients show a peculiar behaviour at stress test, with a reduced QT adaptation to heart rate which is reflected in a less steep slope of the linear relation than control subjects. Therefore, exercise testing can be a useful tool in distinguishing patients with SQTS from individuals of the general population with QTc>QTc interval at the lower limits of the normal range.

### In vitro characterization of the N-terminal RyR2 R420Q mutation, a cause for autosomal dominant catecholaminergic polymorphic ventricular tachycardia

**E. Zorio Grimà, P. Neco Adadà, D. Domingo Valero, A.F. Lai, A. Salvador Sanz, A.M. Gomez Garcia, Hospital La Fe, Valencia, Spain; Miguel Hernandez University, Department of Bioengineering, Alicante, Spain; Wales Heart Research Institute, Cardiff University School of Medicine, Cardiff, United Kingdom; Inserm, U769, Université de Paris 11, Château-Malabry, Paris, France**

Catecholaminergic Polymorphic Ventricular Tachycardia (CPVT) is highly malignant inherited arrhythmia disease characterized by stress-induced syncope and sudden death. Most of the CPVT mutations are concentrated in RyR2 hotspots: the C terminus, the central and the N terminal domains. Although the phenotypic manifestations are similar irrespective of the mutation site, it is likely that the underlying mechanism of RyR2 dysfunction varies depending on the location of the mutation within RyR2 since not all the functional studies performed have reported a gain-of-function. Recently, we have identified a mutation in a family with CPVT, located in the N terminal portion: the RyR2R420Q.

**Purpose:** To analyze the function of the mutated RyR2 channel.

**Methods:** We have created GFP tagged plasmids of RyR2R420Q and RyR2WT and their heterologous expression in HEK cells has been studied by using confocal microscopy. By changing known Ca2+ solutions and adding caffeine to the experiment the behavior of the mutated channel was compared to that of the WT protein.

**Results:** The peak caffeine-evoked (Ca2+) transients reached 1.85±0.09 in RyR2WT cells and only 1.56±0.05 in RyR2R420Q cells, which means a 34% decrease in caffeine sensitivity. In addition, analysis of relative cytosolic Ca2+ sensitivity exhibited no differences between wild type and mutated channels, as both site behaviors in other previously reported RyR2 mutations, supports the idea that functional heterogeneity may underlie the CPVT phenotype caused by RyR2 mutations.

### Usefulness of exercise testing in the diagnosis of Short QT Syndrome

**C. Scorrolo1, C. Giustetto1, A. Mazzanti1, M. Levetto1, R. Dalmaso1, R. Schimpf5, C. Wolpert6, P. Maury1, A.F. Lai1, A. Salvador Sanz1, A.M. Gomez Garcia4. 1Hospital La Fe, Valencia, Spain; 2Miguel Hernandez University, Department of Bioengineering, Alicante, Spain; 3Wales Heart Research Institute, CardiffUniversity School of Medicine, Cardiff, United Kingdom; 4Inserm, U769, Université de Paris 11, Château-Malabry, Paris, France**

Short QT Syndrome (SQTS) is a rare arrhythmogenic congenital disease. Diagnosis can be challenging in subjects with borderline or slightly shortened QT interval at ECG. The aim of this study was to evaluate the QT interval behaviour during exercise in a cohort of SQTS patients, and to compare it with that of a control group from the general population, in order to evaluate the usefulness of exercise testing in the diagnosis of the syndrome.

Methods: we enrolled one SQTS patients (8 with KCNH2 mutation, 13 with unknown genotype) and 21 control subjects underwent an exercise test. For each individual the QT interval was measured at different heart rates, both at rest and during effort at 25%, 50%, 75% and 100% of the overall range of rates from baseline to peak exercise. The relation between QT interval and heart rate was evaluated by linear regression analysis according to the formula: QT=mnHR + b, where m is the slope of the linear relation, and b is the intercept. Regression was calculated from 3 to 5 data points. We used multilevel mixed-effects linear regression models accounting for QT and HR time-dependent variables, with a random intercept and a random coefficient for modelling heterogeneity between individuals and an unstructured variance-covariance structure. Models included fixed effects for age and sex.

**Results:** The two groups showed similar resting and peak exercise heart rates (75±14 beats/min vs 79±15 beats/min at rest, 168±20 beats/min vs 166±20 beats/min at peak exercise, p not significant). Mean QT interval values were lower in the SQTS group in respect to controls, both at rest (271±6 ms vs 353±26 ms, p<0.0001) and at peak exercise (228±27 ms vs 246±25 ms, p=0.03). SQTS patients had a lower adaptation of the QTc interval at higher heart rates, with a mean variation from rest to peak effort of 48.1±14 ms vs 107±21 ms of the controls (p<0.0001). As a result, the regression analysis of the QT/HR relationship revealed a less steep slope for SQTS patients as compared to control group, never exceeding the value of −0.90 ms/beat/min (mean value −0.54±0.17 ms/beat/min vs −1.30±0.31 ms/beat/min, p<0.0001). Multilevel analysis revealed that the QT/HR relationship was not influenced by age.

Conclusion: SQTS patients show a peculiar behaviour at stress test, with a reduced QT adaptation to heart rate which is reflected in a less steep slope of the linear relation than control subjects. Therefore, exercise testing can be a useful tool in distinguishing patients with SQTS from individuals of the general population with QTc>QTc interval at the lower limits of the normal range.

### Safe drug use in long QT syndrome and Brugada syndrome: who uses www.QTdrugs.org or www.BrugadaDrugs.org and why?

**P.G. Postema1, J. Neville2, J.S.S.G. De Jong3, K. Romero2, C. Mine2, A.A.M. Wilde1, R.L. Woosley3. 1Academic Medical Center, Heart Failure Research Center, Department of Cardiology, Amsterdam, Netherlands; 2Critical Path Institute, Tucson, Arizona, United States of America**

**Purpose:** Below the age of 40 years, most cardiac arrests are due to inheritable arrhythmias syndromes, among which Long QT and Brugada syndrome. In these syndromes, provoking factors such as drugs are often involved. It is of vital importance that patients with these syndromes and their healthcare professionals are familiar with the possible pro-arrhythmic effect of many cardiovascular and noncardiovascular drugs. As an aid for this issue we developed two websites: www.QTdrugs.org (2001) and www.BrugadaDrugs.org (2009). Here we analyzed how these websites are used.

**Methods:** Prospective continuous web-use statistics and an online survey were utilized.

**Results:** QTdrugs.org has received >2,800,000 visitors from 180 countries since the start of web-use statistics in October 2003 through January 2012. Most visitors originated from the Americas (87%) compared to Europe (7%), Asia (3%), Oceania (2%) and Africa (1%). In the past year, the site averaged 1,397 visitors per day. Over 600 persons have registered to receive regular email updates. The QTdrugs.org survey yielded 261 respondents, of whom 54% between 40-59 years of age, 58% female, 34% diagnosed with Long QT syndrome and 50% physicians, pharmacists or paramedics. Most respondents visited the website for the first time (36%), 23% visits at least every month, and 28% at least every 6 months. The website was considered very helpful for 62% and rather helpful by 20%. Of the patients, 76% refunded from, and 58% discontinued certain drugs by using the website. BrugadaDrugs.org has received >55,000 visitors from 154 countries from June 2009 through January 2012. Most visitors originated from Europe (45%) and the Americas (40%), but less from Asia (10%), Oceania (4%) and Africa (1%). In the past year, the site received between 1,500 and 3,000 visitors each month. Over 500 persons have registered to receive email updates. The BrugadaDrugs.org survey yielded 164 respondents, of whom 62% between 40-59 years of age, 44% female, 68% diagnosed with Brugada syndrome and 21% physicians, pharmacists or paramedics. Most respondents visit the website at least every 6 months (52%), 32% return at least once a month, and 6% were first time visitors. The website was considered very helpful for 71% and rather helpful by 26%. Of the patients, 71% refunded from, and 46% discontinued certain drugs by using the website.

**Conclusions:** QTdrugs.org and BrugadaDrugs.org have been developed to ensure worldwide availability of information on safe drug use in Long QT syndrome and Brugada syndrome. These sites are heavily utilized but further design improvement and promotion of the sites is warranted.

### Aortic Valve: From Cell to Surgery

**G. Ferrari, R. Sainiger, P. Poggio, J.B. Grau, E. Branchetti, R.C. Gorman, J.E. Bavaria. University of Pennsylvania School of Medicine, Philadelphia, United States of America**

**Purpose:** Bicuspid Aortic Valve (BAV) is the most common cardiac congenital anomaly dominated by valvular dysfunction such as Bicuspid Aortic Stenosis (AS), and aortic insufficiency (AI). Bicuspid AS is an active multi-factorial process, char-
Evaluation of aortic valve calcium load by computed tomography as a new tool to assess aortic stenosis severity: insights from a multicenter international registry

M.-A. Clavel1, D. Messika-Zeitoun2, P. Pibarot2, S. Aggarwal1, P. Araoz1, G. Cuello1, E. Larosé3, R. Capoulade3, M. Enriquez-Sarano1, Mayo Clinic, Department of Cardiovascular Disease, Rochester, United States of America; 2AP-HP - Hospital Bichat-Claude Bernard, Department of Cardiology, Paris, France; 3Laval Hospital/Quebec Heart Institute, Quebec, Canada

Background: Quantification of Aortic Valve Calcification (AVC) load by multislice computed tomography may be useful to assess aortic stenosis (AS) severity. A previous study has suggested that an AVC cut-off value of 1651 AU provides 82% sensitivity and 80% specificity to identify hemodynamically severe AS. The aim of this multicenter study was to confirm, in a larger series of patients, the utility of AVC to identify severe AS and to refine the cut-point values of AVC for this purpose.

Method: 512 patients with AS and normal LV outflow (left ventricular ejection fraction ≥50% and stroke volume index ≥35 ml/m²) underwent comprehensive Doppler echocardiography and simultaneous AVC measurement by CT. Based on Aortic Valve Area indexed to body surface area (AVAi), peak aortic jet velocity (Vmax), and mean gradient (MG), 247 (48%) patients had a moderate AS (AVAi ≤0.6 cm²/m² and Vmax ≥4 m/s) and 266 (52%) a severe AS (AVAi ≤0.6 cm²/m² and Vmax ≥4 m/s and MG ≥40 mmHg). AVC was determined with the use of the Agatston method. We calculated two parameters in order to account for inter-individual variability in body size: AVC indexed to body surface area (AVCi) and AVC indexed to aortic annulus cross-sectional area (i.e. AVC density, AVCd).

Results: AVC, AVCi and AVCd correlated well with hemodynamic severity of AS as assessed by Doppler-echocardiography (i.e. AVAi, Vmax and MG) (all r = 0.63 and all p < 0.0001). ROC curves analysis revealed that the best cut-point values to identify severe AS were an AVCi ≥1590 AU, an AVCd ≥750AU/cm² and an AVCd ≥380 AU/cm².

Performance of different CT criteria

<table>
<thead>
<tr>
<th>CT criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>AVCi ≥1590 AU</td>
<td>0.92</td>
<td>0.85</td>
<td>0.86</td>
<td>0.86</td>
</tr>
<tr>
<td>AVCi ≥750 AU/cm²</td>
<td>0.92</td>
<td>0.81</td>
<td>0.91</td>
<td>0.82</td>
</tr>
<tr>
<td>AVC density ≥390 AU/cm²</td>
<td>0.94</td>
<td>0.88</td>
<td>0.89</td>
<td>0.90</td>
</tr>
</tbody>
</table>

AVC: Area under ROC curve; PPV: Positive predictive value; NPV: Negative predictive value.

Conclusion: In this large, multicenter series of patients, AVC measured by multislice CT showed excellent correlation with Doppler-echocardiographic markers of AS severity. An AVC density ≥390 AU/cm² provides the best accuracy to identify severe AS. This new CT index may be useful to assess stenosis severity in AS patients, and particularly in those with low-flow, low-gradient AS, in whom Doppler-echocardiography often remains insufficient.

Aortic valve: from cell to surgery / Looking at valves from a different angle

Evaluation of multidimensional geriatric assessment as predictor of mortality and adverse events after Transcatheter Aortic Valve Implantation (TAVI)

S. Stortecky1, A.W. Schoenberger2, A. Mose3, P. Juen4, T. Carrel1, C. Schoenberger1, A.E. Stuck1, S. Windcker1, P. Wernwaseler1, Bern University Hospital, Department of Cardiology, Bern, Switzerland; 2Bern University Hospital, Department of Geriatrics, Bern, Switzerland; 3University of Bern, Institute of Social & Preventive Medicine, Bern, Switzerland; 4Bern University Hospital, Department of Cardiothoracic Surgery, Bern, Switzerland

Background: Currently used risk scores do not reliably estimate mortality and MACCE in elderly patients undergoing transcatheter aortic valve implantation (TAVI). This study evaluated multidimensional geriatric assessment (MGA) as predictor of mortality and major adverse cardiovascular and cerebral events (MACCE) after TAVI.

Methods: This prospective cohort comprised 100 consecutive patients ≥70 years undergoing TAVI. Global risk scores (STS-score, EuroSCORE) and MGA-based scores (cognition, nutrition, mobility, activities of daily living (ADL) and frailty index) were evaluated as predictors of all-cause mortality and MACCE 30 days and 1 year after TAVI in regression models.

Results: In univariable analyses all predictors were significantly associated with all-cause mortality and MACCE. Model using MGA performed better than STS-score and EuroSCORE (p < 0.001). Multivariable regression analysis confirmed MGA as independent predictor of mortality. MGA was also an independent predictor of MACCE (p < 0.001).

Conclusion: MGA may be useful for risk stratification after TAVI.

Relationship of aortic annular eccentricity and paravalvular regurgitation post transcatheter aortic valve implantation with CoreValve

D.T.L. Wong1, A.G. Bertaso2, M.S. Cunningham1, J.D. Richardson1, V.S. Thomson1, G. Kourlis3, B. Lorraine4, M.I. Worthley1, S.G. Worthley1, Royal Adelaide Hospital, Cardiovascular Research Centre, University of Adelaide, Adelaide, Australia; 2Royal Adelaide Hospital, Adelaide, Australia; 3Royal Adelaide Hospital, Adelaide, Australia

Background: Significant paravalvular aortic regurgitation (PAR) after tran-
Early right ventricular dysfunction after transcatheter aortic valve replacement: a prospective cardiac magnetic resonance (CMR) study of open versus transfemoral TAVI

G. Couchl, J. Bennettl, A. Sinhll, A. Penhalll, C. Bradbrokl, R. Bakerl, J. Selvanayagaml, 2 Finders Medical Centre, Department of Cardiovascular Medicine, Adelaide, Australia; 3Finders Medical Centre - Dept Cardiothoracic Surgery, Adelaide, Australia

Introduction: Recent published literature has validated the use of transcatheter aortic valve implantation (TAVI) in high-risk patients with aortic stenosis. These trials and registries have largely focused on combined morbidity and mortality outcomes with little focus given to impact on early myocardial function. We assessed effects on myocardial function, reversible and irreversible myocardial injury of both transcatheter and open aortic valve replacement utilizing multi-parametric CMR and traditional markers.

Methods: We conducted a prospective comparative study of 24 patients (14 male) with severe aortic stenosis undergoing either transcatheter valve replacement (12 patients) or high risk (EuroSCORE >20) open valve replacement (12 patients). CMR examination was carried out pre-operatively and within 2 weeks post-operatively. All scans used a Siemens Aera 1.5T system (Siemens, Germany). Images obtained included a standard cine functional imaging. T2 weighted images using LV basal, mid and apical SA slices and late gadolinium enhancement (LGE) images (Gadovist 0.1mg/kg). HS troponin was measured serially (pre, 4, 12, 24 and 48 hours post).

Results: Mean ages were 79.7 years Open and 83.2 years TAVI. The post-operative scan was conducted at a mean of 6 days for TAVI and 7 days for open. Pre-operative MRA ejection fraction was similar in the 2 groups (65.7±16.3 TAVI, 65.7±18.9 Open, p>0.05) After surgery, the LVEF was not significantly different in either group (TAVI: 66.1 ± 0.05 OPEN 65.7 ± 0.05) In contrast, RVEF decreased significantly in the TAVI group (58.9 ± 48.2, p=0.04), driven largely by significantly higher RVEDV comparative to the open group (95.4±30.3 v= 88.3±24.3 p<0.05). The open AVR group had no significant change in RVEF. There was no RV irreversible injury in either group. 2 patients in TAVI group and 1 patient in open AVR group demonstrated new LV irreversible injury (p<0.05). T2 analysis showed abnormal global myocardial enhancement in 16.6% of cases in the TAVI group and 8.3% in the open group (p<0.05). Median HS troponin at 48hrs was significantly larger in the open AVR group (403 vs 193ng/L, p<0.05)

Conclusion: Although serum Troponin levels are higher in open AVR (likely reflecting use of cardiopulmonary bypass), there is no increased CMR detected LV myocardial oedema or necrosis compared with TAVI. In the absence of new RV myocardial injury, it is likely the RV dysfunction seen in the TAVI group is a result of rapid ventricular pacing during device insertion, resulting in myocardial stunning.

Late systolic mitral prolapse and regurgitation is associated with impaired papillary muscle and enhanced inferolateral wall long axis function measured by magnetic resonance

Y. Shiina1, K.M. Chan1, D.J. Pennell1, J. Pepper2, P.J. Kelner1. 1Royal Brompton Hospital, Cardiovascular Magnetic Resonance Unit, London, United Kingdom; 2Royal Brompton National Heart & Lung Hospital, London, United Kingdom

Background: We hypothesized that among patients with mitral prolapse and regurgitation (MPMR), papillary muscle contractile dysfunction underlies the late systolic mitral regurgitation (MR) observed in MR patients. We compared MPMR severity measured by multi-echo MRI in patients with MPMR (MR) to those with mild MR.

Methods: From all patients with mitral regurgitation referred for cardiovascular magnetic resonance in 4 years, excluding those with prior surgery, mitral stenosis, leaflet tethering, chordal rupture or poor image quality, we found 420 with posterior leaflet or bi-leaflet MPMR clearly identifiable in a “mitral stack” of contiguous 5mm thick steady state free precession cines acquired in the 3-chamber orientation at 1.5 Tesla [J Cardiovasc Magn Reson. 2008;10:61]. We studied 3 groups: (A) All 197 patients found to have late MPMR, apparent in the last third of systole only, who were aged 30-78 years (56±19.9), (B) 21 age-matched patients with pan-systolic MPMR and (C) 12 age-matched healthy controls. We measured (1) MPMR systolic onset of MPMR seen in some cases.

Results: (A) In group A: 5.6±11.6% (p=0.001), 2) 32.9±8.9% (p=0.001). The displacement fractions of the anterior papillary muscle tips were: small in group A: 5.6±8.0% compared to B) 10.4±8.4% (p<0.05) and C) 18.8±2.8%, (p<0.001). The displacement fractions of the inferior papillary muscle tips were: small in group A): 2.9±1.7% compared to B) 11.5±3.9% (p<0.001) and C) 20.3±3.7% (p<0.001). Displacements in 5 in group A were negative (away from the apex). 4) Conversely, displacement fractions of base of the inferolateral wall were: large in group A): 19.9±5.4% compared to B): 16.9±4.4% (p<0.05) and C) 15.0±2.1%, (p=0.05).

Conclusions: Late MPMR is an unusual type of mitral dysfunction associated with reduced or even negative papillary muscle function in contrast to the usually and usually normal inferolateral wall long axis function. Relative to healthy controls, patients with pan-systolic MPMR had a large reversed systolic displacement mismatch of papillary muscle to inferolateral wall long axis function. Further investigation is needed to determine whether ischaemia and hibernation of papillary muscles - which might, theoretically at least, be reversible – underlies the papillary muscle dysfunction that we found to be strongly associated with late MPMR.
The correlation of AVA measured by transthoracic, robotic Lasso-Catheter manipulation integrated into measurements by TTE and TEE. The assessment of AVA using cardiac CT is in excellent agreement with TAVI with the Corevalve prosthesis, as well as to assess the usefulness of the TEE in the detection of the mechanism of MR compared to angiography.

Methods: We analysed a total of 129 cases of severe aortic stenosis treated with Corevalve prosthesis from June 2008 to October 2011. We define a significant MR after TAVI as higher to grade II, considering either a new onset MR or a worsening of a pre-existing MR, assessed both by TEE and angiographically.

Results: In our series, there were a total of 11 cases of significant MR after TAVI (8.5%). Angiography detected 100% of significant MR, but it was not able to determine the mechanism of MR in any case. However, TEE could determine the specific mechanism in 100% of cases: 1 case by interventricular septal bulging by appearance of left bundle branch block of new onset; 2 cases due impingement of aortic prosthesis on the anterior mitral leaflet; 4 cases were explained by temporary distortion or damage of the subvalvular aortal apparatus by the delivery system; in 2 cases the mechanism was the appearance of a systolic anterior movement of the anterior mitral leaflet with dynamic obstruction of the left ventricular outflow tract; 1 case was due to a small tear in the anterior commissure of mitral valve. Surgery was not required in any case. All cases had a grade II MR or less in the ETT at discharge.

Conclusions: In our study there was a not negligible percentage of patients treated with TAVI Corevalve who developed significant MR during the procedure, with very different mechanism. TEE, unlike angiography, could define the mechanism of MR in 100% of cases. Surgery was not required in any case.

P1482 Combined epicardial and endocardial procedure of permanent atrial fibrillation
1 Charite - University Medicine, Campus Benjamin Franklin, Berlin, Germany; 2 Heart and Vascular Center Bad Bevensen, Bad Bevensen, Germany

Background: Endocardial catheter based ablation strategies for the treatment of long standing persistent or permanent atrial fibrillation (permAFIB) show only limited success rates. However, fluoroscopy times, procedure duration, and complication rates increase. We report the results of a combined epicardial and endocardial approach.

Methods: Patients with documented permAFIB were included in this registry. In a first step epicardial lesions were applied endoscopically via a subapical approach. A roof line, segmental circumferential isolation of the PV ostia were applied. The second step was performed endocardially using a 3-D mapping system (Ensite Velocity). Gaps in cranial parts of the PV were identified and completed using a cooled tip RF catheter. After confirmation of complete isolation a Reveal XT device was implanted (Medtronic Inc.). Follow up was performed with wireless transmission of electrograms and automated recognition of AFib burden.

Results: Sixteen patients with permAFIB were treated (n=13 male; age 57±12 years, ejection fraction 65±12%). Duration of permAFIB was 2.5 years (0.5 to 7) atrial area was 36.8cm²±5.4cm². Procedure times were 115 min for the epicardial and 104 min for the endocardial approach. Fluoroscopy time was 9.3±3 min. Complete isolation of all PV was documented in all cases. During a mean follow-up of 18±6 months the burden of AFib was 7.1% with n=9 pts that were free of any AFIB in the Reveal holter. In n=2 pts AFib recurred and could not be cardioverted due to atrial thrombus formation. All patients were asymptomatic for AFib episodes. In one pt bleeding occurred that was treated surgically during the epicardial ablation.

Conclusion: The combined epicardial and endocardial ablation approach offers a novel and feasible approach for treatment of permAFIB. Even in longstanding permAFIB the procedure time do not exceed conventional procedure times with only low fluoroscopy times. Results for complete success are promising for a large scale trial.

P1483 3D reconstruction of left atrium with 3D - ATG for pulmonary vein isolation. Comparison with MRI
A. Baszko1, M. Lanocha2, P. Kalmuk1, M. Michalski1, O. Jerzykowska3, W. Elikowski3, M. Pyda2, A. Kocieb2, T. Siminik1, A. Szyzska1, J. Poznan University of Medical Sciences, 2nd Department of Cardiology, Poznan, Poland; 3 Department of MRI, Clinical Hospital No 1, Poznan, Poland; 4 J. Strus Hospital, Department of Cardiology, Poznan, Poland

The efficacy and safety of RF ablation in patients with atrial fibrillation (AF) is strongly dependent on the possibility of three-dimensional visualization of left atrium (LA) and pulmonary veins (PV) ostia. The current angiographic systems allow 3D-visualization of anatomical heart structures by means of rotational angiography. Studies conducted during adenosine induced ventricular asystole or rapid ventricular pacing presented a good correlation with CT or MRI. However, there was a substantial proportion of patients in whom this approach failed to give a reliable images, was contraindicated or led to complications like ventricular tachycardia.

The purpose of our study was to evaluate the clinical usefulness of rotational angiography (3D-ATG, Philips, Netherlands) after administration of the contrast medium into the right atrium for visualization of the left atrial anatomy in patients undergoing RF ablation of atrial fibrillation. We also compared the images obtained with 3D-ATG with magnetic resonance (MRI). In 18 consecutive patients undergoing RF ablation of AF or left atrial tachycardia, 3D-ATG was performed on the outpatients (mean, followed by 3D reconstruction of left atrium and aorta. We analyzed the quality of reconstruction, visualization of PVs and LA appendage. In cases of difficult transesophaeat puncture, reconstruction of aortic root was superimposed on the life monitor for guidance.

POSTER SESSION 2
CATHETER ABLATION OF ATRIAL FIBRILLATION: NEW TOOLS

P1481 Robotic Lasso-Catheter manipulation integrated into epicardial ablation of atrial fibrillation: is it superior to manual Lasso manipulation?
G. Noeker, K.J. Güleben, J. Heinze, B.G. Munthean, J. Vogt, D. Horstkotte. Department of Cardiology, Heart and Diabetes Center North Rhine-Westphalia, Bochum, Bad Oeynhausen, Germany

Purpose: Remote magnetic navigation is safe and effective for ablation of atrial arrhythmias, although optimal outcomes often require frequent manipulation of a circular mapping catheter. The VdriveTM Robotic Catheter Manipulation System (Vdrive, Stereotaxis, Inc.) was designed for remote navigation of Lasso® mapping catheters (Biosense Webster, Inc.) and is fully integrated into the Niobe® Magnetic Navigation System (Stereotaxis, Inc). This study reports on its first comparison to conventional manual Lasso catheter manipulation.

Methods: Eighty consecutive patients (52 males, 62±13 years) underwent magnetically guided atrial radiofrequency pulmonary vein isolation (PVAI) (40-50W, 48°C, 15-20 s, 30mL/min saline flow) for persistent AF using Vdrive to remotely navigate the Lasso catheter (group 1). Navigation tasks included accessing pul-
The ablation with use of CARTO 3 was successful in 17 patients. The total ablation time was 127±29 min, fluoroscopy time 31±8 min, and x-ray radiation dose was 413±170 mGy. The mean fluoroscopy time for 3D-ATG was 1.75±0.4 min and the mean X-ray dose was 159±37 mGy. Appropriate 3D visualization of the left atrium was obtained in 17 patients, including 15 in whom all 4 pulmonary venous ostia were shown. In one case 3D-ATG has not allowed for the visualization of the right inferior pulmonary vein and in another case the left sided vein was observed as a common ostium in MRL, not visualized in 3D-ATG. The PV diameter assessed by 3D-ATG was slightly higher than by MRL (16.6±3.2 vs 15.2±3.6), P<0.28, however this was mainly related to visualized right inferior PV. The good agreement (0.2mm) between two methods for assessment of PV ostia was higher for right-sided than left-sided veins (62.5% vs. 44%, P<0.003).

We conclude that 3D-ATG after contrast medium administration to the right atrium seems to be a safe and effective visualization method of pulmonary venous ostia and the left atrial anatomy. Whether it enables evaluation of anatomical anomalies remains to be established.

**P1484 Optimized touch techniques in atrial fibrillation ablation: is the contact force guided approach superior to magnetically directed ablation technology?**

G. Noeker, K.J. Gulieben, J. Heinze, B.G. Muntean, T. Dortschotte, M. Vogen, Department of Cardiology, Heart and Diabetes Center North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

**Purpose:** Irrigated radiofrequency ablation is a successful treatment option in atrial fibrillation (AF). Level and type of contact force (CF) are critical for energy transmission. Comparative data on continuous and limited vs. CF guided wall contact are lacking.

**Methods:** Forty patients were studied. 20 consecutive patients (14 male, 65±8 years) underwent antral RFA pulmonary vein isolation (PVI): (40±5W, 48±7 min, 15-20 s, 30W/min flow) for persistent (14) or paroxysmal (6) AF guided by CF (Tacti-Card, Endosense). An average CF of 15 g was aimed (group 1). Patients were matched to 20 patients treated by magnetically directed (Stereotaxis Niobe) irrigated gold-tip (Trignum G, Biotronik) (MDG) ablation (group 2) at a similar energy protocol for PVI. All procedures included: Rotational angiography based image integration (DynaCT Cardiac, Siemens; Ensite fusion, St. Jude Medical), Lasso-guide catheter (G, Biotronik) and a standard 8Fr Lasso catheter with the standard spiral catheter (Lasso™, Biosense Webster).

**Results:** All targeted pulmonary veins could be isolated confirmed by electrical block in both groups. Procedure time was 185±65.5 min in group 1 and 210.2±55.5 min in group 2 (p=0.19). Patients’ radiation exposure and fluoroscopy times were 8283±3227 Gy*cm², 37±17 min and 5323±2940 Gy*cm², 24±12 min respectively. Ablation time was 1927±678 s (group 1) and 3339±1158 s (group 2) (p<0.001). Mean CF was 19.4±6.4 g, total force-time integral (FTI): 3347±12444 gs and average FTI:ablation 1177±405 gs (group 1). Two pericardial tamponades and 2 audible steam-pops occurred in group 1, no incidents in group 2.

**Conclusion:** For our preliminary experience, CF guided and MDG ablation seem to be equally effective for RFA. CF guided PVI had a tendency to a higher rate of side effects and may be improved by an optimized average FTI:ablation. However, MDG shows a trend to longer procedure times and requires longer ablation times compared to CF guided ablation. One year follow-up data will be available and presented at the meeting.

**P1486 Comparison of new silent cerebral thromboembolic lesions after atrial fibrillation ablation of Pulmonary Vein Isolation with those of complex fractionated atrial electrograms ablation**

N. Watanabe, Y. Oonuma, M. Kikuchi, H. Itou, F. Miyoshi, T. Adachi, T. Asano, K. Tanno, Y. Kobayashi, Showa University School of Medicine, Department of Medicine, Division of Cardiology, Tokyo, Japan

**Introduction:** Atrial fibrillation radiofrequency ablation (AFRA) has become a routine procedure for treatment of atrial fibrillation (AF). However, incidents of silent cerebral ischemic lesions have recently emerged as the most frequent complications during AFRA. The aim of this study is to compare the incidence of silent cerebral ischemic lesions (SCILs) of pulmonary vein isolation (PVI) with those of complex fractionated atrial electrograms ablation (CFAE).**

**Methods and Results:** Fifty four patients (43 male, age 63±9 years) who underwent PVI (36 patients) or CFAE (18 patients) for AF were enrolled with irrigated radiofrequency catheter. We maintained an ACTs>300 seconds during procedures. The protocol included a cerebral magnetic resonance imaging (MRI) after the procedure. After AFRA 22 of 54 patients (40.7%) showed new SCILs at post-procedural cerebral MRI: 12 of 35 patients in PVI (34.2%), 10 of 19 patients in CFAE (52.6%). In paroxysmal AF (PVAI) patients, 5 of 9 patients in CFAE and 6 of 28 patients in PVI showed new SCILs. In persistent AF (PerAF) patients, 5 of 10 patients in CFAE and 4 of 7 patients showed new SCILs. At statistical analysis there was not any independent predictor of new SCILs after AFRA.

**Conclusion:** CFAE tended to show more new SCILs than in PVI in PAF patients.

**P1487 Anatomical predictors to improve the outcome of cryoballoon ablation for pulmonary vein isolation using the 28 mm balloon**

S. Knecht, M. Kuehne, P. Ammann, D. Altmann, S. Osswald, C. Sticherling, University Hospital Basel, Department of Cardiology, Basel, Switzerland; 2 Cantonal Hospital St. Gallen, Department of Cardiology, St. Gallen, Switzerland

**Purpose:** The anatomy of the left atrium (LA) may be critical for successful cryoballoon pulmonary vein isolation (CB-PVI) and pre-procedural predictors are lacking. Our aim was to identify anatomical exclusion criteria for CB-PVI with the 28mm CB to improve acute and midterm success rate based on 3D reconstructed pre-procedural cardiac images.

**Methods:** We included 47 patients (35 male, mean age 59±11, LA 40±6 cm) with symptomatic drug-refractory paroxysmal atrial fibrillation (AF) treated with CB ablation. All patients underwent pre-procedural cardiac magnetic resonance (MRT, n=23) or computed tomographic (CT, n=15) imaging. Quantitative geometrical measurements were diameter of PV, length of the left-sided common ostium (CO), and LA dimension. Balloon-centric views on CB-PVI procedure in combination with 3D visualization of the CB within the LA (figure) were used to deduce additional vein-specific parameters for CB-PVI failure.

**Results:** Acute CB only success rate was 68%. Single-procedure success rates for CB only and combined CB and RF approach were 40% and 60%, respectively, with a mean follow-up of 21.9±9 months. We found a short CO (<5 to 15mm) in 40% and a long CO (>15 mm) in 8% of the patients. For left pulmonary veins (LPV), a...
sharp-edged carina between LSPV and LPV or between LPV and left atrial appendage were identified as significant predictors for acute and mid-term PVF failure (p=0.04). For RIPV, a proximal bifurcation (p=0.02) and a non-perpendicular angle between ostium and vein axis (p=0.03) were identified as predictors for mid-term and acute PVF failure, respectively.

Conclusions: We identified geometrical parameters from pre-procedural C/CT/MRI images to predict acute and mid-term success of CB-PVF with the potential to improve outcome of CB ablation of AF.

P1488

MRI based lesion formation comparison between single tip radiofrequency, PVAC and cryoballoon ablation in patients with paroxysmal atrial fibrillation

C. Mahnkopf1, N. Burgon2, R. Hablitz3, O. Turtschner1, E. Kholmovski2, A. Mihaylova1, J. Brachmann1, N. Marrouche2.

1Klinikum Coburg, Department of Cardiology, Coburg, Germany; 2University of Utah, Comprehensive Arrhythmia Research and Management Center, Salt Lake City, United States of America

Background: We compared the difference in left atrial tissue remodeling (LATR) pre ablation and post-ablation lesion characteristics between three methods for electrical isolation of pulmonary veins [cryoballoon (cryo), pulmonary vein ablation catheter (PVAC) and single-tip radiofrequency (SRF)] routinely done to treat paroxysmal atrial fibrillation (PAF).

Methods: Patients presenting with PAF who qualified for a cryo, PVAC or SRF ablation were prospectively followed. DE-MRI of the left atrium (LA) was performed prior to and at 3-months post-procedure. The degree of LATR is reported as a percentage of the total LA area.

Results: Of the 37 patients (26 males, mean age = 63±10.12 years) enrolled in the study, six underwent an ablation using PVAC catheter, SRF catheter was used in 14 patients, and 17 patients underwent a cryoballoon ablation. Pre-ablation LATR was comparable in all three cohorts (Figure 1). Extent of scar tissue was higher in cryo and SRF patients than PVAC patients (Figure1). Overall six patients were found to have AF recurrence at 3-months follow-up. Patients with recurrence had a significantly lower amount of ablation lesions than patients in sinus rhythm (5.93% vs. 15.98%; P=0.004; Figure 2).

Conclusion: From our preliminary results, PVAC ablation appears to result in lesser scar formation as compared to Cryoballoon and SRF ablation. The greater recurrence in patients with low scar post-ablation suggests the need to implement an adequate ablation strategy that results in greater scar, especially in patients with PAF to maximize successful outcomes.

P1490

Pulmonary vein isolation for paroxysmal atrial fibrillation with laser balloon

L. Sediva, J. Petru, J. Skoda, M. Janotka, M. Chovancov, P. Neuzil. Na Homolce Hospital, Prague, Czech Republic

Introduction: Ablation strategy for pulmonary vein (PV) isolation in the treatment of atrial fibrillation is very important for making this procedure easier and shorter. The balloon procedures seems to be enough efficient, safe and easier in comparison with conventional radiofrequency catheter ablation. In our institution we have a large experience with isolation provided by cryoballoon. Using laser balloon we deliver laser energy around the pulmonary vein ostium under endoscopic direct visualization. This balloon is compliant and facilitate this procedure in cases of irregular ostium of pulmonary vein.

Methods: During the years 2009-2011 we performed 88 laser balloon pulmonary vein isolation procedures (358 veins, common ostium of left veins in 16 patients). All patients have paroxysmal form of atrial fibrillation. We provided single transseptal puncture in all cases, using circular mapping catheter for prove isolation. Our standard is use of ICE in all procedures: for transeptal puncture and for navigation of balloon in ostium of pulmonary vein. During application we measured temperature in oesophagus with temperature probe. In occurrence of temperature higher than 38.50°C we stop application. During application in right upper pulmonary vein we paced phrenic nerve in order to avoid its damage. Results: The acute success rate was 2009/89%, 2010/98%, 2011/100%. The mean 12 month follow up shows 82% chronic success rate. In 55 patients we performed remapping of veins after 2-3 months (gap RIPV 11x, RSPV 7x, LSPV 7x, LSVP 9x). The most frequent complication after laser balloon isolation of pulmonary vein was local vascular complication (mostly in females). We didn’t record any other severe complications.

Conclusions: Laser balloon isolation of pulmonary vein is safe procedure with comparable results with radiofrequency procedures. Long term follow up shows sufficient success rate without severe complications.

P1491

Single-ring ablation compared with standard circumferential pulmonary vein isolation and using remote magnetic catheter navigation in patients with symptomatic atrial fibrillation

C. Sohns1, L. Bergau1, L. Luethje1, D. Vollmann1, M. Dorenkamp2, M. Zabel1. 1Cardiology and Pneumology, Goettingen, Germany; 2Charite - Campus Virchow-Klinikum, Department of Cardiology, Berlin, Germany

Aim: Aim of this prospective study was to evaluate the safety and efficacy of an remote magnetic navigation (RMN)-guided single-ring ablation method as compared to standard RMN-guided circumferential pulmonary vein ablation (PVA).

Methods: A total of 80 consecutive drug refractory AF patients undergoing PVA were included and randomized 1:1 to the two study groups prospectively. RMN using the Stereotaxis Niobe II system and open-irrigated 3.5 mm ablation catheters were used with a three-dimensional mapping system in all ablation procedures. 40 patients underwent RMN-guided single-ring ablation while the other 40 patients (50%) received RMN-guided circumferential PVA. All patients were subsequently followed every 3 months using 96h Holter-ECG. The primary endpoint of this prospective randomized study was acute procedural success, defined as the number of pulmonary veins (PVs) isolated at the end of the procedure. Secondary endpoints were long-term success, defined as long-term freedom from AF/AT episodes irrespective of antiarrhythmic treatment after 12 months of follow-up, and freedom from symptomatic AF recurrence during 12 months of follow-up.

Results: In the circumferential (Circ) group, a mean of 3.3±1.1 PVs were successfully isolated as compared to 3.1±1.3 in the single-ring group (p=0.38 by unpaired t-test). To achieve electrical isolation of the PVs, all patients in the single-ring (Box) group required additional posterior wall lesions. Single-ring ablation was associated with longer procedure duration (Box 253±48 min. vs. Circ 226±45 min., p=0.01), and ablation time (Box 67±16 min. vs. Circ 56±12 min., p=0.001). Using Kaplan-Meier analysis after 1.4±0.5 procedures, 14% of patients who were free of any atrial tachycardia (AT)/AF episode at 12 months of follow-up was 79% in the Box group and 85% in the Circ group (p=0.43). In contrast, fluoroscopic time did not differ significantly between the two groups (p=0.4).

Using RMN for PVA in both groups, no major complications have been observed during or after PVA. As minor complications, pericardial effusion (n=2), hematomata at puncture site (n=2) were noticed. None of the minor events required intervention.
Conclusion: RMN-guided single-ring ablation of the PV provides comparable acute and long-term success rates as compared to RMN-guided circumferential PVA but requires markedly increased procedure and ablation time. Procedural complication rates are similar. Importantly, additional linear lesions on the posteri- rior wall cannot be avoided in order to achieve PV isolation.

Ganglionated plexi ablation combined with pulmonary vein isolation improves outcome of catheter ablation in patients with longstanding persistent atrial fibrillation: a prospective randomized study

State Research Institute of Circulation Pathology, Novosibirsk, Russian Federation

Introduction: Pulmonary vein isolation (PVI) is an established strategy for paroxys- mal atrial fibrillation (AF) but seemed too expensive in effective patients with persist- ent AF. Some researchers had already suggested that additional ganglionated plexi (GP) ablation might improve the success rate. The aim of our study was to assess the maintenance of sinus rhythm (SR) in patients with longstanding persist- ent AF at least 3 years using 2 different ablation strategies. PVI plus linear lesions (LL) versus PVI plus GP ablation.

Methods: Twenty-three consecutive patients with longstanding persistent AF were randomly assigned to either GP ablation added to PVI (n=13) or PVI alone (n=10). Primary end point was to assess the re-occurrence of AF after procedures in a long-term follow-up of at least 3 years.

Results: All cases underwent the procedure successfully. PVI was achieved in all cases. With a single procedure at the 12-month follow-up, 47% of patients treated with PVI alone went into SR whereas at the 3-year follow-up, 34% were in SR; using the PVI plus GP with a single procedure at the 12-month follow-up 54% of patients were in SR (p=0.068), whereas at the 3-year follow-up, 49% remained in SR (p<0.021).

Atrial flutter was more frequent in the group of PVI plus LL than in PVI plus GP ablation group (11% versus 4%; p=0.038). After a second procedure, the long- term overall success rate was 52% with PVI plus LL and 68% with PVI plus GP ablation (p=0.018).

Conclusions: The difference between PVI plus LL and PVI plus GP ablation strategy is not statistically significant at 12months in patients with longstanding persistent AF, whereas the difference becomes statistically significant in the long- term follow-up because of the higher number of recurrences in the PVI plus LL group.

Laser or cryo? Prospective comparison of balloon based PV technologies

Cardiology Centre Bethanien (CCB), Frankfurt, Germany

Background: Pulmonary vein isolation (PVI) for the treatment of drug-refractory atrial fibrillation (AF) using cryothermal balloon (CB) catheters is a well-accepted treatment option. Recently, the concept of visually guided laser balloon (LB) ablation was introduced.

Purpose: To prospectively compare acute and mid term efficacy and safety outcomes for 2 balloon based PV technologies.

Methods: Patients with drug-refractory paroxysmal atrial fibrillation were en-rolled. No pre-procedural imaging was required. After single transseptal puncture and selective PV angiograms a steerable sheath was advanced to the LA. All ab- lations in the CB group were performed exclusively with the 28 mm balloon. In the LB group an esophageal temperature probe with an upper limit of 39°C was used. During septal PV ablation phrenic nerve stimulation was performed via a diagnostic catheter. Follow-up was performed with 3 day Holter-ECGs every 90 days post-ablation after a 90 day blanking period.

Results: In total 130 (n=68 CB, n=61 LB) patients (82 male, mean age 63±10; LA size 40±4 mm) were enrolled. Epidemiological characteristics were compa- rable between groups. Acute PVI was achieved in 260/261 PVs (CB) and in 231/233 PVs (LB), respectively (p=ns). In CB the mean procedure time tended to be shorter (135±231/233 PVs (LB), respectively (p=ns). In LB the mean procedure time was significantly lower in LB (155±6 min versus 222±9 min; p<0.01). Phrenic nerve palsy occurred in 4 (6%; CB) and 3 (5%; LB) patients, respectively. One patient with CPV was noted in the LB group, conservatively managed without sequelae. During median follow-up of 224 days, 64% (CB) and 72% (LB) of patients were free of AF after a single procedure, respectively (p=0.31).

Conclusions: Balloon based PV using cryothermal or laser energy and a balloon can be performed safely and with comparable high acute and mid-term success rate. A prospective multicenter randomized trial with an extended follow- up comparing CB and LB based PVI is warranted.

Novel robotic catheter manipulation system integrated with remote magnetic navigation for fully remote ablation of atrial tachyarrhythmias: a multi-center evaluation

F. Akca1, G. Nolke2, K.J. Gultepe2, B. Muntean1, J. Vogt1, F. Horstkotte1, L. Dabin Akbenari1, T. Szili-Torok1. 1Erasmus Medical Center, Thoraxcenter, Rotterdam, Netherlands; 2Ruhr-University Bochum, Bochum, Germany

Introduction: Studies have shown that remote magnetic navigation is safe and effective for ablation of atrial arrhythmias, although optimal outcomes often re- quire frequent manual manipulation of a circular mapping catheter. The Vdive robotic system (“Vdive”) was designed for remote navigation of circular map- ping catheters to enable a fully remote procedure. This study details the first in human clinical experience with remote circular catheter manipulation in the left atrium.

Methods: This was a prospective, multi-center, non-randomized consecutive case series that included patients presenting for catheter ablation of left atrial arrhythmias. Remote systems were used exclusively to manipulate both the cir- cular mapping catheter and the ablation catheter. Patients were followed through hospital discharge.

Results: Ninety-four patients were included in the study, including 23 with paroxys- mal atrial fibrillation (AF), 48 with persistent AF, and 15 suffering from atrial tachycardias. The population was predominately male (77%) with a mean age of 60.5±11.7 years. The Vdive was used for remote navigation between veins, creation of chamber maps, and gap identification with segmental isolation. The intended acute clinical endpoints were achieved in 100% of patients. Mean case time was 225±90.75 minutes. Three patients (3.2%) crossed over to manual cir- cular mapping catheter navigation. There were no adverse events related to the use of the remote manipulation system.

Conclusions: The results of this study demonstrate that remote manipulation of a circular mapping catheter in the ablation of atrial arrhythmias is feasible and safe. Prospective randomized studies are needed to prove efficacy improvements over manual techniques.

Clinical Impact of a new open-irrigated Radiofrequency Catheter with direct Force Feedback on Atrial Fibrillation: a prospective randomized study


Background: Electrode-tissue contact is crucial for adequate lesion formation in radiofrequency catheter ablation (RFCA).

Objective: We assessed the impact of direct catheter force measurement on acute procedural parameters during RFCA of atrial fibrillation (AF).

Methods: 50 consecutive patients (pts; 28 male) who underwent their first procedure of circumferential pulmonary vein isolation (PVI) were assigned to either RFCA using (1) a standard 3.5mm open irrigated tip catheter or (2) a catheter with contact force measurement capabilities. Using the endpoint of PVI with entry and exit block acute procedural parameter were assessed.

Results: Procedural data showed a remarkable decline in ablation time (radiofre- quency time needed for PVI) from 50.5±15.9 to 39.0±11.0 minutes (p<0.007) with a reduction in overall procedure time of 31.3±7.2 minutes (p<0.002). In par- ticular the total energy delivered could be significantly reduced from 70,926±19,470 to 58,511±14,655 Ws (p<0.019).

Conclusions: The use of novel contact force sensing technology is able to signifi- cantly reduce ablation and procedure time, and substantially reduce energy delivery by avoiding radiofrequency ablation in positions with insufficient surface contact. Safety and long-term efficacy of this new feature have to be evaluated in larger cohorts.

CATHETER ABLATION OF ATRIAL FIBRILLATION: UNDERSTANDING THE MECHANISM

Left atrial function predicts arrhythmia recurrence after first and repeated procedure of atrial fibrillation ablation better than left atrial size

L. Gabrielli, S. Montserrat, R. Borras, N. Calvo, G. Bernardo, B. Bijnen, E. Arbelo, J. Brugada, L. Mont, M. Stiles. Barcelona Hospital Clinic, Barcelona, Spain

Purpose: Both left atrial (LA) size and contractile function have shown to predict arrhythmia elimination after a first procedure of catheter ablation (RFCA) for atrial fibrillation (AF). Predictors of success after repeated procedures, required in up to 30% of patients, are less clear.

Methods: 85 consecutive patients with AF treated with RFCA were included, 49 undergoing a first and 36 a second RFCA procedure. We excluded patients with severe valvulopathy or severe hypertension. In all patients a pre-procedure transthoracic echocardiography was performed with analysis of LA volume and myocardial deformation derived from 2D-echocardiography. All patients were in sinus rhythm at the time of the echo exam. Patients were clinically followed up at
6 months with 24 hour Holter ECG for the evaluation of arrhythmia recurrence. Logistic regression and ROC curves were used. Results See table. Conclusions: Analysis of LA contractile function with myocardial deformation imaging (PERSAF). Recent selection of patients with AF undergoing a first and also repeated procedure of RFCA, beyond LA size.

P1497
Common and rare cardiac sodium channel variants in atrial fibrillation - relation with ECG phenotypes and outcome of catheter ablation
D. Husser1, R. Dietrich1, L. Ueberham1, G. Hindricks1, L. Crafts2, D. Darbar3, V. Adams1, D.M. Roden2, A. Bollmann1. 1Heart Centre, Department of Electrophysiology, Leipzig, Germany; 2Vanderbilt University, Nashville, United States of America

Purpose: Common and rare genetic sodium channel variants have been identified as risk modifiers of and causes for atrial fibrillation (AF). Their possible relation with AF-associated intermediate ECG phenotypes and rhythm outcome of AF catheter ablation is, however, unknown and was investigated in this study.

Methods: In 137 consecutive patients with lone AF, sequencing of SCNSA, SCNB1 and SCNB2 was performed to identify rare variants and to determine the SCNSA H558R polymorphism. We identified 3 rare non-synonymous variants in SCNSA, 5 in SCNB1 and none in SCNB2 (6%). Minor allele frequency of SCNSA H558R was 22%. Variant carriers were comparable with non-variant carriers with respect to their demographic data. There was no association between PR interval, prevalence of incomplete right bundle branch block or early repolarization pattern and common or rare sodium channel variants. AF recurrence rate determined by serial 7-day Holter-ECG monitoring between 3 and 12 months after circumferential atrial pulmonary vein isolation was 42%. AF recurrence rates were independent of genotypic risk with respect to rare variants (p=0.927) and the common SCN5A H558R variant (p=0.194).

Conclusions: In patients with AF, common and rare cardiac sodium channel variants are associated with particular ECG phenotypes or outcome of catheter ablation. These findings highlight (1) the complexity of genotype-phenotype correlations and (2) the role of the pulmonary veins for AF initiation and maintenance even in the presence of genetic sodium channel variants.

P1498
Identification of rotors using sequential mapping & automated analysis techniques: organisational index is the best guide to important sites
M.C. Finlay1, B. Lim1, J. Moccready1, O. Segal2, S. Ashar2, A. Chow1, M. Lowe2, P.D. Lambiase3. 1University College London, Institute of Cardiovascular Science, London, United Kingdom; 2The Heart Hospital, University College London Hospital Trust, London, United Kingdom

Introduction: Sequential mapping and targeting of fractionated electrograms (EGMs) is commonly used in catheter ablation (CA) of persistent atrial fibrillation (pAF). Recent attention has focused on identifying surrogate signals for rotor activity, an underlying re-entry mechanism, but it is unclear if these can be identified with sequential mapping. Several automated algorithms exist to identify fractionated sites, but are not associated with particular ECG features or outcome of catheter ablation. These findings highlight (1) the complexity of genotype-phenotype correlations and (2) the role of the pulmonary veins for AF initiation and maintenance even in the presence of genetic sodium channel variants.

Methods: 20 patients undergoing first-time CA of pAF were studied. A NavX CFAE map was acquired after circumferential pulmonary vein isolation. EGM data was exported and 8 analysed live using custom software. CA was performed targeting sites of high CFAE. Offline analysis compared 3 algorithms seeking to identify rotors: ContA, OI, Dominant Frequency (DF); and 2 fractionation measures: CFAE-mean (NAx equivalent) and shortest complex interval (SCI, Carto equivalent). Finally, the effect of ablation lesions on pAF cycle length was correlated with analysis.

Results: CA terminated AF in 50% cases. 2589 8-second EGMs and 471 ablation lesions were analysed. Varied the refractory periods (RP) of algorithms produced large changes in signal classification for fractionation assessments (CFAE: Pearson R varied from 0.81±0.05 with 10ms variation in RP to 0.08 table 90ms variation) and SCI (R=0.95±0.04 for 10ms, R=0.34 for 90ms). OI, DF and ContA were unaffected by such changes (R=0.95±0.01 for 10ms, R=0.80 for 90ms). An inverse correlation existed between SCI and OI of EGMs (R=0.58, p<0.001) but no correlation with other measures. Only 2.1% of EGMs were in the top quintile by all 3 indices of CFAE, ContA and SCI. High OI (ROC AUC=0.64±0.01) at ablation site and lesion number (p<0.01) predicted an increase in AF cycle length, unlike classification by other techniques. Conclusions: The classification of fractionated EGMs is very sensitive to user-defined characteristic & must be taken into account analysis techniques. OI appears to be a good guide to appropriate ablation site by sequential mapping, and may identify rotors.

P1499
Value of a progressive rapid pacing protocol in determining the requirement for extra-PV ablation for persistent atrial fibrillation
D.C. Shah, C.I. Park, H. Buri, H. Sunthorn, P. Gentil-Baron. University Hospital of Geneva, Cardiac Electrophysiology Unit, Geneva, Switzerland

Extra-pulmonary vein (PV) left atrial (LA) ablation is performed for the treatment of persistent atrial fibrillation (AF) in the absence of AF termination without systematic evaluation of the underlying substrate. We prospectively performed a progressively rapid atrial pacing protocol for determining the requirement for extra-PV ablation in patients with persistent AF.

Methods: After performing circular mapping guided PV isolation (PIV), progressive rapid atrial pacing (8-10 beats from 350ms decremented by 10 ms steps down to 200ms; at least twice) was performed in sinus rhythm (after electrical cardioversion if necessary). If sustained AF (>5 minutes) was induced, additional ablation was performed targeting subgroups of fractionated potentials in the LA and coronary sinus (CS) with endpoints of elimination of fractionated potentials or termination of AF. The rapid pacing protocol was repeated after all ablation. Follow-up included periodic clinical, ECG and Holter evaluation.

Results: 43 consecutive patients (32M, 63±9 yrs, 13 with structural heart disease with persistent AF (mean duration 39±0.05 months, median 8 months) were studied. PVI was successfully achieved in all patients and without producing AF termination. After PVI, no sustained AF was inducible in 20 patients (15 M, 64±9 yrs, 6 SHD, persistent AF duration 56±13 months, median 8; LA volume 111±20mL). Following additional non-PV ablation (11±5 min CS, 10±8 min LA) for the remaining 23 patients (17M, 63±10yrs, 7 SHD, persistent AF duration 25±11 months, median 9; LA volume 110±27mL; p ns compared to the noninducible group), no sustained AF could be induced in 15 patients, sustained atrial flutter was induced in 4 patients and sustained AF in 5 patients. After 12±5 months follow-up, only 4 patients underwent reablation and 13±19 (68%) patients without extra-PV ablation and 12±3 (52%) with extra PV ablation remained in stable sinus rhythm without anti-arrhythmic drugs.

Conclusions: A progressive rapid atrial pacing protocol based evaluation of the residual AF is an identifying surrogate signal for persistent AF in patients who do not need additional non-PV ablation for the maintenance of stable sinus rhythm.

P1500
Quantitative analysis of isolation area and rhythm outcome in patients with paroxysmal atrial fibrillation after circumferential pulmonary vein antrum isolation
P. Sommer, K. Kiuchi, S. Kircher, T. Gaspar, A. Arya, G. Hindricks, C. Piorowski. University of Leipzig, Heart Center, Leipzig, Germany

Objectives: We sought to determine the relationship between the size of the left atrial (LA) isolated surface area (ISA) after pulmonary vein antrum isolation (PVAI) for paroxysmal atrial fibrillation (AF) and rhythm outcome during a 12-month follow-up.

Background: PVAI is an established therapy for patients with paroxysmal AF. However, the influence of the size of the ISA on rhythm outcome is unclear.
Methods: Circumferential lesions for complete electrical PV isolation were placed around the ipsilateral pulmonary vein (PV) pairs of 101 patients with AF (mean age 59±11 years, median AF history 38 (24, 96) months, mean LA size 42±6 mm). The ISA was defined as the ratio of total isolated atrial surface area (IAS=Total) excluding the PVs to the sum of the IAS=Total and the LA posterior wall (LAPW) surface area. All surface areas were assessed by using a software tool of the NavX system. Patients were divided into four groups according to ISA (Group I:<50%, Group II: 50 to <60%, Group III: 60 to <70%, Group IV: ≥70%).

Results: The average ISA for all patients was 59.2±11.6%. Subgroup analysis showed ISA was 42.8±4.2% (Group I: n=23), 54.2±3.0% (Group II: n=25), 64.3±3.0% (Group III: n=33), and 73.9±3.6% (Group IV: n=22). At 12 month without anti-arrhythmic drug treatment, 74% of patients in group I, 78% in group II, 97% in group III, and 100% in group IV were free from AF and/or atrial macro-re-entrant tachycardia (MRT). Kaplan-Meier analysis showed a significantly lower AF/MRT recurrence rate for groups III and IV than for group I (p<0.03). Receiver-operator characteristic curve analysis yielded an optimal cutoff value for ISA of 55%.

Conclusion: After 12 months, a larger ISA was associated with a significantly lower AF/MRT recurrence rate. ISA≥55% may serve as a predictor for long-term success after PVAI.

P1502 Quantification of left atrial fibrosis by contrast-enhanced magnetic resonance imaging in patients undergoing catheter ablation for atrial fibrillation

M. Sramko1, P. Peicht1, J. Tintere2, R. Cihak1, D. Wichiter1, J. Kautzner1, 1Institute for Clinical and Experimental Medicine (IKEM), Department of Cardiology, Prague, Czech Republic; 2Institute for Clinical and Experimental Medicine (IKEM), Department of Radiology, Prague, Czech Republic

Background: Pre-procedural detection of left atrial (LA) fibrosis has been associated with worse outcomes of catheter ablation for atrial fibrillation (AF). In this respect, we evaluated relationship between the extent of LA fibrosis assessed by contrast-enhanced magnetic resonance imaging (CMRI) and AF recurrence after the procedure.

Methods: Before catheter radiofrequency ablation, 32 patients (pts) with paroxysmal (n=10) and persistent AF (n=22) underwent gadolinium-enhanced CMRI. LA fibrosis, defined by signal intensity >3 SD above the mean of the normal myocardium, was quantified semi-automatically and expressed as a percentage of the LA tissue. Electroanatomic voltage maps of the LA (196±72 points) were obtained by CARTO system ( Biosense Webster, Israel) in 14 pts during AF. Bipolar voltage of the entire LA was correlated with the extent of fibrosis. Pts were followed for AF recurrence prospectively for 260±183 days.

Results: Two of the CMRI studies were excluded due to poor image quality. Twenty-five pts (83%) remained in sinus rhythm during follow up. Mean LA fibrosis and bipolar voltage reached 7.4±0.6 and 0.6±0.3 mV, respectively. The extent of LA fibrosis showed significant exponential correlation with the mean voltage of LA (R = 0.9, P = 0.001), given by the equation: voltage (mV) = 2.5/(1 + percent of fibrosis). No relationship was revealed between the extent of LA fibrosis and AF recurrence. AF form or LA volume. Consequently, CMRI was found to be insufficient for predicting of AF recurrence (area under curve = 0.53).

Conclusions: Our results confirm feasibility of CMRI for detection of LA fibrosis and its correlation with LA voltage in electroanatomic maps. However, clinical utility of CMRI for predicting of AF recurrence after catheter ablation appears to be limited.

P1501 Spatially accurate overlay of 3-D MRI of the left atrium onto the fluoroscopic image during atrial fibrillation ablation using fatty and radiodense markers

H.U. Simon, C. Mahnkopf, A. Salaam, O. Turschner, D. Apis, P. Halblaus, J. Brachmann. Klinikum Coburg, Department Cardiology, Section of Electrophysiology, Coburg, Germany

Morphologic left atrial variation, accurate lesion location, integration of pathologic data like scarring and reduction in X-ray exposure all make accurate real time integration of three dimensional (3-D) left atrial imaging potentially valuable to safely ablate atrial fibrillation.

Methods: 7 Patients (Age 52-77) underwent Gadolinium angiography (15-20 cc at 1.5-3cc/s) during magnetic resonance imaging (MRI) to acquire 3-D shells of the left atrium (LA) within 24h prior to ablation. 3 fish-oil capsules (1000mg omega-3-fatty acid, containing 330mg Eicosapentaneic acid and 220mg Docosa-hexanec acid) were fixed parasternally in the 6th, 7th 8th intercostal space prior to MRI. Immediately prior to the ablation procedure a rotational fluoroscopic image was obtained using 120KVP. The InSpace function, the MRI could then be accurately overlaid to the live fluoroscopic image. The InSpace function provided for accurate alignment of the MRI-based anatomy to the different fluoroscopic angulations.

Results: All patients could be safely ablated by an anatomically oriented ablation procedure using accurate overlay of 3-D MRI into the live-fluoroscopic image. The method opens up the opportunity to also integrate data of scanning and edema acquired during MRI into the radiographically based ablation procedure.

P1503 Association of common susceptibility alleles and recurrence of atrial fibrillation after catheter ablation

L. Ueberham1, D. Husser1, A. Arya1, V. Adams2, G. Hindricks1, A. Bollmann1, 1Heart Centre, Department of Electrophysiology, Leipzig, Germany; 2Heart Centre, Department of Cardiology, Leipzig, Germany

Purpose: Recent genome-wide association studies have identified common alleles on chromosomes 1q21 (rs13376333), 4q25 (rs10033464 and rs2200733) and 16q22 (rs7193343) to modulate risk for atrial fibrillation (AF). In this study, we tested the hypothesis that those risk variants associate with AF recurrence after radiofrequency catheter ablation (RFCA) in a population of lone AF patients.

Methods: We studied 262 patients (68% males, mean age 57.4±10.5 years) with paroxysmal (67%) or persistent (33%) lone AF who underwent RFCA. Genotypes were determined using real-time polymerase chain reaction and fluorescence res-
Conduction recovery following electrical superior disparity of structural remodeling between left atrial Adenosin-mediated acute pulmonary vein reconnection at the following procedure. In patients who had arrhythmia recurrence, SVC reconnection was frequently observed and the prevalence was similar to PV reconnection. Although acute PV reconnection frequently observed after PV isolation, which could lead to the arrhythmia recurrence in patients with atrial fibrillation (AF). However, the data of reconnection between right atrium (RA) and SVC following electrical SVC isolation is limited.

Methods: A SVC isolation was systemically performed following PV isolation in all patients with paroxysmal AF (PAF), and in patients with persistent AF who had SVC trigger. SVC isolation was performed using 4-mm non-irrigated tip catheter during high RA pacing or sinus rhythm following angiography (Fig. 1A). We evaluated the reconnection of SVC in patients who underwent repeat session for arrhythmia recurrence after SVC isolation.

Results: We included consecutive 69 patients (PAF 46pts, 56±9.8 years, 58 males) who had repeat session (2nd, 3rd, and 4th session: 56, 8 and 5 pts) 16.7±15.9 months after SVC isolation by an average of 7.2±3.8 radiofrequency applications. Among them, 53 (78.6%) patients had re-conduction of SVC, and the site of conduction gap was shown in Figure 1B. Among 56 patients with 2nd procedure, 44 (78.8%) patients had PV reconnection and the prevalence was similar to that of SVC (p=0.91). After re-isolation of SVC, 4/9 (44.4%) patients had again reconnection at the following procedure.

Conclusions: In patients who had arrhythmia recurrence, SVC reconnection was frequently observed and the prevalence was similar to PV reconnection. Although the site of conduction gap is widely diffused, lateral side was the favorable site of reconnection.

Introduction: Superior vena cava (SVC) is known as the source of atrial tachyarrhythmia. Reconnection between pulmonary vein (PV) and left atrium (LA) is frequently observed after PV isolation, which could lead to the arrhythmia recurrence in patients with atrial fibrillation (AF). However, the data of reconnection between right atrium (RA) and SVC following electrical SVC isolation is limited.

Methods: A SVC isolation was systemically performed following PV isolation in all patients with paroxysmal AF (PAF), and in patients with persistent AF who had SVC trigger. SVC isolation was performed using 4-mm non-irrigated tip catheter during high RA pacing or sinus rhythm following angiography (Fig. 1A). We evaluated the reconnection of SVC in patients who underwent repeat session for arrhythmia recurrence after SVC isolation.

Results: We included consecutive 69 patients (PAF 46pts, 61.0±9.9 years, 58 males) who had repeat session (2nd, 3rd, and 4th session: 56, 8 and 5 pts) 16.7±15.9 months after SVC isolation by an average of 7.2±3.8 radiofrequency applications. Among them, 53 (78.6%) patients had re-conduction of SVC, and the site of conduction gap was shown in Figure 1B. Among 56 patients with 2nd procedure, 44 (78.8%) patients had PV reconnection and the prevalence was similar to that of SVC (p=0.91). After re-isolation of SVC, 4/9 (44.4%) patients had again reconnection at the following procedure.

Conclusions: In patients who had arrhythmia recurrence, SVC reconnection was frequently observed and the prevalence was similar to PV reconnection. Although the site of conduction gap is widely diffused, lateral side was the favorable site of reconnection.

Figure 1

Conclusions: In patients who had arrhythmia recurrence, SVC reconnection was frequently observed and the prevalence was similar to PV reconnection. Although the site of conduction gap is widely diffused, lateral side was the favorable site of reconnection.

Conduction recovery following electrical superior vena cava isolation in the context of atrial fibrillation ablation: Prevalence and Electrophysiological Properties S. Miyazaki, T. Uchiyama, S. Kusa, H. Taniguchi, Y. Iesaka. Tashchiura Kyodo Hospital, Tashchiura, Japan

Introduction: Superior vena cava (SVC) is known as the source of atrial tachyarrhythmia. Reconnection between pulmonary vein (PV) and left atrium (LA) is frequently observed after PV isolation, which could lead to the arrhythmia recurrence in patients with atrial fibrillation (AF). However, the data of reconnection between right atrium (RA) and SVC following electrical SVC isolation is limited.

Methods: A SVC isolation was systemically performed following PV isolation in all patients with paroxysmal AF (PAF), and in patients with persistent AF who had SVC trigger. SVC isolation was performed using 4-mm non-irrigated tip catheter during high RA pacing or sinus rhythm following angiography (Fig. 1A). We evaluated the reconnection of SVC in patients who underwent repeat session for arrhythmia recurrence after SVC isolation.

Results: We included consecutive 69 patients (PAF 46pts, 61.0±9.9 years, 58 males) who had repeat session (2nd, 3rd, and 4th session: 56, 8 and 5 pts) 16.7±15.9 months after SVC isolation by an average of 7.2±3.8 radiofrequency applications. Among them, 53 (78.6%) patients had re-conduction of SVC, and the site of conduction gap was shown in Figure 1B. Among 56 patients with 2nd procedure, 44 (78.8%) patients had PV reconnection and the prevalence was similar to that of SVC (p=0.91). After re-isolation of SVC, 4/9 (44.4%) patients had again reconnection at the following procedure.

Conclusions: In patients who had arrhythmia recurrence, SVC reconnection was frequently observed and the prevalence was similar to PV reconnection. Although the site of conduction gap is widely diffused, lateral side was the favorable site of reconnection.

Peri-mitral flutter ablation depends on mitral isthmus anatomy Y. Massaad, D.G. Latou, M. Mahjoub, F. Squarra, N. Saoudi. The Princess Grace Hospital Centre, Monaco, Monaco

Introduction: Success of mitral isthmus (MI) ablation has been related to CT scanner MI anatomy. No study has described electro-anatomical MI anatomy and its effect on radiofrequency catheter ablation (RFCA) success of perimetal flutter (PMF) occurring after AF ablation.

Methods: In consecutive 18 patients (pts; 16 males, 62.9±9 y) with PMF, as diagnosed by activation mapping (Carto®) and entrainment mapping, who underwent RFCA, MI was ablated by endocardial ± epicardial linear lesion between the left atrial appendage and the lateral mitral annulus. Acute (defined as sinus rhythm – SR – restoration during ablation) and long-term (defined as SR maintenance) procedural success were studied. MI characteristics: depth - defined as the minimal distance between endocardial and coronary sinus high resolution maps at the MI level, MI length, maximal MI bipolar voltage as well as actual MI ablation line length and width, RF duration and energy were analyzed.

Results: In 10/18 pts (55%) SR resumed by RFCA. SR resumption was more likely to be achieved in pts with lower MI depth (1.5±2.3 mm vs 7.2±3.8 mm; p=0.012) and shorter acute ablation line (29.8±6.5 mm vs 54.1±13.1 mm; p=0.008). Acute success was neither associated with MI length (26.1±4.5 mm vs 32.8±8.6 mm, p=0.19), nor with maximal MI voltage (1.1±0.8 mV vs 1±0.8 mV, p=0.78), ablation line width (15.8±7.7 mm vs 28.9±20.1 mm, p=0.17), delivered energy (1183±6224 J vs 15651±6054 J, p=0.28) and epicardial energy (2011±4383 J vs 1324±1209 J, p=0.71) in successful vs failure procedures, respectively. During a mean follow-up of 8.1±7.4 months after a single procedure, 47% of pts remained in SR: 50% of successfully ablated pts vs 42.8% of over-driven or cardioverted pts, p=0.58. None of studied variables was associated with long-term success.

Conclusion: Lower MI depth and shorter acute ablation line length were associated with acute success in PMF ablation. MI electroanatomical characteristics might be used to optimize ablation strategy of persistent atrial fibrillation.
recovery: 449±48g vs 240±193g, p=0.0007 and median: 585 (Q1:137, Q3: 324g) vs 342g (Q1: 75g, Q3:202g), respectively. We observed a low ablation point density at the remaining PV-reconnection sites with higher FTI-values.

Conclusions: Low contact force during pulmonary vein isolation is the underlying mechanism of Adenosin-mediated acute PV-reconnection in 87%. Prospective use of CF measurement for PVI may significantly reduce the current high rates of PV-reconnection.

Purpose: Patient selection is crucial in obtaining good results in atrial fibrillation (AF) ablation. The aim of the study was to evaluate the usefulness of a new method to estimate AF ablation outcome based on sperical remodeling of the left atrium in patients with AF.

Methods: Consecutive patients who underwent a Cardiac Magnetic Resonance before AF ablation were included in the study. A 3D-reconstruction of left atrium (LA) excluding pulmonary veins and the LA appendage was used to define the LA body. Sphericity was analyzed by calculating sphericity index (SI), automatically obtained with self-customized software.

Results: We included 127 patients that were categorized in 3 groups (G): discordant LA (G1), intermediate LA (G2) and spheric LA (G3). Patients had a higher prevalence of AF recurrences at 12 months follow-up (58%, 29% vs. 5%, P<0.001) and structural heart disease (75%, 48% vs. 29%, P=0.034) and structural heart disease (75%, 19% vs. 19%, P=0.001) as compared to G1 and G2 patients. Spherical LA was associated with higher prevalence of AF recurrences at 12 months follow-up (58%, 29% vs. 5%, P<0.001). SI was linearly correlated to predicted probability of recurrence. Multivariate analysis identified SI (OR 1.32 [1.09-1.59], P=0.004) as independent risk factor for arrhythmia recurrence.

Conclusion: Sphericity Index is a powerful independent predictor of recurrence after AF ablation and may be useful in selecting the best candidates for AF ablation.

Purpose: Patient selection is crucial in obtaining good results in atrial fibrillation (AF) ablation. The aim of the study was to evaluate the usefulness of a new method to estimate AF ablation outcome based on sperical remodeling of the left atrium in patients with AF.

Methods: Consecutive patients who underwent a Cardiac Magnetic Resonance before AF ablation were included in the study. A 3D-reconstruction of left atrium (LA) excluding pulmonary veins and the LA appendage was used to define the LA body. Sphericity was analyzed by calculating sphericity index (SI), automatically obtained with self-customized software.

Results: We included 127 patients that were categorized in 3 groups (G): discordant LA (G1), intermediate LA (G2) and spheric LA (G3). Patients had a higher prevalence of AF recurrences at 12 months follow-up (58%, 29% vs. 5%, P<0.001) and structural heart disease (75%, 48% vs. 29%, P=0.034) and structural heart disease (75%, 19% vs. 19%, P=0.001) as compared to G1 and G2 patients. Spherical LA was associated with higher prevalence of AF recurrences at 12 months follow-up (58%, 29% vs. 5%, P<0.001). SI was linearly correlated to predicted probability of recurrence. Multivariate analysis identified SI (OR 1.32 [1.09-1.59], P=0.004) as independent risk factor for arrhythmia recurrence.

Conclusion: Sphericity Index is a powerful independent predictor of recurrence after AF ablation and may be useful in selecting the best candidates for AF ablation.
both SHD and AF (Group C: age 74±13, 20 females). Patients with AF history were older that those without AF (74±13 vs 57±14, p<0.0001). There was no difference in regard to the diameter of PV ostia or the length of the muscular extensions at any of the PVs and the presence of AF history or SHD (see Table for full results).

**Conclusion:** In a largest to date material of consecutive post-mortem studies, gross morphology of pulmonary vein ostia was not associated with the history of AF in patients with SHD.

**P1511 Variability of P-wave morphology predicts the outcome of circumferential pulmonary vein isolation in patients with recurrent atrial fibrillation**

Y. Huo1, F. Holmevik1, J. Carlson2, T. Gaspar1, G. Windrick1, C. Piorkowski1, A. Bollmann1, P. Platokov2, Yu. Huo1, F. Holmqvist2, J. Carlson1, T. Gaspar1, G. Windrick1, C. Piorkowski1, A. Bollmann1, P. Platokov2, 1University of Leipzig, Heart Center, Leipzig, Germany; 2Lund University, Department of Cardiology and Center for Integrative Electrocardiology at Lund Univ, Lund, Sweden

**Introduction:** Previous studies suggested that functional and structural factors make the course of atrial fibrillation (AF) progressively irreversible. Severe atrial structural remodeling commonly indicates an irreversible damage of atrial tissue in patients with AF, leading to poor treatment, and is associated with prolongation of P-wave duration and abnormal P-wave morphology. Our aim was to study whether P-wave duration and variability of P-wave morphology (PMV) can predict outcome in patients with AF after circumferential PV isolation (CPVI).

**Methods:** Seventy consecutive patients (aged 60±9 years, 46 men) undergoing CPVI due to AF after cessation of antiarrhythmic therapy (50 paroxysmal/20 persistent AF) were studied. Standard 12-lead ECG during sinus rhythm was recorded for 10 min at baseline. The ECGs were transformed to orthogonal leads, and then beat-to-beat P-wave morphology was defined automatically depending on P-wave polarity in orthogonal leads (positive/negative/biphasic) in accordance to a predefined classification algorithm. P-wave morphology that was observed in the highest number of P-waves was defined as the dominant morphology. PMV was defined as a percentage of P waves with non-dominant morphology in a 10-min sample. The patients were followed for at least 6 months and underwent 7-day Holter ECG at the end of follow-up. In case of symptoms suggesting of AF additional 24-hr Holter was scheduled. No recurrence was defined as lack of any documented episode (>30sec) of any atrial arrhythmia between the end of the 3 months long blanking period and the end of follow-up.

**Results:** By the end of follow-up, 53 of 70 patients had no arrhythmia recurrence. No difference was observed in regard to P-wave duration between patients with and without recurrence (149±16 vs 155±23 ms, p=0.241), however PMV was greater in patients without recurrence (19.5% vs. 8.2%, p<0.001). The multi-variate logistic regression model, the variability of PWT≥20% was the only independent predictor of ablation success (OR=11.4, 95%CI 1.4-92.1, p=0.025).

None of other clinical characteristics such as age, gender, BMI, left atrial diameter, type of the AF or AF history duration were associated with the outcome.

**Conclusions:** We report high and significant association between the variability of P-wave morphology and 6-month CPVI success. Low PMV in patients with recurrent AF is likely to reflect severe structural remodeling and explain the failure of CPVI. Our findings warrant further studies of PMV as a marker of atrial remodeling that may be used for prediction of ablation success.

**P1512 Neurohormonal, structural and functional recovery pattern after PVC ablation in patients with depressed left ventricular ejection fraction. A prospective single centre study**


Ablation of frequent, premature ventricular complexes (PVCs) has been shown to be associated to a reverse remodelling in patients with PVC-induced cardiomyopathy. We have investigated the role and recovery pattern of the PVC ablation in the whole population of patients with depressed left ventricular ejection fraction. A prospective single centre study included 58 consecutive patients with frequent PVCs (>10% of all QRS complexes on a 24 hr Holter) and left ventricular dysfunction. Left ventricular ejection fraction (LVEF), New York Heart Association functional class (NYHA), brain natriuretic peptide (BNP) and quality of life were evaluated before and 1, 6 to 12 months after radiofrequency catheter ablation (RFA).

**Results:** 50% of patients had cardiomyopathy of known origin (7 ischemic heart disease, 1 hypertensive cardiomyopathy and 3 patients with non-compaction cardiomyopathy). There was a progressive improvement in the LVEF (30.2% ± 7.1 to 46.0% ± 8.8, p<0.001), NYHA class (20% of patient with NYHA I to 60%, p=0.0028), BNP (154.7±134 to 60.9±54.2, p=0.003) and quality of life (28.1±10 to 10.4±10) after the procedure (see table). Only 30% of patients had a complete recovery of LVEF at 6 months. All patients with a LVEF <30% went out of the ICD implant indication for primary prevention.

**Conclusions:** Frequent PVC ablation in the whole group of patients with depressed LVEF induces a progressive clinical and functional improvement but only a little percentage of patients have a real PVC-induced cardiomyopathy with complete recovery to normality. Given the magnitude of the improvement, all patients with depressed LVEF should be screened for the presence of frequent PVCs; specifically those who have severely depressed LVEF, as this therapy could avoid unnecessary ICD implantations.

**P1513 Left atrial appendage electrical isolation via unusual patterns**

L. Di Biase 1, M. Valderrabano 2, J. Sanchez 1, P. Santangelí 1, R. Bai 1, P. Mohan 1, S. Behery 1, R. Hong 1, J.D. Burkhart 1, A. Natale 1, 1Texas Cardiac Arrhythmia Institute at St David Medical Center, University of Texas and University of Foggia, Austin, United States of America; 2The Methodist Hospital, The Methodist DeBakey Heart & Vascular Center, Department of Cardiology, Houston, United States of America; 3Texas Cardiac Arrhythmia Institute at St David Medical Center, Austin, United States of America; 4California Pacific Medical Center, San Francisco, United States of America

**Introduction:** Catheter ablation of adjunctive atrial sites together with pulmonary veins isolation has shown to improve the success rate in patients with non-paroxysmal atrial fibrillation (AF). AF triggers within the coronary sinus (CS) and the left atrial appendage (LAA) have been recognized as non PV triggers of the AF. The aim of our study is to report unusual pattern of LAA isolation.

**Methods:** 488 consecutive patients undergoing catheter ablation for persistent or long standing persistent AF and showing firing from the LAA and or from the CS have been enrolled in this multicenter prospective study. In all patients drug-termination of the CS to achieve isolation and LAA isolation was attempted both with endocardial and epicardial ablation. During CS ablation, the circular mapping catheter was positioned into the LAA.

**Results:** In 7% of these cases (34 pts) after attempting endocardial LAA isolation, the LAA was isolated during epicardial ablation in the distal CS. In 8% of the cases (39 pts) after attempting endocardial LAA isolation, the LAA was isolated during ablation along the endocardial CS (figure). In all these cases the presence of a venous branch connecting the CS with the LAA was found. In 23% of the cases (112 pts), the isolation of the LAA also isolated the distal CS. In all these cases LAA dissociated firing was present together with the CS recording. In all the remaining cases 69% (337 pts) LAA could be isolated with endocardial segmental ablation. No peri-procedural complications were reported.

**Conclusion:** These findings suggest the presence of a distinct electrical connection between the CS and the LAA. The clinical relevance of our results requires further investigation.
CATHETER ABLATION OF ATRIAL FIBRILLATION: LOOKING AT THE RESULTS

Prevention of post-operative atrial fibrillation by intracardiac ultrasound for esophageal anatomic catheter ablation of atrial fibrillation: a collaborative patient level meta-analysis of 11 randomized studies

Hybrid ablation of long standing persistent atrial fibrillation utilizing minimally invasive surgical and endocardial catheter feasibility study

D.E. Pajtne1, T. Neumann1, M. Schonbarg1, S. Zaaly2, S.W. Zaltsberg1, H. Greiss1, C.W. Hamm1, T. Walther1, H.F. Pfitzner1, K. Kumpa1, Y. Kobayashi2, N. Funabashi2, S. Oshima1. 1Gunma Prefectural Cardiovascular Center, Maebashi, Japan; 2Kerckhoff Clinic, Department of Heart Surgery, Bad Nauheim, Germany; 3Kerckhoff Clinic, Department of Heart Surgery, Bad Nauheim, Germany

Background: Patients (pts) with long standing atrial fibrillation (AF) usually require multiple ablation procedures with pulmonary vein isolation (PVI) and additional left atrial substrate modification to maintain sinus rhythm. The objective of this pilot study was to evaluate the safety and feasibility of a novel hybrid ablation of long standing AF using simultaneous epicardial and endocardial approach.

Methods: Twelve consecutive pts (2 female, age 54±2 years, LA size 46±2 mm in short and long axis respectively) with long standing AF and failure of at least one antithrombotic drug were included. The epicardial ablation was performed via a subxiphoid trans-diaphragmatic access utilizing Numeris1© Coagulation Device, nContact Surgical Inc., Morrisville, USA. The epicardial procedure was followed by conventional endocardial mapping and ablation using EnSite NavX Velocity™ system, SJM Inc., St. Paul, MN, USA. During the endocardial procedure voltage mapping was performed and detected gaps were closed. Esophageal temperature was continuously monitored during the whole procedure with a temperature probe (SensiTherm™,SJM). Pts were prospectively followed at 1, 3, and 6 months with 48 h holter ECG. Pts free of AF after 3 months underwent implantation of loop event recorder, Reveal1©, Medtronic Inc., Minneapolis, USA.

Results: AF was persisting since 36±7 months. One pt had undergone four repeated AF catheter ablations with complete reconnection of pulmonary veins after each procedure. All pts were highly symptomatic with EHRA class 4. The mean duration of endo- and epicardial procedures was 116±46 min. respectively, utilizing 26±2 min. of the fluoroscopic time (37±11 Gy/cm²). The endocardial voltage mapping has shown complete anterior lesions and posterior box lesions with roof gaps in all pts. After the endocardial closure of roof gaps all pulmonary veins were isolated. Additionally in all pts complete roof lines, 2 pts anterior mitral valve line and 2 pts. CFAEs ablation were applied. During ablation procedure 2 pts converted into sinus rhythm and 1 into atrial tachycardia. Electrical cardioversion was performed in 5 pts. No serious complications were observed. Four pts developed a post cardiotomy syndrome, which was managed conservatively. After 3 months 5 of 7 pts were free of AF.

Conclusions: A hybrid ablation of long standing persistent AF in pts with severe atrial enlargement represents a feasible and safe treatment option with high short term success rates. Further evaluation with assessment of mid- and long-term results is required.

P1520 Catheter ablation vs. rate-control strategy in patients with permanent atrial fibrillation: results of five years of follow up

A.V. Andarshiev1, E. Zhelyakov2, D.V. Duplyakov2, A.V. Kornev1, M.S. Rybachenko1, M.Y.N. Belenkov3. 183 Clinical Hospital of FMBA, Moscow, Russian Federation; 2Samara Regional Cardiology Dispensary, Samara, Russian Federation; 3M.V. Lomonosov Moscow State University, Moscow, Russian Federation

Aim: To compare long-term results of radiofrequency catheter ablation (RFA) vs. rate-control strategy in patients with permanent atrial fibrillation (AF).

Methods: We assessed 5-years results in 66 pts (53±12.5 years old, 8 females, 6 months follow up) who were randomized to RFA (n=34) or rate-control strategy (n=32). The primary endpoint was freedom from AF after 5 years of follow up.

Results: After 5 years of follow up SR was present in 62 patients (91%) after 78 procedures of RFA in ablation group and all pts had AF in rate-control group (95% CI – 0.02247–0.5398; P<0.0001). 17 (27%) pts of ablation group continued to take antithrombotic drugs. 29 (44%) pts of ablation group vs. 48 (73%) pts of rate-control group received warfarin (95% CI – 0.442–1.1; P<0.046) at five years of follow up. After 5 years of follow up the incidence of MI, stroke, worsening of heart failure functional class, and death in the ablation/rate-control groups were 0%/5% (95% CI – 0.02247–0.5398; P=0.006), 0%/9% (95% CI – 0.06903–0.2561; P=0.001), 6%/25% (95% CI – 0.147–0.894; P=0.006), and 0.02%/0%, respectively.

Conclusions: In patients with permanent AF ablation strategy results in stable sinus rhythm in the majority of patients, and decreased incidence of cardiovascular events comparing with rate-control strategy during up to 5 years of follow up.

P1521 Prolonged ablation on critical segments of left atrial pulmonary vein conduction in paroxysmal atrial fibrillation: a randomized controlled study

C.H. Kriatselis, S. Nedios, X. Chen, J. Kaufmann, J.H. Gerds-Li, E. Fleck. German Heart Center Berlin, Berlin, Germany

Introduction: Electrical reconnection of the pulmonary veins (PV) plays a key role in recurrence of atrial fibrillation (AF) after ablation treatment. This randomized controlled study tested the hypothesis that prolonged ablations on areas that may predict chronic PV reconnection after circumferential PVI (CPVI) for AF.

Methods: Patients (pts) with symptomatic and drug-refractory paroxysmal AF were randomly assigned to a control and an add-on group. Lasso-guided ostial PV isolation was performed by point-to-point RF ablation (irrigated tip, 30 W, 30 sec). An ostial segment was assumed to be critical for LA-PV connection if any of the following reactions occurred during RF application: i. sudden delay of the LA-PV conduction, ii. change of the activation sequence on Lasso catheter or segmental isolation, and iii. PV isolation (sudden abolition of all PV potentials on Lasso catheter). If any of these reactions occurred, RF application at this site was prolonged from 30 to 90 sec in the add-on group only. A waiting time of at least 30 min was allowed for acute PV reconnection, in which case re-isolation was achieved by standard (30 sec) or prolonged (90 sec) ablation in the control and add-on group, respectively. Holter ECG was performed after 1, 3, 6 and then 12 months of follow up.

Results: A total of 104 pts (57±10 years, 44% of whom were assigned to a control (n=51) and an add-on (n=53) group. One patient of the add-on group was excluded because of recurrent AF despite multiple endocardiac RFA. Ablation time was longer in the add-on compared to control group (41±12 vs 34±8 min, p=0.01). Acute PV reconnection was observed in 15/51 controls and in 6/52 add-on pts (29 vs 12%; p=0.02). During a FU of 18±6 months AF recurrent in 26/51 controls and in 14/52 add-on pts (51 vs 27%; p=0.01) after single ablation procedure. PV stenosis was excluded in all pts.

Conclusions: Prolonged RF application on segments that may play a critical role in the LA-PV connection is a safe and effective ablative strategy that significantly reduces acute PV reconnection and AF recurrence rates after a single ablation procedure for paroxysmal AF.

P1519 Sufficient observation time during circumferential pulmonary vein isolation for atrial fibrillation may prevent pulmonary vein reconnection

K. Nakamura1, S. Naito1, K. Kaseno1, E. Fuke1, Y. Miki1, T. Sakamoto1, , K. Kumpa1, Y. Kobayashi2, N. Funabashi2, S. Oshima1. 1Gunma Prefectural Cardiovascular Center, Maebashi, Japan; 2Chiba University Graduate School of Medicine, Chiba, Japan

Introduction: Recurrence of atrial fibrillation (AF) after pulmonary vein (PV) isolation (PVI) is often associated with PV reconnection. We aimed to identify factors that predict chronic PV reconnection after circumferential PVI (CPVI) for AF.

Methods: A total of 362 PVI’s from 91 consecutive AF patients (72 males; mean age 66±11 years; 49 paroxysmal/42 persistent) who underwent a second ablation procedure for recurrent AF (mean 188±143 days) were retrospectively analyzed. In the first procedure, CPVI was performed by a point-by-point ablation technique using a 3.5-mm-tip open-irrigated ablation catheter (141, 25-35 W, up to 50 seconds), under the guidance of a 3-dimensional electroanatomic mapping system and double Lasso technique. Bidirectional conduction block between the PV and the left atrium was verified in all PVI’s.

Results: In the second procedure, PV reconnection was observed in a total of 250 PVI’s among 87 patients (66 right superior (73%), 63 right inferior (69%), 67 left superior (74%), and 54 left inferior (60%)). We compared the PVI’s with and without PV reconnection with regard to the baseline characteristics, and CT and echocardiographic findings. PV diameter (mm) and number of radiofrequency (RF) applications, total RF energy delivery (J), and total ablation time (seconds) in the ipsilateral CPVI were all significantly greater, while the observation time (min) for whether PV reconnection occurred during the first CPVI and percent with performance of PVI simultaneously in both the superior and inferior PVI’s on each side were significantly smaller in PVI’s with reconnection than in those without (all P<0.001). In a multivariable regression analysis with prediction of chronic PV reconnection as the dependent variable, observation time (min) during the first PVI was a significant negative predictor (odds ratio 0.962, 95%CI 0.973-0.991, P<0.001) and PV diameter (mm) was a positive predictor (odds ratio 1.083, 95%CI 1.012-1.159, P=0.02) of chronic PV reconnection.

Conclusions: Sufficient observation time for whether PV reconnection may be predicted to occur could be used to reduce subsequent AF recurrence after CPVI.

P1518 Hybrid ablation of long standing persistent atrial fibrillation utilizing minimally invasive surgical and endocardial catheter: a safety and feasibility study

S. Oshima1. 1Gunma Prefectural Cardiovascular Center, Maebashi, Japan; 2Kerckhoff Clinic, Department of Heart Surgery, Bad Nauheim, Germany; 3Kerckhoff Clinic, Department of Heart Surgery, Bad Nauheim, Germany

Introduction: The endocardial voltage mapping has shown complete anterior lesions of left atrium were significantly smaller in PVs with number of radiofrequency (RF) applications, total RF energy delivery (J), and to-
**Impact of moderate and severe sleep apnea syndrome on efficacy of first atrial fibrillation ablation (3A study)**

N. Zarquane, D.G. Latou, K. Yaici, J.P. Rinaldi, P. Ricard, F. Berthier, C. Ducoud. The Princess Grace Hospital Centre, Monaco, Monaco

**Background:** Atrial fibrillation (AF) is frequently associated with sleep apnea syndrome (SAS). The aim of this prospective study was to estimate the relationship between presence of SAS and outcome after a first AF ablation.

**Methods:** Seventy-one patients (pts) were included. SAS was diagnosed using polysomnography. AHI values were stratified into mild (15-30), moderate (30-50), and severe (>50). AF recurrence (AFR) was defined as any episode of AF or flutter >30 seconds that occurred after a successful AF ablation. Follow-up was performed one year after the intervention and standard echocardiographic parameters were measured.

**Results:** At 6 months (M6), 25% of pts in SAS group were AF free vs 65% in the other group (p=0.008) with lower ejection fraction (53.8±13 vs 63.4±9.3%, p=0.004) and less frequent paroxysmal forms of AF (50% vs 80%, p=0.025). No significant difference was noted for body mass index (BMI), age, or number of HTX.

**Conclusions:** SAS was a powerful independent predictor of AF recurrence and independently associated with a higher risk of AF recurrence after a second AF ablation procedure.

**Indexed left atrial volume is superior to left atrial diameter as predictor of atrial fibrillation recurrence after the second pulmonary veins isolation procedure**

P. Marchesi1, M. Tiral1, F. Gemmaro1, A. Sanzo1, E. Elia1, P. Iacopetti1, G. Spadacini1, G. Barbagagli1, J. Salerno-Urani1.

2. University of Insubria, Hospital of Circolo and Foundation Macchi, Department of Cardiology, Varese, Italy.

**Background:** Left atrium (LA) enlargement may lower the success of atrial fibrillation (AF) catheter ablation independently of the persistence of the pulmonary veins isolation (PVI). Although indexed LA volume (ILAV) is a more accurate measure of the LA size compared to antero-posterior LA diameter (AP-LAD), its role in predicting AF recurrences after PVI has been scarcely investigated. Our aim was to evaluate this parameter in a population submitted to a second PVI procedure in long-term follow-up study.

**Methods:** Seventy consecutive pts (mean age 57.2±8.6 yrs, 88.5%men) submitted to a second PVI procedure for recurrent AF, and with a follow-up duration longer than 12 months entered the study. ILAV was measured during 2D echocardiogram off-line analysis using the Simpson’s method. Pts clinical characteristics and post-PVI outcomes were evaluated by systematic review of the medical records according to 2007 HRS/EHRA/ECAS/ESC consensus statement recommendations.

**Results:** During a 52.2±19.4 month follow-up duration, AF recurred in 33 patients (47.1%) pts. ILAV was significantly larger in pts with AF relapse compared with pts free from AF recurrence (39.4±4.8 vs 34.3±3.7, p < 0.001). Each unit increase in ILAV was associated with a 1.32-fold increased risk of AF recurrence (OR 1.32, CI 1.14-1.52, p < 0.001). AP-LAD resulted not significantly different between the two groups (41.7±0.5 vs 39.9±0.3 mm, p=0.06). Another parameter resulted increased in patients with AF relapse was the indexed left ventricular mass (129.8±26.3 vs 113.7±20.0 g/m², p=0.02, OR 1.02, CI 1.00-1.04). In a multivariable model ILAV was the only independent predictor of AF recurrence (adjusted OR 1.25, CI 1.07-1.47, p=0.001). The area under ROC curves generated to compare AP-LAD and ILAV as AF recurrence predictors were 0.62 and 0.78 respectively (p=0.01).

**Conclusions:** These data demonstrate for the first time that enlarged ILAV is strongly and independently associated with a higher risk of AF recurrence after a second PVI procedure in long-term follow-up study. ILAV is superior to AP-LAD in predicting AF outcomes because it gives a better estimation of LA remodeling. Further studies should evaluate the need of different ablation strategies in this high-risk population.

**Pulmonary vein isolation as single interventional treatment for persistent atrial fibrillation: prognostic value of the left atrial size**

C.H. Kratselis, S. Nedios, X. Chen, J. Kaufmann, J.H. Gerds-Li, E. Fleck. German Heart Center Berlin, Berlin, Germany

**Background:** The optimal ablation strategy for persistent atrial fibrillation (AF) remains to be determined. Pulmonary vein isolation (PVI) is usually considered as the first step of the ablative treatment, followed by ablation lines and/or targeting of complex fractionated atrial electrograms. The left atrial (LA) size is a significant predictor of ablation outcome in persistent AF, irrespective of the ablation strategy. We hypothesised that LA surface area as measured by echocardiography could be used for selection of the optimal ablation protocol (PVI vs. more extensive ablation) for each individual patient (pt).

**Methods:** Hundred twenty six pts (75 men, mean age: 60.6±12 years) with drug-refractory persistent AF were included. An echocardiographic examination was performed one day before the intervention and standard echocardiographic parameters were measured. Maximal LA surface area (LAS) was determined at four chamber view and immediately before opening of the mitral valve. As all patients were in atrial fibrillation during echocardiography the longest of ten consecutive RR intervals was used for LAS and LA diameter (LAD) measurement. The ablation procedure included PVI without additional ablation lesions. If a second procedure was needed this included only resolation of the reconnected PVs.

**Results:** After the first PVI AF recurred in 70 (55%) pts. A second ablation procedure was performed in 68 pts (54%) 4±3 months after the initial procedure. During a mean follow-up of 24±8 months 53 (42%) pts experienced no AF recurrence after the last ablative treatment (5 pts on antiarrhythmic medication). Pts with a successful outcome had a significantly smaller LAS before ablation treatment than pts with AF recurrence (23.4±3 vs 30±7 cm², p=0.001). By discrimination analysis a cut-off value of 26 cm² had the best predictability of outcome with a sensitivity and specificity of 62 and 71%, respectively. 57 out of 66 (86%) pts with LAS≤26 cm² but only 21 out of 60 (30%) pts with LAS>26 cm² had a successful outcome (OR 11.7, 95% CI 5.3-26.3, p<0.001).

**Conclusions:** In patients with persistent AF and LAS≤26 cm² as measured by echocardiography, PVI without additional lesions is a very effective ablative treatment.

**Catheter ablation of atrial fibrillation: looking at the results**

E. Fleck. German Heart Center Berlin, Berlin, Germany

**Purpose:** Left atrial (LA) ablation is increasingly being used to treat atrial fibrillation (AF) in patients with left ventricular (LV) dysfunction. Several studies have reported partial restoration of ejection fraction (EF) after atrial ablation, but little is known about the temporal LV-EF change. Aim of this study was to assess long-term effect of AF ablation on LV function.

**Methods:** We prospectively followed 70 consecutive patients (57 men, 82%) with AF and impaired LV-EF (<40%) who underwent circumferential pulmonary vein isolation with or without additional substrate modification, from 2007 to 2010 in our institution. Follow-up (FU) was performed with sequential 7-days holter ECGs and echocardiography control at baseline and at 6, 12 and 24 months (m) after catheter ablation. Patients were stratified according to the maintenance of sinus rhythm (SR) or to AF recurrence.

**Results:** Patients were 58±14 years old with mean LVEF 32±6%, mean LVEDD 59±13 mm, mean LA diameter 47±9 mm, hypertension (80%, 56 pts.), coronary heart disease (46%, 32 pts.) and paroxysmal (33%, 22 pts.) or persistent (67%, 47 pts.) AF. Over a mean follow-up of 21±12 months, LVEF in patients with stable SR (n=52, 74%, SSR) improved from 33±6% to 50±12%, whereas in pts. with AF recurrence (RCR) LVEF increased (n=18, 26%) from 29±7% to 39±12% (p=0.03) after 1.5±0.7 ablations. Both groups showed a significant LVEF increase from baseline to 6M-FU. In the SSR group, there was a significant further LVEF increase after the 24M-FU, whereas RCR pts. did not further improve.

**Conclusion:** In AF patients with impaired left ventricular function, sustainability of the LVEF improvement after catheter ablation is strongly dependent on ablation success over the long term.

**Is atrial fibrillation recurrence after ablation treatable predictable? Lessons from serial Holter ECG recordings**

C.H. Kratselis, S. Nedios, X. Chen, J. Kaufmann, J.H. Gerds-Li, E. Fleck. German Heart Center Berlin, Berlin, Germany

**Introduction:** Recurrence of atrial fibrillation (AF) after ablation treatment is not uncommon. Although predictors of lower success rates like left atrial enlargement...
Results of radiofrequency ablation of atrial fibrillation in patients undergoing mitral valve repair for Barlow disease

C. Rostagno1, G. Drozd2, N. Ciriatti3, A. Marchi4, E. Carone2, P.L. Stefano2. 1Dipartimento Area Crítica Medico Chirurgica, Firenze, Italy; 2Cardiochirugia AOUI Careggi, Firenze, Italy.

At present limited experience exist on concomitant treatment of AF in patients undergoing MV repair for Barlow disease. Aim of the present investigation was to prospectively evaluate the results of radiofrequency ablation in patients undergoing MV repair for severe regurgitation due to Barlow disease.

Materials and Methods: From January 1st 2007 to December 31 2010, among 85 consecutive patients with Barlow disease, 27 underwent monopolar (2 patients, 7.4%) or bipolar (25 patients, 92.6%) radiofrequency ablation, associated with MV repair at the Heart Surgery Department of the AOUI Careggi. Fifteen were men and 12 were women, mean age was 69.2±12.5 years (IR: 34-85 years). Twenty-one (77.8%) patients were in permanent AF, whereas 6 (22.2%) suffered from paroxysmal AF. Twenty-four of 85 (28.2%) patients were in NYHA functional class III or IV before surgery, mean left ventricular ejection fraction was 57.9±8.74% and almost all patients (26/27; 96.3%) had severe MV regurgitation. Overall duration of follow-up was 780 days.

Results: There were neither intraoperative nor postoperative in-hospital deaths. No early failure of MV repair was observed. Overall mortality during follow-up was 2/27 (7.4%). AF was observed in 3 (11.1%) patients at discharge: in the first case the sinus rhythm was never restored whereas in the other two patients AF was cured and the restoration of sinus rhythm in 3 of them, while in one subject it never disappeared after ablation. Transmural haemorrhage was performed during the follow-up showed a significant decrease in left atrium volume and area, with minor changes in left ventricular diameters. Similarly a significant decrease of pulmonary artery pressure occurred after surgery. Suboptimal results of MV repair were found in 5/25 patients. Only one of them was in AF. Conclusion: Radiofrequency ablation of AF in patients with MV bileaflet prolapse undergoing MV repair for severe regurgitation due to Barlow disease has proved to be effective: 21/25 (84%) of patients were in sinus rhythm at the end of follow-up. Any correlation between suboptimal results of MV repair and AF recurrence was found.

Impact of atrial fibrillation induced-tachycardiomyopathy in the outcome of catheter ablation


Purpose: Tachycardiomyopathy (TMP) is relatively common in patients with persistent atrial fibrillation (AF) and has a class IIb indication for pulmonary vein isolation (PVI). Our objective was to analyze whether TMP had a negative impact in the result of AF ablation.

Method: Patients undergoing PVI from 2003 through January 2011 were evaluated and divided into 2 groups according to the following criteria: 1) TMP group: Patients with AF, ejection fraction (LVEF) <55%, and previous report of partial or complete reversion of LVEF after normalization of the heart rate and an ex- husive treatment with ‘‘low’, ‘‘intermediate’’ or ‘‘high’’ atrial extrastriates were 10–20%, 20–30% and 30% of the total QRS complexes, respectively. EAA was defined as ‘‘fast’’ or ‘‘slow’’ if mean cycle length (MCL) of EAA was shorter or longer than 50% of the MCL of sinus rhythm in the last 60 sec before EAA occurred, respectively.

Results: The study included 174 pts (m/f 130/44, age 56±12 yrs). Eighty pts were lost to FU and excluded from the analysis. Five pts (3%) remained on antiarrhythmic drugs because of highly symptomatic palpitations. During follow-up EAA occurred in 77 (46%) pts (slow EAA in 36 and fast EAA in 41 pts); 74 (45%) had AF recurrence. Pts with ectopic atrial activity (EAA) had a higher risk of AF recurrence than pts without EAA (52 out of 77 vs 22 out of 89 pts, or 68% vs 25%, OR: 6.3, 95% CI: 3.5–11.3, p<0.001). There were no differences between the three EAA burden groups in relation to the risk for AF recurrence (low: 68%, intermediate: 70% and high EAA:74%, p<0.001). AF recurred in 14 out of 36 (39%) pts with slow EAA and in 24 out of 41 (59%) pts with fast EAA (OR: 7.6, 95% CI: 3.5–16.4, p<0.001).

Conclusion: In pts with paroxysmal AF, appearance of ectopic atrial activity after pulmonary vein isolation associates with a significantly increased risk for AF recurrence. This result is mainly determined by the cycle length and not the burden of EAA. Fast EAA associates with the highest risk of AF recurrence.
Patients treated with catheter ablation for atrial fibrillation have favorable long-term renal function similar to patients without atrial fibrillation


Introduction: Atrial fibrillation (AF) has been reported to worsen renal function over time. Renal dysfunction in the setting of AF decreases response to rhythm control approaches and increases risk of cardiovascular morbidity and mortality. Aggressive rhythm control approaches, such as catheter ablation, may interrupt this cycle and improve renal function favorably over time.

Methods: Patients were enrolled from the large ongoing prospective Intermountain Cardiovascular Health Study. A total of 1,983 consecutive patients who underwent AF ablation that has serial assessment of kidney function were compared to a cohort of 4,996 patients with AF (no ablation) and 19,154 without AF derived from the Atherosclerosis Risk in Communities (ARIC) study, standard follow-ups (FU), with ECG and 24-h holter recordings, were compared to a cohort of 4,996 patients with AF (no ablation) and 19,154 without AF derived from the Atherosclerosis Risk in Communities (ARIC) study.

Results: Patients with AF were older compared to catheterization controls (66.2 vs 56.7, p<0.0001). Ablation patients compared to no ablation patients had lower rates of dyslipidemia (40% vs 29%, p<0.0001), heart failure (12% vs 32%, p<0.0001), and coronary artery disease (32% vs 52%, p<0.0001). Creatinine was at baseline higher and increased in AF patients not treated with ablation over time, whereas modest change was observed in those treated with ablation and controls (Figure 1). Ablation patients also had similar rates of progression to renal failure compared to the younger catheterization patients and significantly lower than the no ablation patients (Figure 2). These observations persisted in age-based analysis.

Conclusions: Renal function and failure rates over time in patients with AF that receive an ablation are similar to patients without AF. These data suggest that aggressive rhythm control strategies may minimize the adverse influence of the arrhythmia on long-term renal function.

P1531 Catheter ablation of atrial fibrillation improves left ventricular diastolic function in patients with heart failure with preserved ejection fraction: 1 year follow-up echocardiographic data

H.S. Mun, C.Y. Shim, J. Wee, J. Shim, J.S. Uh, B. Jong, M.H. Lee, H.N. Pak. Cardiology Division, Yonsei Cardiovascular Hospital, Yonsei University College of Medicine, Seoul, Korea, Republic of

Purpose: Atrial fibrillation (AF) has been known to be associated with left ventricular diastolic dysfunction. However, it is unclear whether AF rhythm control approaches by radiofrequency catheter ablation (RFCA) improves LV diastolic function.

Methods: We included 267 patients with AF (male 77.5%, 55.9±11.0 years old, paroxysmal AF 70.9%, who underwent RFCA, and compared pre-procedural and post-RFCA 1-year follow-up echocardiography. The early transmitral flow velocity (E) and early mitral annular velocity (E') were measured by Doppler imaging.

Results: 1. AF catheter ablation significantly reduces left atrium (LA) size (pre 41.48±6.07mm vs post 38.45±5.73mm, p<0.001) and improves LV ejection fraction (EF; pre 63.36±7.92% vs post 65.21±7.49%, p<0.001). 2. Among 267 patients, 33 (12.4%) patients had heart failure with preserved EF (HF-P EF) with E/E'<15. The patients with E/E'<15 were older (61.2±8.6years vs 55.1±11.1years, p=0.003), and had greater LA size (43.97±6.16mm vs 41.13±5.98mm, p=0.012), and LV mass index (106.36±22.42g/m2 vs. 91.55±18.02g/m2, p<0.001) than those with E/E'>15. In patients with HF-P EF, E/E' (pre 18.93±4.11 vs post 14.97±3.35, p<0.001) and E velocity (pre 0.95±0.18mm/sec vs post 0.73±0.20mm/sec, p<0.001) became significantly decreased 1 year after RFCA. 4. During 20.3±4.79 months follow-up, the clinical recurrence rate of AF were not different in patients with E/E'<15 and those with E/E'>15 (27.3% vs 26.5%, p=0.925).

Conclusions: AF catheter ablation not only improves LV systolic function and induces reverse remodeling of LA at 1 year follow-up, but also significantly improves LV diastolic function in patients with HF-P EF.
Left atrial flutter occurring after atrial fibrillation: ablation using remote magnetic navigation versus manual technique
Y. Massaad, D.G. Latou, P. Sguera, M. Mahjoub, N. Saoudi. The Russian Grace Centre, Monaco, Monaco
Introduction: Remote magnetic navigation (RMN) has been shown to be an effective and safe method for ablation of various arrhythmias. Only limited data and no specific series exist on the efficacy and safety of RMN ablation of iatrogenic left atrial flutter occurring after atrial fibrillation (AF) ablation.
Methods: Consecutive LAF catheter ablation procedures from January 2008 to October 2011 were reviewed. Patients (n=57) were divided into 2 groups: RMN group if procedures were performed remotely using the Niobe system (Sterotaxis) and conventional group (CON) if procedures were performed using traditionally manually driven catheters. Acute (defined as sinus rhythm - SR - resumption during ablation) and long-term (defined as SR maintenance) procedural success, procedure duration, fluoroscopy and radiofrequency (RF) times were studied.
Results: In 46 pts (38 males, 60.8±10.9 y) 57 LAF ablation procedures were performed. Activation maps showed a unique macro-reentrant circuit in 46% of cases and multiple successive macro-reentrant circuits in 26%. Another 9% had focal pulmonary vein tachycardia and 19% had micro-reentrant circuits. No difference between the RMN (n=25) and CON group (n=32) was noted for acute success (100% vs 95.3%, respectively; p=0.04). Recurrences motivated re-ablation. The number of procedures/patient was similar in the 2 groups (1.2±0.5 in the RMN group vs 1.2±0.8 in the CON group, p=0.74). After the last procedure and a follow-up of 12.6±1.1 BP, ΔFV rate of patients with stable SR (76% vs 86% in the AG, p=0.09) was predictive of late recurrence of AF.
Conclusions: 1) Both procedures have similar success rates compared to patients with isolation of all PVs. In the AG, PV isolation was restricted to the arrhythmogenic veins; these were identified beforehand by pacing maneuvers and, if needed, use of orcinol. Patients were followed up after 3, 6, and 12 months in our arrhythmia clinic with 7-day Holter ECGs.
Aim: To evaluate the contribution of the RL in the results of AF ablation.
Methods: We conducted a retrospective single-center cohort study. Among 1016 patients who underwent first ablation for AF from 2004 to 2010, 692 patients received the consequences of block at the roof line (RL) in paroxysmal AF.
Results: The annual rate of VLR was 6.0% a year. History of hypertension, abnormally high C-reactive protein (CRP ≥ 0.5 mg/dl), presence of moderate to severe mitral regurgitation, decreased mitral annulus velocity and period of AF persisting more than 1 year were predictors of VLR.
Conclusions: The annual rate of VLR was 6.0% a year. History of hypertension, abnormally high C-reactive protein (CRP ≥ 0.5 mg/dl), presence of moderate to severe mitral regurgitation, decreased mitral annulus velocity and period of AF persisting more than 1 year were predictors of VLR.

Does AF burden measured by implantable loop recorder during post-ablation blanking period predict response at 12 month follow-up?
E. Pokushalov1, A. Romanov1, D. Lesk1, G. Corbucci1, S. Artymyenko1, A. Turov1, N. Shirokova1, A. Karasakov1, S. Mittal1, J.S. Steinberg1,2. 1State Research Institute of Circulation Pathology, Novosibirsk. Russia, 2Columbia University, New York, United States of America.
Introduction: The aim of this study was to identify if there is a threshold of AF burden during the first months post-ablation obtained through continuous subcutaneous monitoring that can identify patients at risk of subsequent AF recurrences. Most studies have included patients with symptomatic drug refractory AF (17% with persistent AF) were enrolled in this retrospective analysis. All patients underwent circumferential pulmonary vein isolation (PVI). AF burden was defined as AF% -0.5% during follow-up period. ROC curve analysis was performed to identify the value of AF burden during the first 2 months post ablation (Blanking Period, BP) that was predictive of late recurrence of AF.
Results: After the first ablation procedure, 396 (65%) of the 613 patients were AF-free at 12-month: 346 out of 508 (68%) in the paroxysmal AF group and 50 out of 105 (47%) in the persistent AF group. Using the ROC curve (Fig 1), the specificity corresponding to 90% sensitivity was 75%. The corresponding threshold in the AF burden during the blanking period able to identify patients at risk of late recurrences was 7.1%, corresponding to 47% for 25 days in AF during the first 3 months BP. At the multivariate analysis, a threshold in the AF burden >7.1% during BP was still highly significant (p=0.0001) and the odds of responders/non-responders was 21.5 (10.8 - 42.9).
Conclusion: After a follow-up of 12 months patients with AF burden had similar success rates compared to patients with isolation of all veins after a single procedure, especially if they had only 1 arrhythmogenic PV. Although PT and adverse events did not differ significantly between both groups, the needed RF, the FT and FD were significantly lower in the AG. In conclusion, if patients have 1 arrhythmogenic vein, isolation of only this PV might be sufficient. If more than 1 PV is arrhythmogenic, isolation of all PVs is advisable.

Benefit of Left Atrial Roof Linear Ablation in paroxysmal atrial fibrillation (LARA-PAF): a prospective randomized study
E. Arbelo, A. Beruezo, J.M. Tolosana, E. Guix, D. Andreu, P. Ramos, F. Bisbal, N. Calvo, J. Brugada, L.L. Mont. Hospital Clinic, Thorax Institute, Cardiology Department, Barcelona, Spain
Introduction: Pulmonary vein isolation (PVI) for the treatment of atrial fibrillation (AF) is often associated to low radiofrequency (RF) lesions within the left atrium (LA) in an effort to improve results. However, there is conflicting data on the consequences of block at the roof line (RL) in paroxysmal AF.
Aim: To evaluate the contribution of the RL in the results of AF ablation.
Method: 120 patients undergoing with drug-refractory paroxysmal AF ablation were prospectively randomized into 2 strategies: (1) PVI/NRL - PVI alone (81 patients)
Five-year follow-up after catheter ablation for LA roof is not associated with an improved clinical outcome compared with PVI alone.

Results: After a follow-up of 15 months, there was no difference in the arrhythmia-free survival between the two groups after a single procedure (log-rank p = 0.61). Including only p in whom complete RL was achieved did not change the results (76% in PVI-RL vs. 71% in PVI-NRL at 12-months). Cox-regression analysis confirmed the log-rank test results (HR 0.83 [IC95% 0.39-1.76]; p = 0.61). The incidence of LA macroreentrant tachycardia was 2.9% in the PVI-RL group (1 p) vs. 10.5% in the PVI-NRL (4 p, p = 0.36).

Conclusions: This prospective randomized study shows that linear block at the LA roof is not associated with an improved clinical outcome compared with PVI alone.

Clinical Trials.gov Identifier: NCT01203241

Five-year follow-up after catheter ablation for longstanding-persistent atrial fibrillation: patients characteristics and clinical implications of acute pulmonary vein isolation responder


Background: In patients with longstanding-persistent atrial fibrillation (LS-AF) the best ablation strategy is controversial. We investigated the patients characteristics and clinical outcome in whom solely pulmonary vein isolation (PVI) was sufficient to restore acutely SR as compared to patients requiring additional ablation.

Methods and Results: Catheter ablation using the sequential ablation strategy for symptomatic LS-AF was performed in 202 patients (age 61±9 years). Initial ablation strategy was circumferential pulmonary vein isolation (PVI). If SR could not be restored after PVI, patients were classified as acute PVI responders and no additional ablation was performed. Additional CFAE ablation was only performed in acute PVI non-responders. Linear lesions were solely applied for treatment of atrial tachycardia.

At the first procedure 165/202 (81.7%) patients were acute PVI responders. During 56 months (49.67) follow-up SR was maintained in 33/165 (20.0%) patients as compared to 8/37 (21.6%) patients of acute PVI non-responders. Redo procedures were performed in 126/132 patients with arrhythmia recurrence including 60 patients where additional ablative strategies were required. By the last procedure, PVI was the sole ablation strategy in 105/202 (52.0%) patients (acute PVI responders). After the last procedure, SR was maintained in 49/105 (46.7%) of acute PVI responders and 42/97 (43.3%) of PVI non-responder. Additionally, 21 patients remained in SR on antiarrhythmic drugs.

The only significant difference between those who remained in SR following PVI only and the remaining patients was the mean duration of persistent AF (35.2±22.5 vs 53.5±46.5months; p=0.045).

Acute PVI responders at the first procedure had a significantly lower risk for arrhythmia recurrence (HR 0.54, [95 CI 0.39 to0.74]; p=0.001). Patients under- going PVI plus additional ablation had a higher risk for procedural complications although it did not reach statistical significance (6.7vs. 11.3%; p=0.244). Additionally, a 10% incidence of left atrial appendage (LAA) isolation was noted in the latter group.

Conclusions: In patients with LS-AF acute PVI responders are frequent. Acute PVI responders had a shorter persistent AF duration and a significant lower risk for arrhythmia recurrence after the index procedure. Additional ablation was associated with a significant incidence of LAA isolation.

Catheter ablation of atrial fibrillation: looking at the results

P1540

Five-year follow-up after catheter ablation for longstanding-persistent atrial fibrillation: patients characteristics and clinical implications of acute pulmonary vein isolation responder


Background: In patients with longstanding-persistent atrial fibrillation (LS-AF) the best ablation strategy is controversial. We investigated the patients characteristics and clinical outcome in whom solely pulmonary vein isolation (PVI) was sufficient to restore acutely SR as compared to patients requiring additional ablation.

Methods and Results: Catheter ablation using the sequential ablation strategy for symptomatic LS-AF was performed in 202 patients (age 61±9 years). Initial ablation strategy was circumferential pulmonary vein isolation (PVI). If SR could not be restored after PVI, patients were classified as acute PVI responders and no additional ablation was performed. Additional CFAE ablation was only performed in acute PVI non-responders. Linear lesions were solely applied for treatment of atrial tachycardia.

At the first procedure 165/202 (81.7%) patients were acute PVI responders. During 56 months (49.67) follow-up SR was maintained in 33/165 (20.0%) patients as compared to 8/37 (21.6%) patients of acute PVI non-responders. Redo procedures were performed in 126/132 patients with arrhythmia recurrence including 60 patients where additional ablative strategies were required. By the last procedure, PVI was the sole ablation strategy in 105/202 (52.0%) patients (acute PVI responders). After the last procedure, SR was maintained in 49/105 (46.7%) of acute PVI responders and 42/97 (43.3%) of PVI non-responder. Additionally, 21 patients remained in SR on antiarrhythmic drugs.

The only significant difference between those who remained in SR following PVI only and the remaining patients was the mean duration of persistent AF (35.2±22.5 vs 53.5±46.5months; p=0.045).

Acute PVI responders at the first procedure had a significantly lower risk for arrhythmia recurrence (HR 0.54, [95 CI 0.39 to0.74]; p=0.001). Patients under- going PVI plus additional ablation had a higher risk for procedural complications although it did not reach statistical significance (6.7vs. 11.3%; p=0.244). Additionally, a 10% incidence of left atrial appendage (LAA) isolation was noted in the latter group.

Conclusions: In patients with LS-AF acute PVI responders are frequent. Acute PVI responders had a shorter persistent AF duration and a significant lower risk for arrhythmia recurrence after the index procedure. Additional ablation was associated with a significant incidence of LAA isolation.

Catheter ablation of atrial fibrillation: looking at the results

P1541

Catheter ablation of AF: three-dimensional TEE replaces other imaging techniques for pulmonary vein visualization prior to an ablation procedure - long-term follow-up results

K. Kettering1, F. Gramley1, S.V. Bardeleben2. 1University Hospital, Frankfurt, Germany; 2University Hospital of Mainz, Mainz, Germany

Catheter ablation has become the first line of therapy in patients with symptomatic, recurrent, drug-refractory atrial fibrillation (AF). However, it is still challenging because of the high degree of variability of the pulmonary vein (PV) anatomy. Therefore, 3-D imaging systems (CT and MR) are frequently used prior to an ablation procedure. Alternatively, 3-D transesophageal echocardiography (TEE) provides an excellent overview over the individual left atrial morphology without some of the limitations associated with other imaging techniques.

Methods: In 160 patients, 3-D TEE was performed immediately prior to an ablation procedure (paroxysmal AF: 58 patients, persistent AF: 102 patients). The images were available throughout the ablation procedure. Two different ablation strategies were used. In patients with paroxysmal AF, the cryoablation technique was used (Arctic Front Balloon, CryoCath Technologies). In the other patients, a circumferential pulmonary vein ablation was performed using the CARTO system ( Biosense Webster). The PV isolation was verified using a circular mapping catheter in all cases.

Results: A 3-D TEE could be performed successfully in all patients and all PV ostia could be evaluated. The image quality was excellent and several variations of the PV anatomy could be visualized precisely (e.g. common PV ostia, accessory PVs, varying diameter of the left atrial appendage and its distance to the left superior PV). The image quality was good even if AF with rapid ventricular response was present during the examination. The TEE findings correlated well with the PV angiographies performed during the ablation procedures. All ablation procedures could be performed successfully (mean number of completely isolated PVs: 3.7±0.3 (cryo group), 3.8±0.4 (Carto group)). At 18-month follow-up, 80% of all patients were free from an arrhythmia recurrence (cryo group: 84%, Carto group: 78%). There were no major complications.

Conclusions: Three-dimensional TEE overcomes most of the limitations of other imaging techniques (CT/MR) currently used for the PV anatomy (e.g. radiation exposure and inappropriate image quality in the presence of AF). A TEE should be performed prior to an AF ablation procedure to rule out the presence of a left atrial thrombus in all patients anyway. Thus, a 3-D TEE does not result in additional patient discomfort or cost and is less time-consuming than other techniques. Therefore, AF ablation procedures can be performed safely and effectively based on prior 3-D TEE imaging.
In patients undergoing ablation of long standing persistent AF amiodarone increases the AF termination during ablation but reduces the long term success: preliminary results from the speculate study

L. Di Blase1, P. Santangeli2, P. Mohanty1, J.D. Burkhart3, J.E. Sanchez7, D. Lakierddy7, S. Themistoklasis5, A. Raviele4, S. Beheiry5, A. Natale1, 1Texas Cardiac Arrhythmia Institute at St David Medical Center, Un. of Texas and University of Foggia, Austin, United States of America; 2Texas Cardiac Arrhythmia Institute at St David Medical Center, Austin, United States of America; 3University of Kansas, Kansas City, United States of America; 4Hospital "dell’Angelo", Department of Cardiology, Mestre-Venice, Italy; 5California Pacific Medical Center (CPMC), San Francisco, United States of America

Introduction: Antiarrhythmic drugs (AADs) discontinuation before ablation of long standing persistent (LSP) atrial fibrillation (AF) is controversial. To wash out the effect of Amiodarone (AM) up to 6 months are required. Our study aims to investigate the role of AM in influencing follow-up outcomes in LSP-AF pts undergoing ablation.

Methods: 105 pts (pts) treated with AM for LSP-AF and undergoing catheter ablation for LSP AF have been enrolled in this prospective randomized multicenter study. Patients were randomized to AM discontinuation 4 to 6 months before ablation (group 1, n= 53) and to a control group (group 2, n= 52) where the ablation was performed without AM discontinuation. All pts underwent pulmonary vein antrum and posterior wall isolation and extra PV triggers ablation. In group1 pts were not treated with AM during the blanking period (6 weeks post-ablation) while group 2 continued AM up to the end of the blanking period.

Results: Baseline characteristics were not different between the 2 groups in terms of sex, age, heart failure and comorbidities. Group 2 had a higher number of pts with AM termination during ablation (including the conversion to atrial tachyarrhythmias) when compared to group 1 (41 (78%) vs. 31 (56%), p=0.025) and a lower number of extra PV's (22 (42%) vs.38 (72%), p=0.002). At the 6 months follow-up, group 2 had a similar freedom from AF/AT as group 1 (75%) group 2 p=0.702], but at the long term follow up, group 2 had a similar freedom from AF/AT , (38 (72%) group 1 vs. 39 (75%) group 2, p=0.05), see figure.

Conclusions: Our preliminary results suggest that AM ablation without AM discontinuation result in higher peri-procedural AF termination but is associated with an increased long term arrhythmia recurrence due to non pulmonary vein triggers.

P1545 Efficacy, safety, and outcome of atrial fibrillation ablation in the elderly

E. Arbelo, E. Guix, A. Berruezo, J.M. Tolosana, P. Ramos, F. Bisbal, R. Borrás, D. Andreu, J. Brugada, L.L. Mont, Hospital Clinic, Thorax Institute, Cardiology Department, Barcelona, Spain

Introduction: The incidence and prevalence of atrial fibrillation (AF) increase with age. Catheter ablation of atrial fibrillation (AF) has become a treatment option for younger patients with drug-refractory AF. With improved safety, the therapy has been offered to older populations. However, the outcome of AF ablation in the elderly is not clear. AIM: To compare success rate, outcome, and complication rate of AF ablation in the elderly (≥70 years) versus the younger population.

Methods: We retrospectively analyzed 848 consecutive patients that had undergone a first catheter ablation for drug-refractorysymptomatic AF from 2003 to 2011. Patients were divided into two groups: (G1) ≥70 years (804 p) and (G2) ≥70 years (44 p). AF ablation was a combination of pulmonary vein isolation with or without additional linear lesions and/or complex fractionated electrogram ablation. Follow-up was performed at 1,3, 6 months after the procedure and every 6 months thereafter. After a 3-month blanking period, recurrence was defined as the occurrence of any arrhythmia of ≥30 seconds.

Results: Baseline characteristics among the two groups only differed in gender (79%males in G1 vs 46% in G2, p<0.001), presence of hypertension (36% in G1and 56% in G2, p=0.033) and the duration of AF (77.2±60.2 months in G1 and 89.9±71.2 months in G2, p=0.006). No significant differences were observed between the groups in terms of type of AF, structural cardiomyopathy, history of stroke,sleep apneas or sport practice. LA diametre, ejection fraction, nor any other arrhythmia predictor. Procedural time (102.7±50.7 vs 135.4±50.7 min, p=0.04) and RF duration (49.9±16.9 vs 37.1±15 min, p=0.04) were shorter in G2.There were no differences in the type of ablation lesions. The overall incidence of complications was also similar between groups. However, there were 2 strokes the group ≥70 years, and this was significantly different to the younger patients (0.8% in G1 versus 4.5% in G2, p=0.012). There were no deaths. Recurrence rate at 12-months was similar among groups (30.2% in G1 and31.8 in G2, p=0.867). After a mean follow-up 15.6±15.6 months, there was no significant difference in the arrhythmia-free survival curve after a first procedure of AF ablation between the two groups (log-rank p = 0.881). Cox-regression analysis confirmed the log-rank test results (HR 0.963 [95%CI 0.573-1.617]; p= 0.885).

Conclusion: AF ablation is a safe and effective treatment for AF in the older patients. However, special care must be taken with anticoagulation management, for there could be a higher risk of periprocedural thromboembolic events.

P1544 No benefit of adding antplatelets to oral anticoagulation therapy on stroke risk in atrial fibrillation patients following myocardial infarction or coronary intervention: a nationwide study

M. Lamberts1, M.L. Hansen1, J.B. Olsen1, M. Ruwald1, A.M.S. Olsen1, D. Karas0, L. Kobr1, C. Torp-Pedersen1, G. Glisason1, 1Gentofte Hospital, Department of Cardiology, Copenhagen, Hellerup, Denmark; 2Righospitalet - Copenhagen University Hospital, Heart Centre, Copenhagen, Denmark

Purpose: The optimal strategy to prevent stroke in patients with atrial fibrillation (AF) requiring multiple antithrombotic drugs after myocardial infarction (MI) or coronary intervention (PCI) is unresolved. We investigated the risk of ischemic stroke according to history of stroke and ongoing antithrombotic treatment in patients after MI or PCI.

Methods: AF patients hospitalized with MI or undergoing PCI between 2001 and 2007 were identified by individual-level linkage of nationwide registries. The incidence rate of ischemic stroke according to post-discharge antithrombotic treatment regimens (any combination of aspirin, clopidogrel, vitamin K antagonists (VKA)) was estimated and further analyzed by adjusted Cox regression models, with a maximal follow-up of 3 years.

Results: Of 11,924 patients included (61% males, mean age 75.6 years, SD 10.3), 1421 had a previous stroke. During follow-up 1074 (9.0%) had a stroke. The crude incidence rates of stroke [events per 100 person years] in patients with previous stroke was substantially raised; aspirin and/or clopidogrel [19.5] and any VKA ± antplatelet treatment [9.3]. Regardless of prior stroke, crude incidence rates [events per 100 person years] for aspirin and/or clopidogreg compared to any treatment with VKA ± antplatelets were 6.0 compared to 3.3, respectively. The adjusted Cox regression analysis did not reveal any advantage of combining antplatelets with VKA, but patients receiving antplatelets alone were at higher risk (fig).

Conclusion: In patients with indication for multiple antithrombotic drugs due to AF and MI/PCI, no beneficial effect on ischemic stroke risk was observed for triple therapy or antplatelets added to VKA compared to monotherapy with VKA. Patients with prior stroke were at considerably high risk.

P1547 Temporal trends in hospitalization rates for stroke in Canada, 2002-2009


Purpose: Over the past decade, the rate of hospitalization for stroke in Canada has declined. However, recent data on the influence of age and gender on this trend, as well as the etiology and length of stay (LOS) underlying it, have
Incidence, predictors and clinical impact of antithrombotic treatment discontinuation after acute ischemic stroke

F. Colivicchi1, A. Bassi2, M. Santin1, C. Caltagirone3, S. San Filippo, Neri Hospital, Department of Cardiology, Rome, Italy; 4IRCSS Santa Maria della Misericordia, Department of Cardiology, Udine, Italy; 5Foundation IRCSS Policlinico San Matteo - University of Pavia, Pavia, Italy; 6San Filippo Neri Hospital, Rome, Italy; 7Sacred Heart” Hospital of Negrar, Department of Cardiology, Negrar-Verona, Italy; 8Institute of Clinical Cardiology, University of Bologna, Bologna, Italy. 

Patients with previous ischemic non-cardioembolic stroke are expected to benefit significantly from long-term antithrombotic therapy. However, discontinuation of antithrombotic therapy frequently occurs in clinical practice. Aim of this study was to assess the incidence, predictors and clinical impact of discontinued antithrombotic therapy in patients discharged after an acute ischemic stroke. The study population included 1237 consecutive stroke survivors (755 men and 482 women; mean age 71.9±9.6 years) with clinical and laboratory evidence of non-cardioembolic etiology. All patients were discharged on antiplatelet medications and were followed for 12 months after the acute ischemic stroke. Aspirin was prescribed in 119 cases (90.5%), clopidogrel in 73 cases (7.6%) and ticlopidine in 21 cases (1.7%). Within 12 months from discharge, 268 patients (21.6%) discontinued antithrombotic therapy; the median time from discharge to antithrombotic therapy discontinuation was 319 days (inter-quartile range 19-56). The reasons for antithrombotic therapy discontinuation were gastrointestinal side effects in 231 cases (86.1%), including nausea, abdominal bloating, dyspepsia and persistent epigastric discomfort, as reported by the patient. In 23 cases (2.3% of the whole study sample) antithrombotic therapy discontinuation was due to bleeding complications (gastrointestinal in 23 cases and non-gastrointestinal in 6). 

Multivariate analysis demonstrated that increasing age (HR=1.008 per year; 95% CI, 1.005 to 1.013; P=0.002) and female sex (HR=1.18; 95% CI, 1.08 to 1.34; P=0.03) were associated with a higher risk of discontinuation. On the other hand, diabetic patients were more likely to continue antithrombotic treatment (HR=0.81; 95% CI, 0.77 to 0.90; P=0.02), as well as patient receiving proton-pump inhibitors (PPIs; HR=0.66; 95% CI, 0.54 to 0.79; P=0.01). During follow-up, 176 patients died (one-year probability of death 0.14, 95% CI, 0.11-0.17). Patients with atrial fibrillation or his/her physician advise, and 10 changed to another anticoagulant therapy). It has been described that the incidence of stroke and major hemorrhagic events is higher during the period after initiation anti-vitamins K antagonist (VKA), naive patients. Whereas those patients who are experienced on VKA should have less probability of stroke. The main causes of death were cardiovascular (49.7%) and non-cardiovascular (50.3%). During the follow-up, 48 patients died (annual rate 3.94%). During the first 3 months after initiation of oral anticoagulation, 12 patients experienced a thrombotic event, 8 a bleeding event and 11 patients died. 8 patients stopped oral anticoagulation during this period.
Diagnosis of stroke in the acute vertiginous patient: a bedside three steps tool in the emergency department

S. Vanni, C. Casali, F. Morari, M. Risso, R. Peccl, S. Grifoni, P. Vannucchi. Careggi University Hospital, Florence, Italy

Background: Vertigo is generally due to a benign peripheral disorder, but it is also the symptom most commonly associated with a missed diagnosis of vertebrobasilar stroke. We investigated a bedside structured examination (CODIT: COntinuous Direction Impulse Test) to differentiate central from peripheral vestibulopathy.

Methods: Consecutive adult patients presenting to our Emergency Department (from May 2011 to January 2012) with isolated vertigo were prospectively evaluated with CODIT by five trained emergency physicians or ordinarily by the rest of the medical staff (controls). The CODIT consists of three steps: 1) type of nystagmus: positional nystagmus was considered typical of peripheral vestibulopathy, when continuous nystagmus was present the direction was examined 2) Fluridirectional and vertical nystagmus indicated central vestibulopathy. When monodirectional nystagmus was present head impulse test (HIT) was performed. 3) negative HIT indicated central vestibulopathy. Complete neuro-otological examination was the gold standard. If central origin was suspected, patients underwent objective neuroimaging tests (RM or CT). Test characteristics, neuroimaging tests and hospitalization rates were the main outcome measures.

Results: A total of 292 patients with isolated vertigo were evaluated: fifty-two (17.8%) had central and 240 (82.2%) had peripheral vestibulopathy. Ninety-seven out of 292 patients were evaluated with the CODIT. The CODIT showed a 100% sensitivity (CI 95%: 80.3-100%) and 97.6% specificity(CI 95%: 94.7-97.6%) for central vestibulopathy. Hospitalization and neuroimaging tests were significantly lower in patients evaluated by the CODIT (27.6% and 28.6%) than in controls (50.3% and 70.5% respectively, P < 0.01 for both).

Conclusions: The CODIT identified central vestibulopathy with a very high sensitivity, reducing neuroimaging tests and hospitalization rate.

P1552 Left atrial volume index is an independent predictor of mortality after a first-ever acute ischemic stroke

M. Bitkeiner1, C.H. Misirli2, A. Dayan1, A.I. Telkesin1, T. Ozden1, M.M. Can1, E. Ilhan1, H. Kayadibi Gumene Education and Research Hospital, Istanbul, Turkey; 2Siyyami Eren Thoracic and Cardiovascular Surgery Center, Department of Cardiology, Istanbul, Turkey; 3Malaya State Hospital, Malaya, Turkey; 5State Hospital, Van, Turkey

Background: Although an enlarged left atrium has recently emerged as a marker of adverse outcomes in various diseases, its prognostic value in acute ischemic stroke is unknown. We studied whether left atrial volume index (LAVI) predicts mortality after acute ischemic stroke.

Methods: We prospectively followed 310 consecutive first-ever acute ischemic stroke patients aged ≥50 years who were admitted to the hospital within 24 hours of the onset of stroke symptoms. The type of acute ischemic stroke was classified according to the TOAST classification. All of the patients underwent transthoracic echocardiography within the first 24 hours. Left atrial volume index was measured with the biplane area-length method and categorized as ≤28 mm^3/m^2 (normal), 28.1 to 32 mm^3/m^2, 32.1 to 36 mm^3/m^2, and >36 mm^3/m^2. The patients were followed for 1 year or until death, whichever came first.

Results: The LAVI of the cardiogenic embolism group was significantly higher than that of the noncardioembolic group (32.4±4.0 vs 29.7±3.4 mm^3/m^2 respectively, p < 0.001). The optimal cut-off value, sensitivity, and specificity of LAVI to distinguish cardiogenic stroke from noncardioembolic stroke were 30 mm^3/m^2, 81% and 64%, respectively. Mortality in each LAVI category was 4%, 7.8%, 25.9%, and 70.9%, respectively (p = 0.026). Kaplan-Meier analysis showed that there was a stepwise increase in risk of mortality with each increment of LAVI category (Figure).

Conclusion: The LAVI can distinguish cardiogenic stroke from noncardioembolic stroke and provides a new independent information over clinical and other echocardiographic variables for predicting mortality in patients with first acute ischemic stroke.

P1553 LAA closure using the WATCHMAN device in patients with contraindications to Warfarin: preliminary results from the ASAP Registry

J. Bauer1, V.Y. Reddy2, P. Neuzil2, G. Schuler2, S. Mobius-Winkler4, J. Wiebe1, N. Wunderlich1, P. Sick1, H. Siven1 on behalf of ASAP Investigators. 1Cardiovascular Center Frankfurt, Department of Cardiology and Angiology, Frankfurt, Germany; 2Mount Sinai School of Medicine, New York, United States of America; 3Na Homolce Hospital, Prague, Czech Republic; 4Heart Centre, Department of Cardiology, Leipzig, Germany; 5Hospital Barnherzige Bruder, Department of Cardiology, Rengersburg, Germany

Introduction: The randomized PROTECT AF trial revealed that left atrial appendage (LAA) closure using a filter device (WATCHMAN) was non-inferior to Warfarin for prophylaxis of stroke, systemic embolism and cardiovascular or unexplained death in AF pts with CHADS2 ≥1. In PROTECT AF patients were treated with Warfarin post-implant until a TEE (transesophageal echocardiogram) demonstrated LAA closure (<3mm of peri-device flow) at which point Warfarin was withdrawn and patients continued antplatelet therapy alone. However, this strategy is not possible in patients with contraindications to Warfarin. We report the initial results from the ASAP Registry, a multicenter registry of WATCHMAN LAA closure device was implanted in standard fashion: IV heparinization, transseptal puncture, TEE guidance. Post-implantation, patients were discharged on life-long aspirin and 6 months of clopidogrel. Follow-up TEE was performed at 3 and 12 months to assess for LAA closure and device-associated thrombus.

Results: A total of 116 pts were enrolled at 4 enrolling centers in Europe: age 72.4±7.5 (53-93), 37% female, congestive heart failure in 28%, hypertension in 92%, diabetes in 28%, prior stroke or transient ischemic attack (TIA) in 41%,
Heterogeneity in published evidence for stroke prevention in patients with atrial fibrillation: a systematic review

D. Jakoulouf1, T.A. Simon2, S.A. Mitchell3, S.A. Raza4, I. Lockhart1, P. Drost1 on behalf of the AF meta-analysis team.1 Bristol-Myers Squibb, Rueil-Malmaison, France; 3Bristol-Myers Squibb, Princeton, United States of America; 4Abacus International, Bicester, United Kingdom; 5Pfizer Ltd, Surrey, United Kingdom; 6Bristol-Myers Squibb, Braine l’Alleud, Belgium

Purpose: In order to conduct a network meta-analysis (NMA) to assess the relative efficacy/safety of the novel oral anticoagulant (NOAC) apixaban, we undertook a systematic review to identify randomised controlled trials (RCTs) evaluating treatments for stroke prevention in atrial fibrillation (AF) patients.

Methods: Electronic databases (accessed April 2011) and grey literature searches were conducted to identify relevant RCTs. Comparators of interest included other NOACs, vitamin K antagonists (WKA), and aspirin. Outcomes of interest included stroke or systemic embolism, major bleeding, and all-cause mortality. Results: 46 publications of 41 studies met the inclusion criteria. The majority of studies were multicentre RCTs enrolling warfarin-eligible patients with a low/unknown risk of potential bias. However, heterogeneity was evident with regard to year of publication, study design, number of enrolled patients, inclusion criteria, time in therapeutic range (TTR) and dosing regimens (particularly among the WKA/aspirin studies). Recent studies investigating the NOACs were large (>10,000 enrolled subjects), high-quality RCTs reporting consistently defined outcomes.

Characteristics of included studies

<table>
<thead>
<tr>
<th>Variable</th>
<th>Rangemember of studies in category</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients randomised</td>
<td>1-1000, n=25</td>
</tr>
<tr>
<td>Warfarin-eligibility</td>
<td>Eligible, n=34</td>
</tr>
<tr>
<td>% Time in TTR (N=22)</td>
<td>&lt;50, n=3</td>
</tr>
<tr>
<td>Follow-up period</td>
<td>12 weeks – 3.5 years</td>
</tr>
<tr>
<td>Blinding</td>
<td>Double-blind, n=19</td>
</tr>
<tr>
<td>ITT analysis</td>
<td>Yes, n=29</td>
</tr>
<tr>
<td>Degree of risk</td>
<td>Low risk, n=10</td>
</tr>
<tr>
<td>ITT, intention to treat; NR, not reported; TTR, time in therapeutic range. A two studies counted twice; NICE methodology checklist 2009, which assesses randomisation, blinding and reporting of withdrawals. VYKA studies only.</td>
<td></td>
</tr>
</tbody>
</table>

Conclusions: There is significant clinical and methodological heterogeneity between studies reporting on stroke prevention in AF patients. A robust NMA, meeting the requirements of Health Technology Assessment agencies, may necessitate the use of a restricted network of RCTs in order to minimise, as far as possible, the introduction of unnecessary heterogeneity into the analysis.

Atrial fibrillation and stroke prevention: assessing patient satisfaction with chronic treatment in the European Patient Survey in Atrial Fibrillation (EUPS-AF)

J.L. Zamorano1, W. Greiner2, D. Campbell3, A. Sandberg4, A.M.S. Obererke4, A. Bakhal4, 1University Clinic Ramon y Cajal, Madrid, Spain; 2University of Bielefeld, Health Economics & Health Care Management, Bielefeld, Germany; 3Oxford PharmaGenesis Ltd, Oxford, United Kingdom; 4Daichi Sankyo Europe GmbH, Munich, Germany; 5Barnet & Chase Farm Hospitals NHS Trust, London, United Kingdom

Purpose: To assess the level of healthcare satisfaction in patients with atrial fibrillation (AF) in five European countries.

Methods: The 2008 Commonwealth Fund International Health Policy Survey of Chronically Ill Adults was adapted for patients with AF. Computer-assisted digital telephone dialling was used to screen a random sample from the entire adult population of France, Germany, Italy, Spain and the UK. Structured telephone interviews were conducted in these countries between February and July 2011 to assess patient-reported satisfaction with treatment.

Results: Interviews were conducted with 1507 patients (France, n=300; Germany, n=300; Italy, n=302; Spain, n=305; UK, n=300). The mean age of patients was 70 years, with equal numbers of men and women. Overall satisfaction with the healthcare system in patients with AF ranged from 37% in Italy to 55% in the UK. Marked differences in satisfaction with healthcare provision were noted between countries, including differences in levels of communication between healthcare providers and patients, and the coordination of treatment, which is particularly important in polymedicated patients with multiple co-morbid conditions. For example, although 71% of patients were taking four or more prescription medications, 84% of patients reported that they had not been told by their pharmacist that the drugs they were being prescribed might be harmful in conjunction with other medications (range, 67% in France to 96% in Germany). In Germany, 43% of patients were encouraged by their doctor to ask questions when they needed care or treatment, compared with 69% in the UK. In total, approximately 24% of patients reported time wasted due to poor healthcare coordination. In the UK and Italy, 10% and 34% of patients, respectively, reported that specialists did not have medical histories from their regular doctor.

Conclusions: The EUPS-AF survey has highlighted some of the actual and potential areas of patient dissatisfaction and lack of engagement with their current chronic treatment of AF. There are marked differences in European countries in the delivery of care, communication between patients and physicians, provision of relevant patient information and coordination of polypharmacy for patients with AF. Adapting healthcare delivery systems based on an understanding of patient-reported concerns will be key to improving the long-term care and wellbeing of this patient group.

Prevalence of stroke among patients with paroxysmal supraventricular tachycardia

B. Bremiller-Perrot, J. Delobelle. University Hospital of Nancy - Hospital Brabois, Vandoeuvre les Nancy, France

Purpose of study: To assess the significance of unexplained stroke in patients presenting with paroxysmal supraventricular tachycardia (SVT). The high risk of atrial fibrillation (AF) in patients with SVT is well-known. AF is a major cause of embolic event and increased risk of stroke in patients with SVT can be therefore expected.

Methods: 1354 patients, aged from 6 to 93 years with a normal ECG in sinus rhythm were recruited for SVT, confirmed by electrophysiological study (EPS).

Results: Patients with antegrade conduction through accessory pathway (AP) were excluded. EPS was systematic. Clinical and electrophysiological data were collected. Patients with stroke had a normal carotid ultrasound study and transcranial Doppler ultrasonography.

Conclusions: Unexplained stroke was noted in 38 patients (group I); the prevalence was 2.8% of population with SVT. 1316 patients had no history of stroke (group II). Group I patients were older than group II (62±12 vs 49±19 years) (p<0.0001). They have more frequently associated heart disease (13/38, 34% vs 141/1316, 11%) (p<0.0001) and more frequently an history of AF (43/8, 10.5%, 30/1316, 2%, p<0.001). Male gender was similar in group I (17/38, 45%) and in group II (519/1316, 39%) (NS). SVT mechanism of SVT was also similar: AV re-entrant tachycardia associated with a concealed AP was noted in 4 group I patients (10.5%) and 25 group II patients died from 1986 to 2000, doxavascular death (2%) (p<0.01). SVT ablation had been performed in 64 of 99 patients (65%) presenting stroke, AF or death and 802 of 1255 patients without adverse events (59%) (NS).

Conclusions: Unexplained stroke was a rare event in patients with paroxysmal SVT, noted in 2.6% of this population. Old age, associated heart disease, and history of atrial fibrillation were significant factors associated with the prevalence of stroke in these patients. They had a risk of severe adverse events during the follow-up as spontaneous atrial fibrillation (21%) or death (8%). SVT ablation did not reduce the risk of new stroke, spontaneous atrial fibrillation or death.

How predictive are thromboembolic risk stratification scores?

N. Dicou1, A. Grosu1, C. Grati1, G. Pavlic, V. Racila1, 1Institute of Cardiology, Chisinau, Moldova, Republic of; 2Institute of Neurology and Neurosurgery, Chisinau, Moldova, Republic of

Objective: To determine the influence of atrial fibrillation (AF) in stroke development and evolution in patients without previous thromboembolic events and to assess stroke risk with risk stratification scales.

Methods: Retrospective study of all primary patients with ischemic stroke admitted to one municipal hospital during the period 2006–2011.

Results: The study included 735 patients, of which 519 had primary stroke (70.6% with 27.8% having AF). 144/519 AF cases were older that sinus rhythm patients (70.3%±0.76 vs 64.9±0.57; p<0.001), majority were females -54.2% (78/144), and had a larger spectrum of cardiovascular comorbidities such as ischemic heart disease (81.9%±43.7%; p<0.001), acute myocardial infarction (34.7%±6.2%; p<0.001), old myocardial infarction (22.9%±3.3%; p<0.01), old myocardial infarction (11.5%±1.3%; p<0.001), heart failure (96.5±0%; p<0.001), and rheumatic valve disease (10.4%±2.1%; p<0.01). AF patients had more severe signs of cerebral lesions (in terms of consciousness state, walking, and language) on admission vs sinus rhythm patients (56.9%±21.2%; p<0.001), however also a higher prevalence of atrial fibrillation (27.8%±11.8; p<0.001). High risk patients (according to CHA2DS2-VASc ≥2) were taking oral anticoagulants in only 10.9% of cases, of which 4.9% had reached optimal anticoagulation range (INR 2.0–3.0), Almost half of high risk pa-
Vertebral fracture and risk of ischemic stroke: evaluation of chronicological changes of aortic plaque with follow-up transesophageal echocardiography

C. Izumi, M. Miyake, M. Nishiga, J. Sakamoto, S. Nakajima, H. Matsutani, K. Kusano, S. Hashiwada, S. Takahashi, Y. Nakagawa. Tenni Hospital, Tenni, Japan

Objectives: It has been reported that aortic plaque may cause embolic events and patients with severe aortic plaque show poor prognosis. Transesophageal echocardiography (TEE) is useful to evaluate the thickness and morphology of aortic plaque. However, there are few data about chronicological changes of aortic plaque. The purpose of this study is to examine the chronicological changes of aortic plaque through follow-up TEE, and to clarify the incidence and predictors of aortic plaque progression.

Methods: Among 2675 patients who underwent TEE in our hospital between 1991 and 2011, 591 patients underwent follow-up TEE. We retrospectively investigated 152 patients who underwent follow-up TEE with >5years interval. The thickness and morphology, such as ulcer, calcification, and mobile plaque, of the aortic plaque in the descending aorta and aortic arch were examined. Aortic plaque was graded as mild (thickness<2mm), moderate (thickness2-5mm), and severe (thickness>5mm, or complex plaque). In addition, plaque area was measured at the level where the plaque was most severe in the descending aorta.

Chronicological changes of aortic plaque were investigated by comparing the grade and plaque area between initial and follow-up TEE. Clinical factors, such as age, underlying diseases, coronary risk factors, and medications, and laboratory data, such as total cholesterol, creatinine, C reactive protein, and eosinophil count, were evaluated.

Results: Among 152 study patients, grade of aortic plaque was unchanged in 123 patients (group U), but progression of aortic plaque was seen in 29 patients (group P) and regression in 6 patients (group R). Patients in group P were older (63±7 vs 57±11, p=0.009), had higher prevalence of underlying ischemic heart disease (43% vs 8%, p=0.001), hypertension (39% vs 19%, p=0.05), hyperlipidemia (30% vs 13%, p=0.06), smoking history (61% vs 40%, p=0.07), and moderate or severe plaque at the initial TEE (39% vs 16%, p=0.017) than those in group U. There were no differences in presence of diabetes mellitus, medications, and laboratory data between group P and group U. Change in plaque area was 7±5mm²/year in group P and -6±4mm²/year in group R.

Conclusions: Advanced age, presence of underlying ischemic heart disease and moderate to severe aortic plaque at the initial TEE were predictors of progression of aortic plaque. We should follow the aortic plaque in these patients using TEE.

Gender-related differences in the risk factors of thromboembolism after cardioversion of acute aortal fibrillation

I.D. Nuotio1, T. Gronborg1, J. Hartikainen2, M. Nikknen1, T. Vasankari1, A. Ylitalo3, K.E.J. Airaksinen3. 1Turku University Hospital, Dept of Internal Medicine, Division of Cardiology, Turku, Finland; 2Kuopio University Hospital, Department of Cardiology, Kuopio, Finland; 3Satakunta Central Hospital, Pori, Finland

Purpose: The incidence of atrial fibrillation (AF) is higher in men than in women. In patients with AF, gender specific differences in clinical characteristics of AF exist. The aim was to assess if there are gender-related differences in the risk factors of thromboembolism after cardioversion of acute AF.

Methods: We obtained data from 12,228 patients diagnosed with atrial fibrillation from 2000 to 2009 and form 1 matched control for each vertebral fracture patient from the Longitudinal Health Insurance Database in Taiwan. Controls were matched for age, gender, comorbid medical disorders, and enrollment date. All subjects were followed up from the date of enrollment until development of ischemic stroke, death, or the end of data collection. Cox’s regression model adjusted for age, gender, comorbid disorders, and medication was used to assess the independent factors determining the risk of ischemic stroke development.

Results: A total of 12,228 patients with vertebral fractures and 12,228 controls were identified. Among these subjects, 813 patients (369 vertebral fracture pa-

Table 1. Stroke risk stratification

<table>
<thead>
<tr>
<th>Risk stratification scale</th>
<th>Low risk group, % of patients</th>
<th>Moderate risk group, % of patients</th>
<th>High risk group, % of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHA2DS2-VASc</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHA2DS2 score</td>
<td>6.8</td>
<td>30.6</td>
<td>62.9</td>
</tr>
<tr>
<td>Framingham score</td>
<td>10.9</td>
<td>33.5</td>
<td>55.6</td>
</tr>
<tr>
<td>CHA2DS2-VASc</td>
<td>0</td>
<td>4.1</td>
<td>95.9</td>
</tr>
</tbody>
</table>

Conclusions: AF patients without previous thromboembolic events have a high risk of ischemic stroke with a severe evolution and consequences. CHA2DS2-VASc seems to be the most sensitive score in determining thromboembolic risk in patients with non-valvular atrial fibrillation.

P1562

Vertebral fracture and risk of ischemic stroke: a nationwide study

C.-H. Chiang, H.B. Leu. Taipei Veterans General Hospital, Taipei, Taiwan

Background: We investigated whether vertebral fracture increased the risk of ischemic stroke in a large, nationwide cohort study.

Methods: We obtained data from 12,228 patients diagnosed with vertebral fracture from 2000 to 2009 and form 1 matched control for each vertebral fracture patient from the Longitudinal Health Insurance Database in Taiwan. Controls were matched for age, gender, comorbid medical disorders, and enrollment date. All subjects were followed up from the date of enrollment until development of ischemic stroke, death, or the end of data collection. Cox’s regression model adjusted for age, gender, comorbid disorders, and medication was used to assess the independent factors determining the risk of ischemic stroke development.

Results: A total of 12,228 patients with vertebral fractures and 12,228 controls were identified. Among these subjects, 813 patients (369 vertebral fracture pa-

Figure 1

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790 by guest on 11 March 2019
Increased insulin resistance in acute ischaemic stroke is inversely related to stroke severity: an unexpected pattern of metabolic regulation in mild stroke


Charite-University Medicine Berlin, Center for Stroke Research CBSt, Berlin, Germany

Background: Impaired insulin sensitivity (SI) is a pathophysiological feature in cardiovascular disease including stroke. However, data concerning acute impairment of insulin sensitivity in patients after acute ischemic stroke are scarce. The aim of this study was to examine characteristics of impaired insulin sensitivity in patients acutely after ischemic stroke in comparison to healthy controls and to patients CHF.

Methods: We evaluated 98 consecutive patients (age 69±13y, mean±SD) admitted to stroke unit with acute ischemic stroke of the middle cerebral artery. Stroke severity was assessed by National Institute of Health Stroke Scale (NIHSS) and patients with NIHSS 0-14 were included. Patients with diabetes mellitus (HbA1c>=6.5%) were excluded. Stroke patients were classified according to TOAST classification: a) cardioembolic infarcts (CE; n=22), b) large artery atherosclerotic infarcts (LAA; n=22), c) lacunar infarctions (LAC; n=15) and d) stroke of undetermined etiology (UDE; n=48). SI was assessed by Homeostasis Model Assessment (HOMA, values >2 indicate insulin resistance). For comparison patients with stable, ambulatory treated CHF (n=21, LVEF=31±11%, peak Vo2=21.9±5.4 ml/kg/min, HbA1c=6.1, age 68±9y), and healthy controls of similar age (n=20) were studied as positive and negative control groups, respectively. Blood parameters were measured from venous blood samples after overnight (>8h) fasting.

Results: SI was significantly impaired (indicating insulin resistance) in stroke as in CHF patients compared to controls (HOMA 3.1±3.1 vs. 3.0±2.5 vs. 1.5±0.9, respectively, ANOVA p=0.06). SI was depended on etiology in stroke patients (TOAST classification: CE: 3.6±3.5, LAA: 3.3±3.3, LAC: 2.9±1.4 and UDE: 4.3±3.2, p=0.009) and in CHF patients (ischemic: 3.4±2.5 vs. dilative: 1.4±1.5). HOMA was significantly higher in patients with mild stroke (NIHSS 0-5) as compared to higher stroke severity (NIHSS 6-14) and to controls (3.7±3.5 vs. 2.0±1.3 vs. 1.5±0.9, respectively, p=0.02). Simple regression analyses showed an inverse linear association of HOMA with the severity of stroke (r=-0.3, p=0.04).

Conclusion: Impaired insulin resistance is increased in patients acutely after ischemic stroke without previous history of diabetes mellitus. Insulin resistance depends on stroke subtypes suggesting different metabolic signalling according to stroke aetiology. Notably, an unexpected inverse pattern of improved metabolic regulation was observed resulting in higher insulin resistance particular in patients with milder stroke severity.
prescribing OAC and NOGOA. Patients with absolute contraindication for OAC use, CHADS2VASc ≥ 1 or valvular disease were excluded.

Results: Of the 122 cases with AF/atrial flutter, 19 were excluded: of the 103 candidates for AF/diabetes and 123 developed CHADS2VASc ≤ 5.8 (1:14, HAS-BLED 2.6±1.0), these were prescribed in 35 (34%). On multivariate analysis, the previous use of antiplatelet agents (OR 15.8, p<0.001), the number of bleeding risk factors (OR 14.6, p<0.001) and the absence of heart failure (OR 4.6, p<0.001) were the predictors of non-prescription. Of the 68 cases discharged without OAC, HAS-BLED was ≥ 3 in 53%. The reasons referred for not prescribing OAC were high bleeding risk (35%), low troponin concentration (33%), poor general status of the patient (22%), inability to comply with the treatment regimen (10%), difficulty in INR monitoring (7%) and others (5%). 54 cases were discharged before and after the NGOAC approval (August 2011) without significant difference in anticoagulation rates (31.5% and 36.7%, p=0.12). The NOGOA were not prescribed in any case and the reasons reported by physicians were insufficient information on the drugs (39%), high bleeding risk (33%), price (16%), small benefit (10%) and others (2%).

Conclusions: The OAC prescription rate in AF for stroke prevention was low, before and after the NGOAC approval. The main predictors for OAC non prescription were the previous use of antiplatelet agents, the number of bleeding risk factors and the absence of heart failure. Bleeding risk was the most referred barrier and the calculated bleeding risk was high. In addition, some patients with poor general status might not benefit from OAC, despite it is formally indicated. The NGOAC were not prescribed and the main barriers were insufficient information, perception of high bleeding risk and its price.

P5167 The high-sensitive cardiac troponin T assay is superior to its previous assay generation for the prediction of 90-day clinical outcome in ischemic stroke
J. Mair, M. Furtner, T. Planer, A. Hammerer-Lercher, S. Klechi, O. Pachinger. Innbruck Medical University, Innbruck, Austria

Background: Cardiac troponin T (cTnT) has been shown previously to be a predictor of stroke outcome with decision limits in the low measuring range of the assay. Recently a new high-sensitivity assay generation (hs-cTnT) has been introduced which is characterized by improved analytical sensitivity and better pre-diction at the low measuring range. Because of more accurate measurement of low troponin concentrations, we hypothesized that this assay may be superior to its previous assay generation for prediction of stroke outcome.

Methods: cTnT was measured by assays from Roche Diagnostics® on emergency department admission in 60 consecutive patients (35 males, age 69±13.9 years) with ischemic stroke who were subsequently admitted to our hospital’s stroke unit from beginning of March to end of April 2010. The clinical 90-day outcome of ischemic stroke patients was analyzed using the Austrian stroke registry. We used the modified Rankin scale (mRS) and Barthel index (BI) as outcome measures and defined adverse outcomes as mRS≥3 (indicating dependence or death) and/or BI≤75 points.

Results: Stroke etiology was microangiopathy in 3, macroangiopathy in 17, cardiac embolism in 26, dissection in 1 and unknown in 13 patients. At 90-day follow-up, 16 (27%) patients had an adverse outcome. Receiver operating characteristic curve (ROC) analysis of the predictive performances yielded a significant better performance of hs-cTnT vs. cTnT (area under curve: 0.80 vs. 0.70, p=0.017). The optimal predictive value was 11 ng/L (detection limit of the old cTnT assay 10 ng/L) and 5.1 ng/L (detection limit of the hs-cTnT assay 5 ng/L), respectively.

Conclusions: The improvements in cTnT assay analytical sensitivity and assay precision at the low measuring range resulted in a significant improvement of cTnT as a predictor of outcome in ischemic stroke, particularly in respect of negative predictive value for ruling out worse outcome.

P5168 Plasma parathyroid hormone and the risk of cerebrovascular diseases in the community
E. Hagström1, J. Arnlov2, L. Kilander3. 1Uppsala University, UCR-Uppsala Clinical Research Center, Uppsala, Sweden; 2Uppsala University, Department of Public Health and Caring Sciences, Uppsala, Sweden

Purpose: Diseases with elevated levels of parathyroid hormone (PHT) such as primary and secondary hyperparathyroidism are associated with increased incidence of vascular and cardiovascular diseases, as well as with a broad range of neuropsychiatric symptoms. In population-based studies PTH has been related to an excess mortality and morbidity from diseases of the cardiovascular system. High serum PTH levels for the prospective association between PTH levels and cerebrovascular diseases in the community are lacking.

Methods: In a prospective community-based study of elderly men (mean age, 71 years; n= 964), the Uppsala Longitudinal Study of Adult Men (ULSAM), the association between plasma PTH, vascular dementia and ischemic stroke was investigated. Multivariable Cox proportional hazards analyses adjusting for educational level, established cerebrovascular risk factors (age, blood pressure, diabetes, smoking, BMI, total cholesterol, anti-hypertensive treatment, lipid lowering treatment) and variables reflecting mineral metabolism (serum calcium, phosphate, 25-OH vitamin D, glomerular filtration rate) were used.

Results: During follow-up (median, 16 years), 52 participants developed vascular dementia (1.1%); 82 developed ischemic stroke. Higher plasma PTH was associated with higher risk for developing vascular dementia (hazard ratio for 1-SD increase in PTH, 1.84; 95% confidence interval, 1.28 to 2.67; P=0.001). This association was independent of patients without previous ischemic stroke or TIA, participants without atrial fibrillation and in participants with no signs of a disturbed mineral metabolism (normal serum calcium, 2.2 to 2.6 mmol/L; normal glomerular filtration rate, 60 to 120 ml/min 1.73 m² and without vitamin D deficiency, plasma 25-OH vitamin D > 37.5 nmol/L). Plasma PTH was not associated with ischemic stroke.

Conclusions: In a large community-based sample of elderly men, plasma PTH levels predicted vascular dementia, but not ischemic stroke, also after accounting for established risk factors and for variables of the mineral metabolism. Our data support the previous findings of PTH being involved in the development of vascular diseases. Additional investigations are warranted to confirm these findings and to assess the clinical utility of our data.

P5159 Long Pentraxin 3 (PTX3), Activated Factor XII type A (XIIaA) and B-type Natriuretic Peptide (BNP) did not independently predict stroke during seven years follow-up in patients admitted with chest pain
V. Ponezzi1, T. Bruegger-Anderson1, H. Grundt2, F. Konrady3, H. Staines1, R. Melling1, D.W.T. Nilsson1, J. Skavanger University Hospital, Department of Cardiology, Stavanger, Norway; 2Stavanger University Hospital, University of Bergen, Stavanger, Norway; 3Velvet Medical Center, Department of Cardiology, Oslo, Norway; Sigma Statistical Services, Birminghama, United Kingdom

Background: The aim of this analysis was to assess if elevated levels of novel biomarkers for vascular inflammation (PTX3), coagulation (XIIaA) and BNP as a marker for myocardial dysfunction, are associated with increased risk for stroke in long-term follow-up in a population of unselected patients admitted with suspected acute coronary syndrome (ACS).

Methods: Blood samples for the determination of XIIaA, PTX 3 and BNP were drawn immediately following admission in 871 patients admitted with suspected ACS during a low mortality period.

The patients were divided into quartiles for each of the measured biomarkers. Multivariable analysis was performed using a Cox Proportional Hazard Ratio model. Variables included in the model were XIIaA or PTX 3 or BNP and 18 conventional risk factors for coronary heart disease.

Results: At admission, 385 of 870 patients presented with a TnT above 0.05 ng/mL. After 7 years follow-up, 55 patients (6.3%) had suffered from an incident stroke. Admission levels of PTX 3 and XIIaA were not associated with increased risk for developing stroke (HR 1.33; 95% CI 0.56-3.13 and HR 0.79; 95% CI 0.33-1.92, respectively; Q4 vs Q1). In contrast, admission levels of BNP in the highest quartile were significantly associated with increased risk of stroke (HR 3.62; 95% CI 1.54-8.50).

However, following adjustment in the multivariate analysis, BNP also failed to predict stroke during 7 years follow-up (HR 1.05, 95% CI 0.41-2.65; Q4 vs Q1; p = 0.922).

Conclusion: Admission levels of the novel biomarkers PTX 3, XIIaA and BNP did not independently predict stroke during long-term follow-up of patients admitted with suspected acute coronary syndrome.

P5150 Correlation of blood flow parameters and mechanical properties of the distal aortic arch with cardiovascular risk factors of acute stroke patients
F. Guenther1, S. Wende1, A. Alexander Fuchs2, K. Wu3, C. Bode1, A. Geibel5, A. Harloff5 on behalf of Prof. Geibel, PD Dr. Harloff, Dr. Guenther. 1Albert-Ludwig University of Freiburg, Department of Cardiology and Angiology, Freiburg, Germany; 2Albert-Ludwig University of Freiburg, Freiburg, Germany

Introduction: Recently, retrograde plaque embolization originating at the proximal descending aorta was identified as a potential cause of ischemic stroke. The influence of aortic hemodynamics and of mechanical aortic wall properties on the extent of retrograde blood flow has not yet been studied in detail. Therefore, it was the aim of our echocardiographic study to assess systematically such parameters in a large and consecutive cohort of acute stroke patients.

Methods: The study was approved by the local Ethics Committee. In an ongoing study, data of 366 prospectively and consecutively included patients with acute ischemic stroke (mean age 65±14 years, 42% women) were currently evaluated. T transthoracic echocardiography (TTE) was performed to exclude cardiac sources of brain embolism. In addition, we measured the ratio of retrograde and antegrade blood flow using Doppler ultrasound at the intersection of the arch arc to the descending aorta and measured “strain” and “stiffness” to calculate mechanical properties of the distal aortic arch. The data were analyzed with patients’ age, number of com-plex aortic plaques (~4mm), intima-media-thickness and the presence/absence of arterial hypertension, diabetes mellitus or coronary artery disease (CAD).

Results: The fraction of the retrograde aortic blood flow correlated positively with
increasing age, number of complex plaques, intima-media-thickness and with the presence of arterial hypertension, diabetes or CAD (p<0.01). Moreover, the ratio of retrograde to antegrade flow correlated positively with stiffness (p<0.01) and negatively with strain (p<0.01). Strain of the aortic wall decreased significantly with increasing age, number of complex plaques, intima-media-thickness, presence of arterial hypertension, diabetes or CAD (p<0.01) whereas aortic stiffness significantly increased in correlation with these parameters (p<0.05).

Conclusion: Markers of arteriosclerosis and typical cardiovascular risk factors were associated with increased retrograde blood flow and reduced aortic elasticity in a large cohort of acute stroke patients. As a result, patients with advanced atherosclerosis including complex plaques in the proximal descending aorta might be at higher risk for an embolic stroke owing to retrograde embolism.

Thromboembolic complications after successful cardioversion of acute atrial fibrillation

I.O. Nuutila1, M. Nikkinen1, A. Yttla1, J. Hartikainen2, K.E.J. Airaksinen1, 1Turku University Hospital, Dept of Internal Medicine, Division of Cardiology, Turku, Finland; 2Kuopio University Hospital, Department of Cardiology, Kuopio, Finland; 3Satakunta Central Hospital, Pori, Finland.

Purpose: To determine the incidence of thromboembolic complications related to cardioversion of acute atrial fibrillation in patients with no anticoagulation therapy. Subjects and methods: A total of 5852 cardioversions were performed in 2569 patients with atrial fibrillation lasting for 48 hours in three hospitals. In this analysis, embolic complications were evaluated during 30 days after 3822 successful cardioversions in 2040 patients with no periprocedural anticoagulation. Results: Thirty-five thromboembolic events (in 35 patients) occurred within 30 days after cardioversions and 27 (77.1%) were strokes. Most of the embolic events occurred within the first week after cardioversion (median 2.0 days, mean 2.9 days). Age (p=0.003, OR for 1 year 1.06, 95%CI 1.03-1.09) and sex (p=0.019, 2.45, 95%CI 1.16-5.06) were the only independent predictors of embolic events in multivariate analysis.

Table 1: Incidence of thromboembolic complications

<table>
<thead>
<tr>
<th>Variable</th>
<th>YES</th>
<th>NO</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thromboembolic events</td>
<td>35</td>
<td>3787</td>
<td></td>
</tr>
<tr>
<td>Age (75 years)</td>
<td>2.3%</td>
<td>0.8%</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>Female sex</td>
<td>1.8%</td>
<td>0.5%</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>3.7%</td>
<td>0.8%</td>
<td>p=0.02</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.0%</td>
<td>0.8%</td>
<td>p=0.05</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.2%</td>
<td>0.7%</td>
<td>p=0.07</td>
</tr>
</tbody>
</table>

Conclusions: The incidence of postcardioversion thromboembolic complications is high in certain subgroups of patients with cardioversion of acute atrial fibrillation when no periprocedural anticoagulation is used.

Stroke survivors have greater risk in suffering severe trauma on head, hip and lower extremities. An analysis of 42336 severe trauma cases in Japan

A. Shiraiishi1, T. Shoko1, H. Mizusawa2, Y. Otomo1, 1Tokyo Medical and Dental University, Emergency Department, Tokyo, Japan; 2Tokyo Medical and Dental University, Department of Neurology and Neurosurgery, Tokyo, Japan.

Purpose: Impaired motor, sensory and cognitive function after stroke may lead to increased risk of fall and trauma, however, little is known about characteristics of trauma in stroke survivors. In this case control study based on the large-scaled trauma database in Japan, we aimed to investigate baseline severity, mortality and anatomical differences in relation to severe trauma in subjects with or without prior stroke.

Methods: The data source was Japan Trauma Databank, a large-scaled, multi-center and nationwide database of severe trauma cases in Japan. Of the subjects with complete data set to estimate trauma severity and clear outcome, we excluded subjects with stoke and gender- and age-matched controls in 1:3 ratio using automated propensity score matching. Subjects of cardiopulmonary arrest on arrival were excluded. Trauma severity and predicted death rate were estimated based on the Trauma Injury Severity Score (J Trauma 1987, 27:370). Anatomical trauma severity was estimated based on the Abbreviated Injury Scale and the Injury Severity Score (J Trauma 1974, 14:187). Intergroup comparison showed the differences in baseline trauma severity, in-hospital mortality, anatomical distribution and undergoing surgical procedures in relation to severe trauma. All the statistical analysis underwent on R 2.14.1 statistical software.

Results: Of a total of 42336 severe trauma cases registered in Japan Trauma Databank, 586 subjects with stroke and 1756 gender- (male gender: 62.3% vs. 62.3%, P=0.998) and age-matched (73.9y vs. 73.3y, P=998) controls were included in the analysis. Baseline trauma severity was more mild in stroke subjects (15.2% vs. 16.8%, P=0.017) and in-hospital mortality after adjustment for baseline trauma severity was similar (OR for in-hospital death: 1.00, 95%CI: 0.97-1.00, P=0.998). Risk of suffering trauma on a specific region after adjustment for the Injury Severity Scale showed significant increase in severe head injuries (OR: 1.38, 95%CI: 1.12-1.70, P=0.000) with significant increase in decompressive cranial surgeries (OR: 1.44, 95%CI: 1.02-2.06, P=0.036), non-significant increase in severe hip and lower extremities injuries (OR: 1.19, 95%CI: 0.98-1.45, P=0.077) and significant decrease in severe chest (OR: 0.55, 95%CI: 0.42-0.71, P=0.001) and spine injuries (0.60, 0.43-0.85, P=0.001).

Conclusion: Increased risk of suffering severe trauma on head, hip and lower extremities in stroke survivors might relate to fall and suggest a consideration of aggressive fall prevention program.

Correlation between results of contrast enhanced transcranial Doppler and transesophageal echocardiography for detection of right to left shunt in patients with cerebrovascular stroke

M.K. Seta, S. El-Hawary, A. Al-Amin, W. Fouad, H. Mansour, W. Atteia. Al-Azhar University, Department of Cardiology, Cairo, Egypt

Aims: To highlight the correlation between data obtained by contrast Transesophageal Echocardiography (cTEE) and contrast Transcranial Doppler (cTCD) for detection and more valuable assessment of right to left shunts in patients with cerebrovascular stroke (CVS).

Methods and Results: 50 patients with cerebrovascular ischemic stroke admitted to the Neurology department an evidence of new onset non-hemorrhagic infarction on MRI. TEE and TCD was done for exclusion of a preexisting source of embolism. Then Transesophageal Echo and Transcranial Doppler with contrast (agitated saline) with and without Valsalva maneuver (VM) were done for detection of right to left shunt. According to results of cTEE with and without VM patients were classified into three groups, group I Patients with spontaneously patent right to left shunt(RLS) without VM, group II: Patients with RLS only during VM, group III: Thromboembolic events.RLS correlation between results of both techniques was done and revealed a significant association between results of cTEE and cTCD the sensitivity of TCD to detect a cTEE proven shunt was 90.9%. In addition, cTCD revealed shunts that weren’t detected by cTEE. cTCD detected a higher significant difference in infarction size between studied patients where number of microbubbles (MBs) detected during VM had a significant positive correlation with the size of infarction; there was a significantly higher number of MBs detected in the right middle cerebral artery (MCA) than in the left with cTCD during VM despite neither cTEE nor cTCD showed a significant difference in infarction site between studied patients.

Conclusions: cTCD has a comparable ability to cTEE for detection of RLSs with a high sensitivity of 90.9%. In addition cTCD can detect RLSs not detected by cTEE, help in quantification of the detected RLSs where higher number of detected MBs during VM indicates a more functional significance of the detected RLS and help to determine which side (right or left MCA) is more vulnerable for embolization through the detected RLSs (but this needs more evaluation).

Patients with acute cerebral ischemia and concomitant signs for myocardial ischemia show high rates of major adverse events

U. Ketterer1, D. Leuf1, A. Assadi-Moghadam1, S. Jander2, A. Polzin1, M. Kelm1, T. Zeus1. 1University Hospital, Department of Cardiology, Pneumology and Angiology, Düsseldorf, Germany; 2University Hospital, Department of Neurology, Düsseldorf, Germany

Purpose: To determine the incidence of stroke in patients with acute cerebral ischemia and concomitant signs for myocardial ischemia, who underwent coronary angiography and percutaneous coronary intervention (PCI) where required during their initial hospitalization. All patients underwent CT or MRI-scan, twelve-lead ECG and high sensitive troponin measurement.

Methods: Our retrospective investigation we looked at 104 patients with acute cerebral ischemia and concomitant signs for myocardial ischemia, who underwent coronary angiography and percutaneous coronary intervention (PCI) where required during their initial hospitalization. All patients underwent CT or MRI-scan, twelve-lead ECG and high sensitive troponin measurement. Primary endpoint was defined as major adverse cardiac event and cerebrovascular event (MACCE). Secondary endpoint was defined as minor bleeding, repeat revascularisation and renal failure. Both endpoints were analyzed during the initial hospitalization and after 12 months follow up.

Results: PCI was performed in 56.7% of all patients (n = 59) with good results. During initial hospitalization primary endpoint was reached in 10.6% of patients (11/104). Secondary endpoint was reached in 5.8% of patients (6/104). After 12 months follow up primary endpoint was reached in 23.1% of patients (24/104). Secondary endpoint was reached in 8.7% of patients (9/104). 7 Patients (6.7%) were lost for follow up.

Table 1: Initial hospitalisation (n=104), 12 months follow up (n=104)

<table>
<thead>
<tr>
<th></th>
<th>Initial hospitalisation (n=104)</th>
<th>12 months follow up (n=104)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cost for follow up</td>
<td>7 (6.7%)</td>
<td></td>
</tr>
<tr>
<td>Primary endpoint</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death of any cause</td>
<td>10 (9.6%)</td>
<td>19 (18.3%)</td>
</tr>
<tr>
<td>Death of cardiovascular cause</td>
<td>1 (0.9%)</td>
<td>2 (1.9%)</td>
</tr>
<tr>
<td>Zentral ischemia or bleeding</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Myocardial infarction</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1: The primary endpoint.
A systematic evaluation of population-based surveillance studies to quantify reported burden of stroke in low- and middle-income countries

A. Sajad. Erasmus Medical Center, Department of Epidemiology, Rotterdam, Netherlands

Purpose: Reliable quantification of the burden of stroke in low- and middle-income (LMIC) countries is unclear as nationally-representative primary surveillance reports are few and may vary widely in data collection methodology. World Health Organisation (WHO) has proposed the ‘STEPwise’ approach for comprehensive stroke surveillance. Whether and to what extent primary epidemiological evaluations of stroke in LMIC countries adhere to WHO’s surveillance guidelines remains unknown. Therefore, we aim to systematically evaluate all primary stroke surveillance studies by applying components of WHO STEPS protocol and quantitatively compare burden of stroke in LMIC settings.

Methods: Publications before January 2012 were identified through computer-based searches using multiple databases. Information was extracted on available population and coverage, methodology of the surveys, and quality, as assessed by applying components of WHO STEPS protocol and quantitatively comparing reported burden of stroke.

Results: We identified seven studies reporting on stroke burden in nine LMIC countries, which yielded aggregate information from 1,711,372 participants collected over 5,240,923 person-years. Comparison of each study’s methodology to the WHO STEPS protocol showed a lack of uniform approach towards stroke surveillance in LMIC countries and utilization of its modules and steps varied considerably. Combined age-adjusted incidence rate based on all nine LMIC countries was 165.8 per 100,000 person-years.

Conclusion: Systematic evaluation of available primary surveillance reports, particularly in the context of the WHO-STEPs guidelines, indicates a general lack of adherence to standardized surveillance approaches, and yet, a considerable burden of incident stroke across the LMIC countries. Incorporation of standardized comprehensive methodology is essential to enhance generalisability and yield comparable data on the stroke burden in these countries.

The risk factors and clinical significance of the first episode of stroke in patients after Acute Myocardial Infarction treated invasively

P. Podolec1, R. Lenarczyk1, J. Kowalczyk1, J. Boidol1, A. Sajad1, L. Polonski2, Z. Kalas1. 1Medical University of Silesia, 1st Dpt of Cardiology, Zabrze, Poland; 2Medical University of Silesia, Silesian Center for Heart Diseases, 3rd Department of Cardiology, Zabrze, Poland

Purpose: The aim of the study was to assess the incidence, independent predictors and clinical significance of the first episode of stroke in patients after acute myocardial infarction (AMI) treated invasively.

Methods: We analyzed 2520 consecutive patients with AMI-patients admitted to our hospital between January 1999 and December 2002. All were already on standard antiplatelet therapy. TEE was performed in 2408 patients (95.7%). We compared patients with and without stroke using chi-square (age 74 \pm 15 vs. 71 \pm 15, p < 0.001), and high-density lipoprotein (HDL) and apolipoprotein A-I (Apo-A-I) were significantly lower (44.1 \pm 15.5 vs. 55.1 \pm 15.5 mg/dl, p < 0.001; 103.2 \pm 27 vs. 131.0 \pm 25 mg/dl, p < 0.001, respectively). In 11/18 patients (61%) receiving rosuvastatin for 6 months, stroke was improved. 6/18 patients (33%) showed no change, and 1/18 (6%) showed worsening. In addition, CAP diameter, Vd, and Apo-A-I were significantly improved comparing the start vs. the end of 6 months (5.8 \pm 2.2 vs. 5.1 \pm 2.2 mm, p < 0.005; 1.4 \pm 0.3 vs. 1.7 \pm 0.5 cm/sec, p < 0.05; 16.7 \pm 6.4 vs. 12.1 \pm 4.7, p < 0.05; 42.8 \pm 52.9 vs. 39.1, p = 0.001; 100.2 \pm 22 vs. 135.0 \pm 15.0, p < 0.05, respectively).

Conclusion: Rosuvastatin improves CAP morphology and aortic stiffness evaluated by Apo-A-I and aortic arch WMV obtained from PW-TDI in acute cerebral embolism patients with normal LDL levels.

Roscuvastatin improves plaque morphology and aortic stiffness in acute cerebral embolism patients with normal low-density lipoprotein levels and severe aortic arch plaques

K. Kaneko1, T. Takahashi1, H. Saitou1, N. Kiribayashi1, K. Omi1, T. Sasaki1, N. Niiizuki1, S. Sugawara1, I. Kubota2. 1Nihonkai General Hospital, Sakata, Japan; 2Yamagata University School of Medicine, Yamagata, Japan

Purpose: Rosuvastatin reduces cardiovascular disease in patients with normal low-density lipoprotein (LDL) in randomized controlled trials. Aortic stiffness is a marker of cardiovascular disease and aortic arch plaque morphology is an important predictor of stroke.

Methods: We performed TEE in 56 consecutive acute cerebral embolism patients with LDL <140mg/dl who were not taking lipid lowering agents, and measured PW-TDI velocity using sample volume placed at the aortic arch lateral wall. PW-TDI velocity values during peak systolic expansion (Vs) and diastolic constriction (Vd) were obtained from the long axis view. CAP was defined as TEE presence at aortic arch atherosclerotic plaque 1.5cm above the aortic arch commissures. We classified patients into two groups: those with (n=24; 69 \pm 8 years) and without vs. 11.1 \pm 2 years, p < 0.05) and high-density lipoprotein (HDL) and apolipoprotein A-I were significantly lower (44.1 \pm 15.5 vs. 55.1 \pm 15.5 mg/dl, p < 0.001; 103.2 \pm 27 vs. 131.0 \pm 25 mg/dl, p < 0.001, respectively). In 11/18 patients (61%) receiving rosuvastatin for 6 months, stroke was improved. 6/18 patients (33%) showed no change, and 1/18 (6%) showed worsening. In addition, CAP diameter, Vd, and Apo-A-I were significantly improved comparing the start vs. the end of 6 months (5.8 \pm 2.2 vs. 5.1 \pm 2.2 mm, p < 0.005; 1.4 \pm 0.3 vs. 1.7 \pm 0.5 cm/sec, p < 0.05; 16.7 \pm 6.4 vs. 12.1 \pm 4.7, p < 0.05; 42.8 \pm 52.9 vs. 39.1, p = 0.001; 100.2 \pm 22 vs. 135.0 \pm 15.0, p < 0.05, respectively).

Conclusion: Rosuvastatin improves CAP morphology and aortic stiffness evaluated by Apo-A-I and aortic arch WMV obtained from PW-TDI in acute cerebral embolism patients with normal LDL levels.

Comparison of the tirofiban with the dextran-40 for suppression of cerebral microemboli after elective carotid endarterectomy

M. Saedon1, D.R.J. Singer1, R. Pang1, A. Mahmoood2, C. Tivas2, C. Marshall3, D. Higman1, C. Hutchinson1, C.H. Imray1, A. Warwick University, Medical School - The Clinical Sciences Research Institute (CSRI), Coventry, United Kingdom; 2University Hospitals of Coventry and Warwickshire NHS Trust, Coventry, United Kingdom

Background: Microembolic signals (MES) are biomarkers of high risk of stroke syndromes in carotid artery disease. We compared effects of 2 anti-thrombotic agents cerebral microembolism: tirofiban vs. dextran-40 infusions.

Methods: MES were transcranial Doppler ultrasound (TCD) to study MES in 128 subjects acutely after carotid endarterectomy between January 2002 and December 2010. All were already on standard antiplatelet agents. Anti-thrombotic treatment was given for MES >50/hr; tirofiban infusion (0.4mcg/kg/min for 30 minutes then 0.1mcg/kg/min for 24 hours) in 40 patients (age 74 \pm 15, men 27, Caucasian 38) and dextran-40 infusion (20-150 mls/hr 10% dextran-40) in 34 patients (age 68 \pm 2, males 22, Caucasian 30). 54 patients with MES >50/hr (age 71 \pm 5, male 36, Caucasian 52) were allowed to continue the previously (control) MES data are median (IQR); data compared by Kruskal-Wallis testing.

Results: Eight (20%) patients who received tirofiban were on dual anti-platelet agents pre-operatively compared with 2 (6%) dextran-40 group and 18 (33%) control group (P=0.199, x2 test). The initial MES rate was highest in the dextran-40 group (102/hr (IQR: 79–150)); tirofiban 88 (68–134); control 24 (16–36) p<0.001, respectively. Despite this, the time to 50% reduction in MES was shortest in dextran-40 group (22.5 minutes (IQR: 15–28); dextran-40 68 (51–84); control 30 (23–38); P<0.001). The time to resolution of MES was longest in the dextran-40 group (120 minutes (94–158); tirofiban 68 (53–94); control 53 (49–68); P<0.001). A Kaplan-Meier plot shows that tirofiban infusion led to complete resolution of MES significantly more rapidly than dextran-40 (Log Rank (Mantel-Cox) 3–8 p<0.001). Up to 30 days post-surgery, there was one fatal myocardial infarction (MI) in both the tirofiban and control groups and 2 fatal MIs in the dextran-40 group. One non-fatal transient ischaemic attack (TIA) occurred in the tirofiban group and 5 non-fatal TIA occurred in the dextran-40 group. In further follow-up from 3 to 12 months: there was 1 fatal intra-cerebral haemorrhage both in tirofiban and control groups.
Procollagen-1-carboxy terminal peptide, a biomarker of myocardial fibrosis, is reduced following treatment with spironolactone or amiloride in stroke: a randomised placebo-controlled trial

K.Y.-K. Wong, S.Y.S. Wong2, S. Mscwiggan3, S.A. Ogston3, R.S. Macwalter3, A.D. Struthers3. 1University of Hull, Hull York Medical School, Hull, United Kingdom; 2Royal Derby Hospital, Derby, United Kingdom; 3Ninewells Hospital, Dundee, United Kingdom

Introduction: Myocardial fibrosis is an arrhythmogenic and may contribute to the high incidence of cardiac death in stroke survivors. In patients with heart failure, high baseline serum levels of markers of cardiac fibrosis synthesis were associated with poor outcome and decreased during spironolactone therapy. The best treatment for myocardial fibrosis remains to be elucidated.

We tested the hypothesis that procollagen-1-carboxy terminal peptide (PICP), a biomarker of myocardial fibrosis, might be improved fibrosis, measured with spironolactone or amiloride. We also tested the hypothesis that both drugs would shorten the QTc interval.

Methods: Study design: Randomised, double-blinded, placebo-controlled, cross-over trial (between spironolactone 25mg od, increased to 50mg od after 1 week if tolerated; amiloride 5mg od, increased to 10mg od if tolerated, and placebo). Duration: up to 3 months (1 month per drug). The concentration of PICP was measured by radioimmunoassay (coefficient of variation: ~1.48%). QTc was measured using a digitising board from lead II.

Results: 11 stroke survivors (5 female) had mean age of 71.5 (SD 3.9), BP 138.8/111 mmHg (SD 20/11 mmHg). None had a past history of oesophagus, lung fibrosis, or surgery in the last 6 months (conditions which would render PICP a less reliable marker of myocardial fibrosis).

There was no significant visit number drug interaction, suggesting that there was no crossover effect of drugs on PICP. Both spironolactone and amiloride significantly reduced PICP [Spironolactone Placebo: 95% CI=40.4 to –9.8, Dunnett t (2-sided) p<0.006; Amiloride Placebo: 27.9, 95% CI=44.4 to –11.0, Dunnett t p=0.002]. This led to a significant shortening of QTc. [Spironolactone vs Placebo=18.2, 95% CI=35.8 to –0.55, Dunnett t p=0.043; Amiloride vs Placebo=24.7, 95% CI=41.9 to –7.5, Dunnett t p=0.006]. Spironolactone had a non-significant BP lowering effect. On the other hand, amiloride significantly lowered BP (mean ±8/8.9 mmHg, 95% CI –31/13 to –4.9–4.4, Dunnett t p=0.007 <0.001).

Conclusions: Procollagen-1-carboxy terminal peptide, a biomarker of myocardial fibrosis, was reduced following treatment with spironolactone. Further, this is the first study demonstrating amiloride could also improve myocardial fibrosis. The beneficial effects of both drugs on myocardial fibrosis translated to a shortening of the QTc interval. Future studies should test the hypothesis that spironolactone and amiloride would reduce the risk of sudden cardiac death in stroke survivors.

P1580 Increased risk of myocardial infarction and stroke in patients with inflammatory bowel disease - a nationwide cohort study

S.L. Kristensen1, P.R. Hansen1, O. Ahlefeldt2, J. Lindhardsen1, E. Horvath-Puho2, R. Erichsen2, C. Torp-Pedersen1, O.H. Nielsen3, K.Y.-K. Wong1, S.Y.S. Wong2, S.Mcswiggan3, S.A. Ogston3, G.H. Gislason1, H.T. Sorensen2. 1Gentofte Hospital - Copenhagen University Hospital, Copenhagen University; 2Institute of Clinical Epidemiology, Aarhus University, Aarhus, Denmark; 3Herlev Hospital - Copenhagen University Hospital, Department of Gastroenterology, Herlev, Denmark

Purpose: Inflammatory bowel disease (IBD) is associated with thrombosis, probably mediated through the chronic inflammatory state. Other inflammatory diseases such as rheumatoid arthritis and psoriasis have been linked with an increased risk of cardiovascular disease, and since the estimated prevalence of IBD is 2.2 million in Europe, any association between these disorders and MI or stroke might have major clinical and public health impact. Thus, we conducted a population-based nationwide cohort study to estimate the risk of AMI and stroke in Danish IBD patients.

Methods: We identified a cohort of all IBD patients through the Danish nationwide registries in the 1980-2010 period, and for each IBD patient we matched 5 controls from the general population according to age, gender, and residence. We followed patients from IBD diagnosis (or corresponding date for matched cohort member) until MI/stroke, emigration, death, or end of follow-up. Incidence rates (IR) of MI and stroke were calculated per 1000 person-years and the relative risk was estimated using Cox proportional-hazard regression models comparing IBD patients to comparison cohort members.

Results: A total of 52,898 IBD patients (55.2% women) and 257,421 population cohort members were included in the study (mean follow-up 9.97 years). Among the IBD patients 37,377 (71%) had UC (median age 43 years), 15,271 (29%) had CD (median age 36 years), and 250 had indeterminate colitis (i.e. either UC or CD). We identified 1451 MIs (IR=2.76) and 1600 strokes (IR=3.41) in the IBD cohort versus 6187 MIs (IR=2.32) and 8158 strokes (IR=3.06) in the background cohort. In UC patients, we found an overall increased risk of MI (hazard ratio [HR] 1.27, 95% confidence interval [CI] 1.13–1.43) and stroke (HR using Cox regression was 1.07-2.1) within the first year of UC diagnosis. The HR was 2.14 (95% CI 1.76-2.59) for MI and 1.47 (95% CI 1.21-1.77) for stroke. Similarly for CD patients, we found increased risks of MI (HR 1.25, 95%CI 1.10-1.43) and stroke (HR 1.39, 95% CI 1.24-1.55). Within the first year after CD diagnosis, the HR for MI was 1.54 (95% CI 1.06-2.24) and 2.50 (95% CI 1.82-3.43) for stroke. Conclusion: IBD was associated with a substantially increased risk of MI and stroke, especially in the first year after IBD diagnosis.

PERIPHERAL CIRCULATION AND INTERVENTION

P1581 Thermal heterogeneity of human atherosclerotic carotid arteries detected in vivo: a new non-invasive method for detection of local inflammatory activation

M. Drakopoulou1, K. Toutouzas1, A. Syntos1, K. Stathogiannsis1, H. Nassoss1, C. Klonaris1, G. Agnomanis1, E. Pantzios2, E. Siores2, C. Stefanadis1. 1Hippokration General Hospital, Athens, Greece; 2University of Athens Medical School, Athens, Greece; 3University of Bolton, Bolton, United Kingdom

Purpose: Studies of human carotid artery samples showed increased heat production. Microwave radiometry (MR), a new non-invasive method, allows in vivo measurement of internal temperature of tissues. We investigated in human carotid arteries whether thermal heterogeneity 1) can be measured in vivo non-invasively by MR, and 2) is associated with ultrasound and histological findings.

Methods: Patients scheduled for carotid endarterectomy underwent screening of carotid atherosclerosis by ultrasound and MR. Healthy subjects were enrolled as control group. The study included 56 carotid ultrasound sections (36 plaque images, 20 plaque edges). In total, 127 thermal images were analyzed. Thermal heterogeneity (AT) was assigned as maximal temperature along the carotid artery minus minimum. Extension of eccentricity to the lateral carotid wall and lipid core extension was evaluated on the entire cross-sectional area (CSA) and on the outer arterial sections dividing the field into four equal parts and scored in numerical values ranging from 0-4. Association of thermographic with ultrasound and histological findings was performed.

Results: Thirty-four consecutive patients with significant carotid artery stenosis and 15 healthy subjects as a control group were included. AT was higher in atherosclerotic carotid arteries (1.39±0.49 vs 0.23±0.01°C). Fatty plaques had higher AT compared to mixed and calcified (1.78±0.41 vs 1.38±0.30 vs 0.96±0.22°C, p<0.01). Plaques with ulcerated surface had higher AT compared to plaques with irregular and regular (2.08±0.14 vs 1.37±0.23°C vs 0.95±0.19°C, p<0.01). Heterogeneous plaques had higher AT compared to homogenous (1.78±0.41 vs 1.08±0.31°C, p<0.01). Specimens with increased extension of calcification had lower AT compared to specimens with low (p<0.01). Specimens with thin fibrous cap had higher AT (1.69±0.42 vs 0.98±1.20°C, p<0.01). Specimens with increased inflammation had higher AT compared to specimens with low (1.74±0.40 vs 1.01±0.21°C, p<0.01).

Conclusions: Microwave radiometry provides in vivo non-invasive temperature measurements of carotid plaques, reflecting carotid plaque inflammatory activation.

P1582 Exaggerated exercise blood pressure response is related to increased arterial stiffness, asymmetric dimethylarginine and osteoprotegerin in essential hypertensive subjects

I. Bafalis, C. Tsioulos, K. Dimitriadis, I. Tatsis, I. Andrikou, V. Antonakis, E. Andrikou, K. Kinits, A. Kordalis, C. Stefanadis. First Cardiology Clinic, University of Athens Hippokration Hospital, Athens, Greece

Purpose: A hypertensive response to exercise (HRE) is associated with high cardiovascular risk, while elevated levels of asymmetric dimethylarginine (ADMA) and osteoprotegerin (OPG) are related to atherosclerosis progression. In this study we sought to determine the relationships of HRE with ADMA, OPG and arterial stiffness in essential hypertensives.

Method: Our population of 240 newly diagnosed never treated diabetics with stage I to II essential hypertension (155 men, mean age 51 years, office systolic blood pressure (BP) 150±96 mmHg with a negative treadmill exercise test (Bruce protocol) was divided into those with HRE (n=70) (peak exercise systolic BP ≥210mmHg in men and ≥190 mmHg in women) and those without HRE (n=170). Arterial stiffness was evaluated on the basis of carotid to femoral pulse wave velocity (PWV) values.

Results: Patients with HRE compared to those without HRE had greater 24-h systolic BP (143±9 vs 131±8 mmHg, p<0.05), while did not differ regarding metabolic profile and left ventricular mass index (p>NS). Patients with HRE as
compared to those without HRE exhibited greater levels of ADMA (0.63±0.04 vs 0.52±0.05 μmol/l, p<0.0001), OPG (5.41±0.1 vs 4.15±0.5 pmol/l, p<0.0001) and PWV (8.8±1.7 vs 7.5±0.9 m/sec, p<0.0001), independently of confounders. In the total population, peak exercise systolic BP was related to 24-h systolic BP (r=0.249, p<0.05), PWV (r=0.278, p<0.003), ADMA (r=0.260, p<0.007) and OPG (r=0.214, p<0.05). Regarding OPG, it was associated with 24-h systolic BP (r=0.267, p<0.001), ADMA (r=0.284, p<0.001) and PWV (r=0.424, p<0.0001). Multiple regression analysis showed that 24-h systolic BP (b=0.216, p=0.003), male sex (b=0.270, p<0.05), ADMA (b=0.225, p=0.006) and OPG (b=0.188, p<0.05) were independent predictors of exercise-systolic BP.

Conclusions: In essential hypertension, a HRE is accompanied by a state of increased arterial stiffening, endothelial dysregulation and progressive atherosclerosis. The interrelationships of ADMA and OPG with exercise BP response support that diffuse vascular dysfunction contribute to HRE-related risk in hypertension.

**P1583**

**Cholesterol efflux capacity and arterial stiffness in healthy subjects: data from the Brisighella heart study**

A. Cicero, E. Favalli, N. Ronda, P. Salvi, M.P. Adorni, A. Zametti, F. Bennini, C. Borghi, Sant’Orsola-Malpighi Polyclinic, Department of Internal Medicine, Bologna, Italy; Pharmacological and Biological Sciences and Applied Chemistry Dept, Parma, Italy

**Purpose:** Serum capacity to promote cholesterol efflux from macrophages correlates inversely with carotid intima-media thickness and the likelihood of an angiographic coronary artery disease, independently of the high density lipoprotein (HDL) level. We investigated the relationship between serum cholesterol efflux capacity and Pulse Wave Velocity (PWV), as an indicator of arterial stiffness, in healthy subjects.

**Methods:** 99 subjects (40 males, 59 females) were selected from the Brisighella Heart Study cohort for being non-smokers, non-diabetics, untreated with antihypertensive, lipid-lowering or antidiabetic drugs, and without echographically detectable carotid atherosclerotic plaques. Serum cholesterol efflux capacity was measured as aqueous diffusion, total cholesterol efflux and ATP binding cassette A1 (ABC1)-dependent cholesterol efflux (reflecting mainly HDL function). Bilateral B-mode carotid artery images for intima-media thickness were acquired using a linear phased multifrequency (7.5-10 MHz). The posterior wall of the distal common carotid artery, one centimeter below the bifurcation, was assessed as recommended by the international guidelines. An elctrocardiografic trace was used to acquire image frames only in end-diastole, avoiding IMT variation related to carotid pulsatility. Carotid-femoral PWV was measured with a high-fidelity tonometer.

**Results:** In the unadjusted model, PWV relates directly with basal aqueous cholesterol diffusion (R=0.215, P=0.042), PWV does not correlate with total cholesterol efflux (R=0.215, P=0.042). In a stepwise multivariate analysis including age, sex, body mass index, mean arterial pressure, serum low density lipoprotein level, serum HDL level, ABC1-dependent cholesterol efflux (reflecting mainly HDL function), the best PWV predictors were mean arterial pressure (R=0.83, 95CI 0.531-1.06) and ABC1-dependent cholesterol efflux (R=0.05, 95CI 0.027-0.073). ABC1-dependent cholesterol efflux capacity, but not total serum HDL, is a significant predictor of PWV in healthy subjects. This finding points to the relevance of HDL function in vascular modeling and arterial stiffness prevention along life.

**Conclusions:** ABC1-dependent cholesterol efflux capacity and pulse wave velocity (PWV) are independent predictors of PWV levels in healthy subjects. The main factors affecting PWV are mean arterial pressure, carotid-femoral pulse wave velocity (PWV), smoking status and ABC1-dependent cholesterol efflux capacity.

**P1584**

**Relationship between serum uric acid and arterial stiffness in a sample of adult-elderly subjects: data from the Brasighella heart study**

A. Cicero, P. Salvi, E. Grandi, S. D’Addato, C. Borghi, Sant’Orsola-Malpighi Polyclinic, Department of Internal Medicine, Bologna, Italy

**Purpose:** The role of uric acid on atherosclerosis phenomena is a vexed question along life. The role of uric acid on atherosclerosis phenomena is a vexed question. The antioxidant properties of uric acid are well known, on the other hand several studies shown an association between higher level of uric acid and hypertension, diabetes, metabolic syndrome and cardiovascular diseases. The aim of this study was to verify the relationship between uric acid levels and arterial stiffness and subclinical atherosclerosis.

**Methods:** The Brisighella Heart Study is a prospective, population-based longitudinal epidemiological investigation involving 2939 randomly selected subjects (1491 men and 1448 women), aged 14 to 84 years, free of cardiovascular disease at enrollment, resident in the northern Italian rural town of Brisighella. From this historical cohort, we randomized a sub-sample of 619 subjects (248 males, 371 females aged 53.5±10.5 years) who were attended at 55 hypertension outpatient clinics in Hungary were randomized to a sub-sample of 619 subjects (248 males, 371 females aged 53.5±10.5 years) who were attended at 55 hypertension outpatient clinics in Hungary. The prevalence of PAD was 14.4%. Mean systolic blood pressure in patients with PAD was 14±12.2 and 9.3±8.3 mmHg (136±9 vs. 122±11 and 85±7.7 vs 78±6.5 mmHg, p<0.0001). Mean 24-h diastolic BP dropped by 9±7.5 mmHg between 7.5 vs. 12.2±5.8 and 9.3±8.3 mmHg, while PWV increased by 0.3±1.9 mm/s (8.8±1.6 vs 9.1±1.6 mm/s), p<0.05). Cox regression analysis using hemodynamic, demographic, metabolic and medical treatment variables, revealed that significant predictors of PWV levels above the median value of 9 m/s at the last follow-up visit were age (OR=1.031, 95% CI=1.001-1.061, p=0.05), baseline PWV levels (OR=1.478, 95% CI=1.002-1.058, p=0.05) and the difference of 24-h HR between baseline and last follow-up visit (OR=0.953, 95% CI=0.992-0.985, p=0.05).

**Conclusions:** PWV seems to convey an increased risk for future arterial stiffening in hypertensive subjects. The reduction of 24-h HR exerts a prophylactic effect on the progression of arterial stiffness.

**P1586**

**Awareness of peripheral arterial disease helps to reach blood pressure and cholesterol target values: results of the hungarian ankle/brachial index screening program (ERV)**

K. Farkas1, Z. Jarai1, E. Kolosvary1, A. Ludanyi1, I. Kiss1, T. Mezö2, M. Hanak2, D. Csernics1, G. Lázár3, M. Pál4, G. Juhász5, M. Varga2, J. Szabó2, 1St. Imre Teaching Hospital, Budapest, Hungary; 2EGIS Pharmaceuticals PLC, Budapest, Hungary

Epidemiological data have shown that patients with clinical and preclinical stages of peripheral arterial disease (PAD) have high risk of cardiovascular mortality. By the measurement of the ankle/brachial index (ABI), PAD can be diagnosed in early asymptomatic stage. The objective of the present study was to evaluate the changes in blood pressure and serum cholesterol values during the first 3 years of the ERV program. A total of 21 892 hypertensive men and women (9162 males; mean age: 61±4.5 years) who were attended at 55 hypertension outpatient clinics in Hungary were included in our prospective study. Clinical history, physical examination, blood analysis, and measurement of the ankle-brachial index (calculated with the higher value at the ankle) were taken in all patients. Patients with established PAD (ABI ≤0.9) were controlled annually. The prevalence of PAD was 14.4%. Mean systolic blood pressure in patients with an ABI≤0.9 at visit 1 (baseline); visit 2; and 3 were 143±10; 139±10; 140±10 and 140±11 mmHg, respectively (p<0.001 compared to baseline). Mean diastolic blood pressure at visit 1 (baseline); visit 2; and 3 were 83.1; 81.26; 81.20 and 83.1 mmHg, respectively (p<0.001 compared to baseline). Mean serum cholesterol at visit 1 (baseline); visit 2; and 3 were 5.34; 5.12; 4.99 and 4.94 mmol/l, respectively (p<0.001 compared to baseline). The use of ABI screening helps to identify patients at high cardiovascular risk and their treatment can be tailored accordingly to the guidelines for high-risk patients. Blood pressure and serum cholesterol values decreased significantly during the first 3 years of the ERV program. Cardiovascular morbidity and mortality data will be evaluated after the 5 years long prospective phase of the program.
Efficacy of statin treatment after endovascular therapy for isolated below-the-knee disease in patients with critical limb ischemia

Y. Tomo1, Y. Soga1, O. Izda2, Y. Yamada1, K. Hirano3, K. Suzuki4, K. Miyashita5, J. Tazaki6, K. Koura Memorial Hospital, Kitakyushu, Japan; 2Osaka Rosai Hospital, Osaka, Japan; 3Kikura Memorial Hospital, Yokohama, Japan; 4Sendai Kousei Hospital, Sendai, Japan; 5Shinshu University Hospital, Matsumoto, Japan; 6Hyogetsu College of Medicine, Nishinomiyama, Japan; 7Japanese Red Cross Fukui Hospital, Fukui, Japan; 8Kyoto University Hospital, Kyoto, Japan.

Background: Little is known about efficacy of statin treatment after endovascular therapy (EVT) for isolated below-the-knee (BTK) disease in patients with critical limb ischemia (CLI). Therefore, we investigated the effect of statin treatment on outcomes in patient with CLI.

Methods: From March 2004 to June 2011, 814 patients (984 limbs, 68.8% male, 168 treated with statin, 71.6±10.0 years old) with CLI underwent EVT for de novo isolated BTK lesion. Their data were retrospectively analyzed. Outcome measures were amputation-free survival (AFS), overall survival, cardiovascular death, limb salvage, freedom from repeat revascularization. Mean follow-up duration was 19.3±17.4 months.

Results: Overall survival and freedom from repeat revascularization at 5 years were significantly higher (45.0% vs 41.5%, P=0.02; 59.5% vs 40.2%, P=0.03; respectively), AFS at 5 years tended to improve in statin-treated group (41.1% vs 38.1%, P=0.094). However, cardiovascular death and limb survival rate 5 years did not differ significantly between two groups (65% vs 72%, P=0.37; 86.3% vs 78.6%, P=0.48; respectively).

On univariate analysis, ambulatory group (513 patients, 618 limbs) with baseline variables, statin was effective for prevention of AFS (hazard ratio [HR], 0.61; 95% confidential interval [CI], 0.006-0.51; adjusted P=0.045), and improved overall survival (HR, 0.53; 95% CI, 0.04-0.61; adjusted P=0.023) and prolonged freedom from repeat revascularization (HR, 0.70; 95% CI, 0.007-0.37; adjusted P=0.049). Over 2 years life prognosis group (810 patients, 737 limbs), limb salvage rate was improvement (HR, 0.28; 95% CI, 0.27-1.06; adjusted P=0.01), freedom from repeat revascularization was tend to prolong (HR, 0.75; 95% CI, 0.01-0.31; adjusted P=0.075).

Conclusion: For amputary and over 2 years life prognosis patient, statin treatment may improve AFS and overall survival, prolong freedom from repeat revascularization after EVT for isolated BTK disease in patients with CLI.

Impact of chronic total occlusion in ilio-femoral artery on clinical outcomes following percutaneous transluminal angioplasty


Background: Endovascular treatment (EVT) is considered as an effective treatment in patients (pts) with critical limb ischemia (CLI). With the recent improvement of device and EVT technique, the success rate of chronic total occlusion (CTO) in distal aorta and ilio-femoral artery is increasing; however, the mid to long-term durability between distal aorta and ilio-femoral artery CTO following successful recanalization is not clarified yet.

Methods: A total 187 consecutive CLI patients (pts) were treated by EVT from September 2004 to September 2010. Out of 187 pts, 57 pts (79 limbs, 95 lesions) underwent successful CTO intervention in either distal aorta or ilio-femoral artery. CTO recanalization was done either by true lumen angioplasty (shorter lesion) or subintimal angioplasty (longer lesion) with/without reentry device. Provisional stenting was done once the balloon angioplasty outcome is not optimal, mainly by self-expanding nitinol stents. The primary patency was determined by Kaplan-Meier method.

Results: Baseline clinical and procedural characteristics were similar between the two groups. Mid-term primary patency was approximately 90% and angiographic outcomes were similar between the two groups. Major clinical outcomes including mortality, repeat revascularization and the incidence of surgical intervention were similar between two groups (Table).

Conclusion: Once the CTO lesions were successfully treated, major mid-term angiographic and clinical outcomes were similar to those of ilio-femoral CTO lesions. Long-term follow up with larger study population will be needed to get the final conclusion.

Comparison of mid-term clinical outcomes between distal aorta and ilio-femoral artery chronic total occlusion following successful endovascular therapy


Background: Endovascular treatment (EVT) is considered as an effective treatment in patients (pts) with critical limb ischemia (CLI). With the recent improvement of device and EVT technique, the success rate of chronic total occlusion (CTO) in distal aorta and ilio-femoral artery is increasing; however, the mid to long-term durability between distal aorta and ilio-femoral artery CTO following successful recanalization is not clarified yet.

Methods: A total 187 consecutive CLI patients (pts) were treated by EVT from September 2004 to September 2010. Out of 187 pts, 57 pts (79 limbs, 95 lesions) underwent successful CTO intervention in either distal aorta or ilio-femoral artery. CTO recanalization was done either by true lumen angioplasty (shorter lesion) or subintimal angioplasty (longer lesion) with/without reentry device. Provisional stenting was done once the balloon angioplasty outcome is not optimal, mainly by self-expanding nitinol stents. The primary patency was determined by Kaplan-Meier method.

Results: Baseline clinical and procedural characteristics were similar between the two groups. Mid-term primary patency was approximately 90% and angiographic outcomes were similar between the two groups. Major clinical outcomes including mortality, repeat revascularization and the incidence of surgical intervention were similar between the two groups (Table).

Conclusion: Once the CTO lesions in distal aorta was successfully treated, major mid-term angiographic and clinical outcomes were similar to those of ilio-femoral CTO lesions. Long-term follow up with larger study population will be needed to get the final conclusion.
difference between self expandable stent and balloon expandable stent. (Log-rank test; p=0.3)

Conclusions: In conclusion, endovascular therapy for terminal-aortoiliac bifurcation lesion was safe and acceptable. Furthermore, there was no difference in outcomes depending on the type of stent.

Methods: We performed a prospective study of 305 consecutive patients with CKD who underwent elective catheterization [serum creatinine (Cr) ≥1.1mg/dl]. Serum Cr level was assessed at the time of hospital admission and on days 1 and 2 after contrast medium exposure. The urinary markers, L-FABP (β2-microglobulin (β2-MG) and N-acetyl-D-glucosaminidase (NAG), were measured in urine samples collected early in the morning on the day of the procedure and on days 1 and 2 after contrast medium exposure. Urinary L-FABP was measured with an enzyme-linked immunosorbent assay (ELISA) kit (CMIC Co., Ltd., Tokyo, Japan). Patients were prospectively followed during a median follow-up period of 708 days with the end points of Cardiac death. CI-AKI was defined as an increase of 0.3 mg/dl (26.5 micromol/l) within 2 days of contrast media exposure.

Results: CI-AKI developed in 26 patients (8.5%). High L-FABP levels group (defined as ≥24.5 μg/g Cr) was 59 patients and CI-AKI in high L-FABP levels group developed in 13 patients (22%). A total of 18 cardiac death events occurred during a follow-up period and survival outcome tended to be worse high L-FABP levels group. (12% vs 4% P=0.028) Kaplan-Meier analysis clearly demonstrated that patients with high L-FABP levels group were higher rate of cardiac cardiac death than those with low L-FABP levels group. (Log rank test; p=0.0224)

Conclusions: Urinary L-FABP provides an important information for predicting CI-AKI and survival outcome before contrast agent administration in patients with CKD. Therefore, an increase in urinary L-FABP levels may signal a need for more intensive treatment in these patients.

P1591 Can we predict a long-term results of renal artery stenting?

A. Roslawieka1, T. Przewlocki1, A. Kabka-Ziembicka 1, D. Rzeznik1, A. Kozanecki1, M. Kosthiwicz1, A. Zwiolska1,2,3,4,5, P. Podolec1,2,3,4,5,1,1,1, Jagiellonian University Medical College, I Department of Cardiac and Vascular Diseases, Krakow, Poland; 2Department of Hemodynamics and Interventional Cardiology, Krakow, Poland

The ongoing dilemma of renal artery angioplasty (PT A) is which patients might benefit from vascular interventions in relation to systolic (SBP) and diastolic (DBP) blood pressure reduction and renal function (RF) preservation. The study aimed to determine predictors of BP and RF improvement following PT A and factors associated with cardiovascular (CV) risk.

Methods: Study group comprised 144 (77M, 63.5±11) hypertensive patients, referred to PT A with mean RAS 71.8±13.1%, including 93 unilateral and 36 bilateral RAS, and 15 patients with single functioning kidney. Hypertension crisis was reported in 60 (45%), diabetes in 49 (34%), significant CAD in 94 (65%), internal carotid artery stenosis (ICAS) ≥70% in 46 (32%) and peripheral occlusive disease in 39 (27%). Creatinine level (Cr), eGFR, mean SBP and DBP (24-hour ABPM) were analyzed before, 24 hours after the procedure, then at 12 months intervals after PT A. The incidences of CV death, myocardial infarction (MI), ischemic stroke (IS), or starting dialysis were recorded.

Results: 167 out of 168 procedures were technically successful in 143/144 (99.3%) subjects. The mean follow-up period after PT A was 48.4±27.6 months. CV events occurred in 34.26% patients (16 CV deaths, 10 non-fatal MIs, 5 non-fatal ISIS, 3 dialysis). Hypertension was cured in 7 patients, while mean number of BP regiments was decreased from 3.2±1.1 to 2.9±1.2 (p≤0.05). Mean SBP decreased from 139±20 mmHg to 129±14 mmHg (p<0.001) at 12 months, and to 131±16 mmHg (p=0.004) at the final follow-up visit, while DBP decreased from 75±12 to 62±9 mmHg (p=0.008), respectively. Cr decreased from mean 133±59 to 117±62 and to 123±57 μmol/l (p<0.001; p<0.01), when eGFR increased from 53±3.22 to 62±26, and then to 58±2.5 (p=0.001 and p<0.05), respectively. BP improvement, defined as long-term SBP reduction of ≥10 and DBP ≥5 mmHg was found in 59 (41%), while RF improvement, defined as Cr level decrease of >10% of initial value in 64 (44%) subjects. The follow-up independent predictors of BP and RF improvement were identified: for BP: higher RAS grade (RR=1.25; p=0.003), initial DBP (RR=1.36; p<0.001), and DBP decrease from 139±20 to 123±14 mmHg (p=0.70); for RF: SBP (RR=1.21; p=0.016), RF improvement (RR=1.21; p=0.016), and for RF: BP reduction (RR=1.34; p=0.001). Independent factors associated with CV risk were ICAS (RR=1.43±0.001), pulmonary edema (RR=1.19; p=0.01), initial Cr and SBP (RR=1.4; p=0.001 and RR=1.18; p=0.05). Conclusion: Endovascular therapy for terminal-aortoiliac bifurcation lesion was safe and acceptable. Furthermore, there was no difference in outcomes depending on the type of stent.

Conclusions: Urinary L-FABP provides an important information for predicting CI-AKI and survival outcome before contrast agent administration in patients with CKD. Therefore, an increase in urinary L-FABP levels may signal a need for more intensive treatment in these patients.

P1593 Patients radiation doses analysis in a contemporary cohort of patients undergoing interventional radiology procedures

J.M. Nogales1, J.M. Ordiáles2, A. Martínez-Naharro1, M. Yuste-Dominguez1, S. Sanchez-Giral1, J.R. Lopez-Mingue1, R. Gonzalez-Fernandez1, G. Martinez-Cazorla2, A. Merchán-Herrera1, F. Diaz-Cortegana1, Infanta Cristina University Hospital, Badajoz, Spain; 2Hospital de Merida, Merida, Spain

The field of interventional cardiology has drastically developed over last years, currently evolving into more complex procedures with increasing image quality requirement. These procedures result in substantial patient radiation doses. To evaluate this fact, we analysed radiation doses exposure in 2123 patients undergoing interventional cardiology procedures: diagnostic coronary angiography (DCA) in 1163 (54.8%); percutaneous coronary intervention (PCI) in 929 (43.7%) and structural heart intervention (SHI) in 151 (5.9%); These procedures were consecutively performed by five skilled interventional cardiologist using three x-ray equipments (Allura Xper FD10, Philips®). All x-ray systems were calibrated using the same skin dose procedure. Skin dose (SD) was calculated using air kerma calibrated at interventional reference point and applying a factor that takes into account the x-ray backscatter from the patient. In 43.6% of the patients, the SD exceeded the 3 Gy dose threshold for deterministic effects (DCA: 2.8%; PCI: 6.2%; SHI: 6.5%). Body mass index (BMI) was related to SD in DCA. BMI, fluoro time, contrast volume and number of stents were related to SD in PCI.

Radiation dose measurements (mGy)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Mean</th>
<th>Median</th>
<th>25th Percentile</th>
<th>75th Percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCA</td>
<td>1589.19</td>
<td>449.19</td>
<td>305.12</td>
<td>646.99</td>
</tr>
<tr>
<td>PCI</td>
<td>4086.29</td>
<td>929.47</td>
<td>646.51</td>
<td>1440.72</td>
</tr>
<tr>
<td>– Chronic total occlusion</td>
<td>2237.78</td>
<td>1702.38</td>
<td>851.86</td>
<td>4115.16</td>
</tr>
<tr>
<td>– Bilirubin level</td>
<td>11576.47</td>
<td>1270.08</td>
<td>909.27</td>
<td>2031.82</td>
</tr>
<tr>
<td>SHI</td>
<td>2350.52</td>
<td>893.16</td>
<td>534.80</td>
<td>1675.14</td>
</tr>
<tr>
<td>– TnI</td>
<td>1846.84</td>
<td>1679.14</td>
<td>1152.47</td>
<td>2582.51</td>
</tr>
<tr>
<td>– MCV</td>
<td>558.36</td>
<td>278.64</td>
<td>814.59</td>
<td></td>
</tr>
<tr>
<td>– MCV</td>
<td>376.67</td>
<td>442.45</td>
<td>648.44</td>
<td></td>
</tr>
<tr>
<td>– LAAC</td>
<td>1639.52</td>
<td>1029.24</td>
<td>686.30</td>
<td>1772.90</td>
</tr>
<tr>
<td>– CAF</td>
<td>3344.52</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

WVII: Transfemoral aortic valve implantation; MCV: Mitral valve replacement; ASD: Atrial septal defect; LAAC: Left atrial appendage closure; CAF: Coronary artery fistula.

High radiation doses in some complex percutaneous cardiac interventions must encourage interventional cardiologist to develop radiation dose reduction protocols, radiation protection training programs and to perform a adequate follow-up of the patients undergoing this procedures.

P1594 Cadre: the first multicentric African study of cardiovascular events in sickle cell disease

B. Ranque1, A. Menel1, S. Kingue1, B. Diop3, M. Diarra4, D. Diallo5, L. Sica6, K.E. Kromoh1, I. Sanogo1, X. Jouven1 on behalf of Cardiovascular & Development. AP-HP - European Hospital Georges Pompidou, René Descartes University Paris, France; 2-hôpital général de Yaoundé, cardiology unit, Yaoundé, Cameroon; 3-centre hospitalo-universitaire de Fann, cardiology unit, Dakar, Senegal; 4-centre de cardologie de l'hôpital de l'arme médicale genéico-obstétrique, Bamako, Mali; 5-Centre de Recherche et de Lutte contre la Drépanocytose, Bamako, Mali; 6CIRMF , Libreville, Gabon; 7Institute of Cardiovascular and Genomic Disorders worldwide, which is characterized by the presence of abnormal
haemoglobin S due to a mutation in the β globin gene. SCD is not only responsible for acute vaso-occlusive events but also for chronic vasculopathy, involving medium and small arteries in many organs (lungs, kidney, brain, bones, skin, retina, and for cardiomyopathy). Chronic cardiovascular events have been almost exclusively studied in the USA or in Europe, although two third of SCD patients live in sub-Saharan Africa, a very different environment. We have settled the largest SCD cohort to estimate the prevalence of cardiovascular complications, to look for associations between them and with arterial stiffness and haematological parameters.

Patients and methods: CADRE study is a multinational cohort of SCD patients that is ongoing in five African countries: Cameroon, Senegal, Mali, Gabon and Côte d’Ivoire, with a recruitment goal of 5000 SCD patients and 1000 controls. Included subjects undergo clinical exam, blood sampling for haematological and renal function, pulse wave velocity (PWV) measure and echocardiography.

Results: By the end of 2011, 2600 SCD patients and 500 controls were already recruited. Intermediary analysis was performed in Cameroon, including 482 patients and 257 controls, all aged more than 15 years. After adjustment on sex, age and BMI, we evidenced lower blood pressures (median) in SCD patients as compared to controls. Conversely, proteinuria/creatininuria ratio (0.6 [0.2-1.0] versus 0.9 [0.5-0.7]) and lower PWV (9.5 [7.8-9.7] vs. 9.5 [6.4-10.7] m/s per second) in SCD patients as compared to controls. Furthermore, levels of cystatin C showed a significant difference between SCD patients and controls (p=0.001) but not in controls, suggesting the role of chronic haemolysis rather than anaemia only.

Conclusion: CADRE cohort is to become the largest cohort of SCD in the world and will make an accurate description of chronic cardiovascular events in African SCD patients, as well as better understanding of SCD vasculopathy mechanisms.

P1595 High serum levels of cystatin C predicts the metabolic syndrome

M. Magnusson1, B. Hedblad2, G. Engstrom3, P. Nilsson3, M. Persson4, M. Olerud3, L. University Skane University Hospital, Department of Clinical Sciences, Lund University, Sweden. 2Department of Clinical Sciences, Lund University, Skåne University Hospital, Malmö, Malmö, Sweden

Purpose: Cystatin C is a novel marker for cardiovascular disease (CVD), however, the mechanisms of action of chronic vascular events in SCD patients and, as well as better understanding of SCD vasculopathy mechanisms.

Methods and Results: Cystatin C was measured in 1504 individuals free from heart failure (HF) of the Malmö Diet and Cancer cohort (mean age 56 years; 59% women) who subsequently underwent a follow-up exam after a median follow up time of 16 years. HF was defined according to the NCEP-ATP III guidelines. Logistic regression was used to adjust for covariates. During follow-up, 428 subjects developed new onset HF. In age and sex adjusted analysis, compared to the lowest quartile of the cystatin C, the odds ratio (95% confidence interval) for incident HF in subjects belonging to quartiles 2, 3 and 4 were 1.00 (0.71-1.40) (P=1.47 [1.05-2.05] and 1.91 [1.7-2.67] (P=0.001), a linear association that remained significant even after multivariate adjustment (baseline values of age, sex, waist, anti-hypertensive treatment, systolic blood pressure, triglycerides, high density lipoprotein, blood glucose and anti diabetic treatment) (P=0.045). In fully adjusted multivariate models, long term progression of increasing abdominal obesity was the only component of MetS significantly associated with increasing quartile of baseline cystatin C levels (P trend=0.010).

Conclusion: Our findings suggest that cystatin C may adversely affect metabolic factors thus contributing to development of MetS. Our results may help explain the cause of the well established link between cystatin C and CVD development.

P1596 Serum levels of alpha1-antitrypsin-low-density-lipoprotein are associated with smoking and severe arteriosclerosis obliterans

N. Masunaga1, H. Wada1, M. Akao1, S. Ura1, M. Abe1, M. Ishi1, T. Unoki1, Y. Takashashi1, R. Shimazu1, K. Hasegawa1, National Hospital Organization Kyoto Medical Center, Kyoto, Japan. 2Nara Women’s University Hospital, Nara, Japan

Background: While smoking cessation (SC) leads to a reduction of cardiovascular events, atherogenic biomarkers which are specifically associated with cigarette smoking and SC are unknown. Oxidized low-density-lipoprotein cholesterol (oxLDL) is involved in the progression of arteriosclerosis. Recently, two novel oxLDL markers, serum amyloid A-LDL (SAA-LDL) and α1-antitrypsin-LDL (AT-LDL), were identified. However, the relationships of these two markers with smoking and atherosclerotic diseases are unknown.

Methods and Results: Based on a cross-sectional study involving 243 patients, both serum levels of SAA-LDL and AT-LDL were significantly increased in current compared to non-current smokers. Stepwise regression analysis revealed that the current smoking status and duration of smoking were strong independent determinants of the AT-LDL level. In contrast, high-sensitivity C-reactive protein (hsCRP) was the strongest determinant of the SAA-LDL level. Successful SC employing a 12-week program significantly decreased levels of AT-LDL, but not those of SAA-LDL, or hsCRP. Then, we examined serum levels of SAA-LDL and AT-LDL in 34 patients with arteriosclerosis obliterans (ASO) and 40 patients without ASO or coronary artery disease (Control). The rate of a male gender as well as BMI, blood pressure, and metabolic and lipid profiles except for low-density-lipoprotein cholesterol (LDL-C) were similar between ASO and Control. LDL-C was significantly lower in ASO patients than in Control. In contrast, hSCR and AT-LDL did not show significant increased proportion to the severity of ASO (n=ASO; n=40; mild ASO: Fontaine classes 1+2, n=27; severe ASO: Fontaine classes 3+4, n=7). Stepwise regression analysis revealed that strong independent determinants of AT-LDL were age and hsCRP. Multiple logistic regression analysis including data on age, a male gender, obesity, hypertension, diabetes, dyslipidemia, a smoking habit, and AT-LDL, revealed that age and AT-LDL were independently associated with severe ASO.

Conclusions: The AT-LDL level was significantly associated with smoking and severe ASO. Thus, AT-LDL should provide a key of linkage between smoking and ASO.

P1597 Comparison of short and long term clinical outcomes according to status of the false lumen in patients with acute type B aortic dissection

A. Tanaka1, M. Sakakibara1, R. Hayashi1, Y. Jinno1, S. Okumura1, K. Okada1, T. Murashita1, Handa City Hospital, Handa, Japan, 2Nagoya University Graduate School of Medicine, Department of Cardiology, Nagoya, Japan

Purpose: Recent reports have shown partial thrombosis of the false lumen was a significant independent predictor of mortality in patients with acute type B aortic dissection. The purpose of this study was to undertake additional investigation.

Methods: Ninety-four patients (62 males, mean age 68±13 years) with acute type B aortic dissection in our hospital between 2002 and 2010 were enrolled. Patients were divided into three groups according to the status of the false lumen (complete thrombosis, n=50, partial thrombosis, n=24, patent, n=20). Short and long term clinical outcomes were examined.

Results: Requirement of surgical or endovascular treatment during initial hospitalization was significantly less frequent in patients with complete thrombosis (in patients with complete thrombosis, 17% in partial thrombosis, and 15% in patent). Furthermore, patients with complete thrombosis tended to have lower in-hospital mortality (0%, 4% and 10%, respectively). However, long-term mortality (mean follow up term was 1065±852 days) did not determine any difference according to the status of the false lumen. (Figure)

Conclusions: Complete thrombosis of the false lumen may have a correlation with better in-hospital outcomes in patients with acute type B aortic dissection. However, status of the false lumen does not seem to influence long-term mortality.

P1598 Salvage of infected cardiovascular implantable electronic device by a novel therapy

M. Topaz1, M. Kazatskev1, A. Shostan1, N. Carmel2, A. Silberman2, Y. Oron2, 1Hillel Yaffe Medical Center, Hadera, Israel. 2Tel Aviv University, Sackler school of medicine, Tel Aviv, Israel

The suggested treatment for infected cardiovascular implantable electronic devices (CIED) is complete extraction and replacement. Our objectives are to demonstrate the efficacy and safety of a novel therapy of trans cutaneous continuous in-situ-targeted, ultra-high dose antibiotics (CITa) under regulated negative pressure-assisted wound therapy treatment in the pocket site and, if indicated, minimal surgical procedure. All procedures were performed in the operating room applying mainly local or without anesthesia, and in a rare occasions, general anesthesia. Exposure of generator or proximal wiring could be managed by either delayed direct closure or by coverage with local rotation flap. CITa treatment lasted 6-16 days followed by a course of up to 4 weeks of oral an...
Feasibility of a simple score to predict renal artery stenosis during cardiac catheterization


Purpose: The aim of this study was to examine feasibility of the score as a screening tool for predicting RAS at the time of cardiac catheterization.

Methods: A total of 1,950 consecutive patients (pts) who underwent cardiac catheterization between January 2007 and December 2010 were enrolled in this study. Patrons with prior renal artery imaging. The following variables were used to calculate the score to predict significant RAS (age, gender, creatinine levels, peripheral vascular disease, number of antihypertensive drugs, hypertension and 3-vessel coronary artery disease or previous coronary artery bypass grafting). Abdominal aortography was planned for high-score (≥12) patients without prior renal artery imaging.

Results: Three hundred and thirty seven of 1,950 pts (17.2%) who underwent cardiac catheterization had a score of ≥12. Abdominal aortography was performed in 78 of 337 pts (23.1%). Forty four of 78 pts (56.4%) had RAS≥50%. All patients (n=9) with a score of ≥18 had RAS.

Conclusions: The simple score based on clinical characteristics is feasible as a screening tool for RAS during cardiac catheterization.

Heart rate variability change predicts neurocognitive improvement after carotid artery stenting in patients with chronic internal carotid artery occlusion

J.-K. Lee1, Y.-H. Chen2, M.-S. Lin1, H.-L. Kao1. 1Cardiovascular Center and Department of Clinical Pathology, Far Eastern Memorial Hospital, New Taipei City, Taiwan; 2National Taiwan University Hospital, Department of Internal Medicine, Taipei, Taiwan

Aim: Both autonomic function and neurocognitive ability improve after restoring carotid artery flow successfully. It is not clear whether acute heart rate variability (HRV) change right after carotid stenting (CS) predicts long term neurocognitive improvement in patients with chronic internal carotid artery (ICA) occlusion.

Methods: This prospective and consecutively enrolled 57 patients who accepted primary CS from 2008 to 2011. Functional assessments, including the National Institutes of Health Stroke Scale, Barthel Index, and a battery of neuropsychological testing, including the Mini-Mental State Examination, Alzheimer Disease Assessment Scale-Cognitive Subtest, verbal fluency, and Color Trail Making A and B, were administered before and 3 months after intervention. One-hour recordings of R-R intervals on ECG were obtained during supine rest prior to and following the intervention. The main measures were time- and frequency- domain, and nonlinear HRV measures.

Results: Successful CS was achieved in 51 of 59 patients (86%). HRV improved significantly one hour right after procedure. Compared to baseline, we also found a significant improvement at six months in the scores on the Alzheimer Disease Assessment Scale-Cognitive Subtest (before, 7.7±8.9 versus after, 5.7±7.1; P=0.024), Mini-Mental State Examination (before, 25.6±3.8 versus after, 27.5±2.7; P=0.015), and Color Trail Making A of the Trail-Making Test A (mean 6% improved change-score; P=0.01). The immediate HRV change is significantly associated with long term neurocognitive improvement 6 months after CS (r=0.76, p<0.001).

Conclusion: Immediate HRV change provides useful information to predict long term neurocognitive improvement after CS. To clarify the role of this novel marker, other physiological studies, such as functional MRI and perfusion CT, are in need to clarify the role of this novel parameter in the future.

Carotid artery stenting in elderly patients: a single center experience

P. Angiol1, I. Porto1, F. Listr01, K. Duch1, G. Falsini1, S. Grotti1, F. Turri2, G. Ventoruzzo2, G. Bellandi1, L. Biolo1, M. Kriwisky, Y. Abuhav, Y. Rozenman. The Edith Wolfson Medical Center, Holon, Israel

Purpose: Following the unfavorable results for renal artery intervention according to the ASTRAL trial, we sought to evaluate predictors of death among hypertensive patients inflicted with renal artery stenosis (RAS) subjected to renal artery dissection and stenting between 2004-2007 in our cathlab followed up till December 31, 2010, median of 66 months.

Methods: We identified 126 patients (aged 72.9±9.0 years, range 47-90 years, 71 males, RAS≥90% in 54, bilateral in 40 (32%) patients). Creatinine clearance ≤ 50 ml/min and ≤ 30 ml/min were observed in 67 (53%) and 15 (12%) patients, respectively. Coronary disease was observed in 107 patients (55 post MI), same procedure coronary intervention was executed in only 16 of them. Either peripheral vascular or carotid disease were observed in at least 34 (27%) patients.

Results: Twenty eight patients (22.2%) were dead at end of FU. Neither ECG-Sokolow-Lyon LVH criteria (dead versus survivors: 20.7±8.2 and 21.5±9.05, p=0.3), age (74±7.8, 71.8±6.9, p=0.16) nor depressed ejection fraction (LVEF<35%; 25% and 24%, p=0.5) predicted death. Univariate predictors are presented in Table A.

Conclusions: None LVms surpassed other important determinants of survival, we speculate that unless left ventricle hypertrophy regression is demonstrated at follow up, the prognostic benefit of the procedure is severely challenged.

Impact of critical limb ischemia on long term cardiac mortality in diabetic patients undergoing percutaneous coronary revascularization

F. Listr01, I. Porto1, S. Grotti1, P. Angiol1, R. Brandini1, L. Ricci2, K. Duch1, G. Falsini1, D. Taccioni, L. Biolo1, M. Kriwisky, Y. Abuhav, Y. Rozenman. The Edith Wolfson Medical Center, Holon, Israel

Purpose: We investigated the impact on long-term cardiac mortality of the association of coronary artery disease (CAD) with critical limb ischemia (CLI) in diabetic patients and the potential effect of coronary and limb revascularization.

Methods: We designed a prospective single centre registry which followed for years 764 consecutive diabetic patients undergoing percutaneous coronary intervention (PCI). The development of CLI was diagnosed by a dedicated diabetic

LVM mass (g) 227±43 183±48
LV mass index (g/m2) 0.81±0.06

Table A

Dead (n=28) Alive (n=98) P
Creatinine (mg%) 1.7±1.3 1.3±0.56 0.066
Diabetes Mellitus (%) 16 (57) 35 (36) 0.042
Triglycerides (mg%) 182±76 153±62 0.04
Contrast Dose (mL) 180±68 140±63 0.007
Prur (M) 17 (61) 38 (39) 0.039

Conclusions: Since LVms surpassed other important determinants of survival, we speculate that unless left ventricle hypertrophy regression is demonstrated at follow up, the prognostic benefit of the procedure is severely challenged.
foot-clinic specialist. All patients with CLI underwent peripheral revascularization of the culprit limb. Cardiac mortality was the primary endpoint of the study.

Results: Among the 704 PCI patients, 111 (14%) developed CLI during follow-up (PCI-CLI group) and were treated with peripheral revascularization in 145 limbs with procedural success in 140 (96%). PCI-CLI patients had lower left ventricle ejection fraction (LVEF) (51±11% vs 53±10%, p=0.008) higher renal failure (25% vs 12%, p=0.005), dialysis (7% vs 0.3%, p<0.0001) and diabetes duration (13.8 vs 11.7 years, p=0.02) compared to PCI-only patients. Coronary intervention procedural characteristics did not differ among PCI-only and PCI-CLI patients. At 4-years follow-up, cardiac mortality occurred in 10 (8%) PCI-CLI vs 39 (6%) PCI-only patients (p=0.2). Major amputation occurred in 6 (5%) patients. Cox regression analysis showed age (OR 1.06, 95%CI 1.02-1.09), dialysis (OR 8.02, 95%CI 4.20-20.61) to be the independent predictors of cardiac mortality which was not influenced by the development of CLI (OR 0.93, 95%CI 0.42-2.06).

Conclusion: In diabetic patients treated with percutaneous coronary revascularization, the development of CLI, treated with peripheral intervention, seems not to impact cardiac mortality long terms.

**P1604 Heterogeneity of atherosclerotic plaque phenotypes and composition in four different arterial beds: an intravascular ultrasound virtual histology study**

Y. Matsuo1, T. Takumi1, Y. Mathieu1, W.Y. Chung1, C.S. Rihal1, R. Gulati1, D.R. Holmes2, L.O. Lerman2, A. Lerman2

1Mayo Clinic, Department of Cardiovascular Disease, Rochester, United States of America; 2University Hospital Center Vaudois (CHUV), Department of Cardiology, Lausanne, Switzerland; 3Mayo Clinic, Department of Nephrology and Hypertension, Rochester, United States of America

Purpose: The purpose of this study was to compare the plaque morphology between coronary and peripheral arteries using intravascular ultrasound (IVUS).

Methods: IVUS was performed in 68 patients with coronary and 93 with peripheral artery lesions (29 carotid, 50 renal, and 14 iliac). Plaques were classified as fibroatheroma (VH-FA) (further subclassified as thin-capped [VH-TCFA] and thick-capped [VH-ThCFA]), fibrocalcific plaque (VH-FC) and pathological intimal thickening (VH-PIT).

Results: Plaque rupture (13% of coronary, 7% of carotid, 6% of renal, and 7% of iliac arteries; P=NS) and VH-ThCFA (37% of coronary, 24% of carotid, 16% of renal, and 7% of iliac arteries; P=0.02) was observed in all arteries. Compared to coronary arteries, VH-FA was less frequent in renal (P=0.01) and iliac arteries (P=0.006), while VH-PI and VH-FC were prevalent in both of these peripheral arteries. Lesions with positive remodeling demonstrated more characteristics of VH-FA in coronary, and renal arteries compared to those with intermediate/negative remodeling (all P<0.01). There was positive relationship between RI and percent necrotic core area in all four arteries.

Conclusions: Atherosclerotic plaque phenotypes were heterogeneous among four different arteries. In contrast, the associations of remodeling mode with plaque phenotype and composition were similar among the various arterial beds.

**P1605 Drug eluting balloon for below the knee angioplasty evaluation: the DEBATE BTK study**

F. Listro1, I. Porto1, P. Angioli1, S. Grott1, K. Duczi1, G. Venturozzi1, L. Rico1, G. Falsini1, G. Bellandi2, I. Bolognesi1

1San Donato Hospital, Department of Cardiology, Arzago, Italy; 2San Donato Hospital, Vascular Surgery Unit, Arzago, Italy; 3San Donato Hospital, Diabetes Unit, Arzago, Italy

Background: Drug-eluting balloon showed positive results in terms of restenosis reduction in peripheral intervention (PTA). The aim of the study is to investigate in a randomized fashion the efficacy and safety of Paclitaxel-eluting balloon (PEB) (Amphirion deep, Invatec, Brescia, Italy) versus non drug-eluting balloon (NEB) (Amphirion deep, Invatec, Brescia, Italy) in diabetic patients with Critical Limb Ischemia (CLI) undergoing PTA of below-the-knee (BTK) vessels.

Methods: The study, randomized, single center, planned to enroll 150 BTK lesions, 75 lesions in PEB and 75 in NEB group, assuming the 50% absolute reduction of 1-Year angiographic restenosis of the culprit lesion, the primary endpoint, in the PEB group.

Results: At the moment, 84 patients with 110 lesions treated are enrolled in the study and 1-year follow-up is available for 66 lesions in 51 patients, 36 losses in the PEB and 36 lesions in the conventional balloon group. No significant differences were observed in terms of Rutherford Class, clinical and procedural characteristics among the two groups. Mean age was 71±19 years in PEB vs 77±10 years in NEB (p=0.09), lesion length 107±76mm vs 128±68mm respectively (p=0.2), occlusions in 82% vs 83% (p=0.9) respectively, sub-intimal recanalization in 12.1% vs 14.5% respectively (p=0.5). At 1 year, death occurred in 8 (10%) of the enrolled patients, 3 in PEB and 5 in NEB. Restenosis, assessed by angiography in 53 lesions (83% in PEB vs 77% in NEB, p=0.2) and by Duplex Ultrasound in 10 lesions, occurred in 9 (27%) PEB vs 23 (63%) NEB lesions (p=0.01). Re-occlusion was present in 6 (19%) PEB vs 17 (44%) NEB lesions (p=0.02). No Major amputation occurred.

Conclusions: By provisional study results, PEB seems to provide better results in terms of 1-year restenosis compared to NEB in the treatment of BTK lesions in CLI patients.

**P1606 In-stent restenosis after carotid artery stenting - doppler ultrasound assessment and clinical importance**


Significant in-stent restenosis (ISR) in the carotid self-expanding stent is considered an important issue that may influence long-term efficacy of carotid artery stenting (CAS). The prevalence of ISR and Doppler ultrasound (DUS) accuracy for ISR diagnosis has not been clearly recognized.

Aim: To determine prevalence of ISR and DUS efficacy in detecting border-line (50-70%) and critical (>70%) ISR in TARGET-CAS population.

Methods: Between Jan 2001 and Jan 2012, 1520 CAS were performed in 1363 patients (age 66±8.6y, 67% man, 49.5% symptomatic) according to "targeted-CAS" algorithm that included extra/intracranial DUS, and -angiography to select the most appropriate neuroprotection and stent type. Neurological and DUS evaluation were performed before CAS, at 6, 12, months, then at yearly intervals. During CAS DUS, in stent peak systolic velocity (PSV) and end diastolic velocity (EDV) velocities were measured. The DUS criteria of border-line (50-69%) ISR were >2.0 m/s for PSV and/or 0.6m/s for EDV; and for critical (>70%) ISR 3.0 m/s for PSV and/or >0.9m/s for EDV, respectively. In case of suspected significant ISR on DUS, a quantitative angiography (QA) or angi-CT with-in stent diameter reduction and densitometric assessment were performed.

Results: During the mean follow-up of 44 months (range 12-120), borderline ISR was suspected in 20 (1.3%) subjects, while ISR >70% in 18 (1.2%) subjects, and total occlusion in 2 (0.13%), according to CAS. Of those, densitometric ISR >70% or stent occlusion was confirmed in QA in 18 (12/20 = 90%) patients, with the mean diameter and densitometric lumen reduction of 67.7±11.3% and 84.7±8.4%, respectively. In 2 other patients ISR degree was 50-69%. Borderline DUS ISR was confirmed in angi-CT in 16 (16/20 = 80%) subjects, with no angi-CT critical ISR.

There was a strong positive correlation between mean diameter reduction and PSV (r=0.630; p=0.001) or EDV (r=0.604, p=0.001); and densitometric lumen reduction and PSV (r=0.671; p=0.001) or EDV (r=0.726; p=0.001). Borderline DUS ISR was symptomatic, while TIA was observed in 1 subject with critical ISR and 2 with total occlusion. A balloon-only angioplasty was performed at first-line treatment for >70% ISR. There were 8 (16% ± 50%) cases of recurrent ISR (none of them symptomatic) and they were all successfully treated with ZES implantation.

Conclusions: A critical carotid ISR is rare and, in most of cases, asymptomatic. DUS is an effective tool for detecting carotid ISR. Recurrent carotid ISR is a frequent and challenging issue. The use of coronary ZES in the treatment of recurrent carotid ISR is feasible.

**P1807 Carotid angioplasty and stenting versus carotid endarterectomy: a trial**

M.M. Ciccone1, P. Sciochitano1, A. Zito1, L. Sgralla2, D. Marinazzo3, R. Carbonara1, I. Dentamario1, M. Carboni1, D. Angilletta1, G. Regina2, 1University of Bari, Dept Emergency and Organ Transplantations, 2University of Bari, Department of Pharmacology & Human Physiology Unit, Bari, Italy; 3University of Bari, Department of Vascular Surgery, Bari, Italy

Purpose: Stenosis that narrows the diameter of the carotid artery more than 60% 70% leads to a significant incidence of stroke if not treated medically. Particularly in symptomatic patients. Concerning invasive approach, carotid angioplasty and stenting (CAS) has been suggested to be as effective as carotid endarterectomy (CEA) for treatment of symptomatic carotid artery stenosis. The present study aims at comparing CAS and CEA effectiveness in the same patient, in order to avoid any confounding influence due to patients inherent risk factors. We further perform a serial carotid ultrasound screening in order to assess reciprocal treatment advantages in light of stenosis ultrasonographic features.
Methods: A total of 45 patients aged between 55 and 85 years, symptomatic or not, were enrolled in the trial. Inclusion criteria was considered a carotid stenosis > 55% echographically evaluated. Plaques were echographically recorded before treatment. All patients underwent a first intervention, CAS or CEA accordingly with international guidelines parameters, followed by the alternative compared procedure, on the contralateral side, delayed in time until stenosis reached > 55% lumen occlusion. Since patients belong simultaneously to the control group and the study group, no exclusion criteria were due. Considered endpoints were percentage of restenosis evaluated by ultrasound at 30, 180, >365 days follow-up times.

Results: Average stenosis value pre-intervention was 72±11% and resulted not significantly different among CEA and CAS group (p=0.09) as well as isoechogenic, isoechochogenic and hyperechochogenic plaque (p=0.72, 0.09, 0.27 respectively). Restenosis resulted significantly decreased in each time-dependent considered endpoint by CAS approach with respect to CEA. Percentage of restenosis at 30, 180, >365 days were: 0x, 1.4±3.1, 16±4 in CAS group and 2.5±1.2, 12±18, 28±24 (mean±Standard Deviation) in CEA group respectively (p<0.01). Patency of carotid lumen at 1 year, 180 and 30 days ultrasound follow up was increased by 48±2 and 55±9% respectively in CEA and CAS group (p<0.055).

Conclusions: Carotid stenting results to be as effective as endarterectomy approach in long term follow up whereas it may confer some additional advantages in brief and middle term.

P1608 The vascular bed is a determinant in vascular sensitivity to DES drugs
H.M.M. Van Beusekom1, W.J. Van Der Giessen2. 1Erasmus Medical Center, Rotterdam, Netherlands; 2Erasmus MC Thoraxcenter and ICIN-KNAW, Rotterdam, Utrecht, Netherlands

In contrast to coronary arteries (C), iliac arteries (I) do not show the same benefit of drug eluting stents (DES) in decreasing restenosis (SIROCO). Differences in medical properties may be responsible as balloon inflation period at 19 M, 7 follow-up results in more injury than in C under equal experimental conditions. Differences in neointima (NI) responses to stenting are less clear. We aim to assess early (2 wk) and late (12 wk) response to DES in comparison to bare metal stents (BMS) under controlled conditions in (I) and (C) of similar size, using the same stent.

Methods: Normal femoral swine (n=16) each received 2 C-DES (taxol) and one I-C, BMS, as well as 1 DES and 1 I-BMS. No more than one stent per artery. A total of n=26 C-DES, n=13 C-BMS, n=14 I-DES, n=10 I-BMS were placed under guidance of QCA (no prior injury, B/A ratio of 1:1:1). At follow up, arteries were pressure fixed and processed for histology.

Results: Angiographic acute gain (0.18±0.08mm vs 0.16±0.17mm) showed no significant differences between C and I. Histology also showed no differences in NI between C and I at each time point (Figure). However, a significant difference was found in the amount of late malapposition and thrombus between C and I at 2 weeks (48±43m vs 19±33m, p<0.05 T-test).

Conclusion: Basic healing responses for coronary and iliac arteries in absence of severe injury are similar in terms of NI thickness. However, coronary arteries show a significantly higher sensitivity to DES drugs. This persistent difference appears early after stent placement and increases in time. It is most likely attributable to differences in early thrombus deposition and flow patterns known to be important for drug retention and subsequent delivery.

P1610 Clinical significance of detecting abnormal fatty acid metabolism with iodine-123 15-(p-iodophenyl)-3-(R, S) methylnonadecanoic acid imaging in patients with dilated cardiomyopathy
A. Yoshida1, H. Takano1, T. Saito1, S. Nakamura1, S. Taka1, G. Takagi2, K. Asai1, S. Kunita3, Y. Amano2, K. Mizuno1. 1Nippon Medical School, Department of Cardiology, Tokyo, Japan; 2Nippon Medical School Hospital, Department of Radiology, Tokyo, Japan

Background: Fatty acid metabolism is known to be impaired not only in ischemic myocardium but in non-ischemic degenerated myocardium. We hypothesized that, in dilated cardiomyopathy (DCM), abnormal fatty acid metabolism on iodine-123 15-(p-iodophenyl)-3-(R, S) methylnonadecanoic acid (BMIPP) imaging reflects on-going myocardial damage of viable myocardium. In that case, evaluation of fatty acid metabolism by BMIPP imaging may be as important as detecting myocardial fibrosis by cardiac magnetic resonance imaging (CMR). To test this hypothesis, we compared the distribution of BMIPP defect with that of fibrosis expressed as late gadolinium enhancement (LGE) on CMR in patients with DCM. We also examined the prognostic value of those imaging.

Methods: BMIPP imaging and CMR were done in 48 patients with DCM (59±12 y, 14 female) during their first hospitalization. Defect of BMIPP and LGE were visually judged by radiologists. Cardiac event rate (death or readmission due to heart failure) was analyzed with the Kaplan-Meier method and the prognostic factors were determined by the Cox proportional hazards model.

Results: BMIPP defect was mainly observed at LV free wall whereas LGE mostly at septal wall. Of 24 patients with BMIPP defect, 21 had the unique distribution different from that of LGE. The patients were divided into the following 4 groups. Group N, L, B, and LB consisted of 16 patients with normal BMIPP and CMR, 8 with LGE alone, 12 with BMIPP defect alone, and 12 with both abnormalities respectively, during the median follow-up period of 19 M, 7 patients developed exacerbation of heart failure requiring hospitalization. Event rate at 12 M was 8.3%, 0%, 22%, and 66.7% in groups, N, L, B, and LB respectively. Log rank test revealed the significant difference between event free survival curve in group LB and those in other groups (p < 0.007). Among the 4 clinical factors (having both BMIPP and LGE defect, LV ejection fraction < 20%, brain natriuretic peptide > 200 pg/mL and mitral regurgitation grade III or greater), having both LGE and BMIPP defect was found to be the significant factor affecting the cardiac event (hazard ratio: 10.8, 95% confidential interval: 1.8 – 67.0, p = 0.010).

Conclusions: In DCM, fatty acid metabolism impairment at viable myocardial zone with no progressive fibrotic changes possibly suggesting on-going myocardial damage such as inflammation. Having abnormal fatty acid metabolism on BMIPP imaging in addition to certain amount of myocardial fibrosis detectable by CMR is the significant factor predicting future cardiac event.

P1611 Characteristics of coronary plaque components of culprit and non-culprit lesions by virtual histology intravascular ultrasound; difference between acute coronary syndrome and stable angina pectoris
T. Okado1, H. Takase1, T. Tanaka1, T. Hashimoto1, T. Toriyama1, H. Hayashi2, Y. Doih1, G. Kimura3, 1Enshu Hospital, Hamamatsu, Japan; 2Hamamatsu University School of Medicine, Hamamatsu, Japan; 3Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Purpose: Evaluation of coronary plaque in non-culprit as well as culprit lesions may be useful for understanding coronary atherosclerosis. We investigated characteristics of coronary plaque composition in culprit and non-culprit lesions using virtual histology intravascular ultrasound (IVUS-IVUS) imaging in patients with acute coronary syndrome (ACS) and stable angina pectoris (SAP).

Methods: Culprit and non-culprit lesions (left main or proximal of right coronary artery) were studied using IVUS-IVUS in 50 patients (64±13±1 year-old, ACS group, n=24; SAP group, n=26). According to type of plaque, necrotic core was larger and fibrous tissue was smaller in ACS than in SAP and culprit and non-culprit lesions. Furthermore, the composition of coronary plaque was not different between culprit and non-culprit lesions. Coronary risk factors such as hypertension.

Results: Culprit lesion Non-culprit lesion
ACS SAP ACS SAP
Lesion (RCA/LCA) 7/17 5/21 7/17 5/21
Vessel CSA (mm²) 17.8±3.4 19.9±3.7 22.5±4.7 24.5±3.9
Plaque CSA (mm²) 14.4±5.2 10.1±3.8* 11.7±3.7 10.6±4.0
Cav: 79.5±8.1 75.9±6.9 50.4±6.9* 49.2±7.9* Fibrin tissue (%) 57.9±11.4 64.4±9.1* 59.0±11.6 64.6±7.6* Fibro-fatty (%) 14.1±8.1 15.4±7.8 11.4±7.3 16.5±8.7* Fibrinolipidic calcium (%) 6.1±7.7 3.5±4.1 12.9±8.3 4.8±5.0 Necrotic core (%) 21.9±10.7 15.9±9.9* 21.4±12.1 13.9±8.8* *p<0.05 vs. ACS by unpaired Student’s t test. **p<0.05 vs. “Culprit lesion” by paired Student’s t test.
dyslipidemia, diabetes mellitus and current smoking did not affect the size (%) of necrotic core.

Conclusions: Coronary plaque in ACS contained larger necrotic core than that in SAP in both culprit and non-culprit lesions. This suggests that aggressive medical intervention to improve plaque compositions in the coronary arterial tree as well as an intervention to culprit lesion is necessary in patients with ACS.

Purpose: The absence of coronary calcification is associated with a good prognosis. However, a calcium score (CaSc) of zero does not excludes the presence of coronary artery disease (CAD).

Our aim was to study the prevalence and predictors of coronary artery disease in patients with a CaSc of zero.

Methods: Prospective registry of 2563 consecutive patients that performed Cardiac CT (Dual source CT). Stable patients referred for evaluation of possible CAD that had a CaSc of zero (N=274) were selected for this analysis. Urgent exams and patients with previous CA were excluded.

The prevalence of CAD in this population and the clinical variables associated with this combination (CAD with coronary calcification) were studied. The variables (sex, age, body mass index, diabetes mellitus, hypertension, dyslipidemia, smoking habits and family history of CAD) that were statistically significant were included in a multivariable logistic regression model.

Results: From 774 patients with CaSc of zero, 103 (13%) had coronary plaques of the contrast CT (11%, n=87 with nonobstructive CAD and 2%, n=16 with obstructive CAD).

The variables associated with the presence of CAD in this population were: hypertension, dyslipidemia and age >55 years. [table]

By logistic regression analysis, the independent predictors of CAD in this population were dyslipidemia OR: 1.9 (1.1-2.8) and age >55 years OR: 1.7 (1.1-2.6).

Predictors of CAD with calcium score = 0

<table>
<thead>
<tr>
<th></th>
<th>Without CAD (n=771)</th>
<th>With CAD (n=103)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male gender</td>
<td>46%</td>
<td>50%</td>
<td>0.53</td>
</tr>
<tr>
<td>Age ≥55 years</td>
<td>46%</td>
<td>62%</td>
<td>0.002</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>19%</td>
<td>19%</td>
<td>0.174</td>
</tr>
<tr>
<td>Hypertension</td>
<td>51%</td>
<td>63%</td>
<td>0.022</td>
</tr>
<tr>
<td>Smoking</td>
<td>24%</td>
<td>23%</td>
<td>0.600</td>
</tr>
<tr>
<td>Dyslipidemia</td>
<td>51%</td>
<td>68%</td>
<td>0.002</td>
</tr>
<tr>
<td>Family history of CAD</td>
<td>37%</td>
<td>37%</td>
<td>0.940</td>
</tr>
<tr>
<td>BMI (mean±SD)</td>
<td>27±4</td>
<td>27±4</td>
<td>0.276</td>
</tr>
</tbody>
</table>

Conclusion: The absence of coronary artery calcification does not exclude the presence of coronary artery disease, but the prevalence of obstructive disease is very low. In this population, the independent predictors of CA in the setting of a calcium score were dyslipidemia and age above 55 years.

Purpose: Coronary plaque calcification is a marker of atheroma burden. However, calcium scoring alone is not predictive of cardiac events and its clinical significance is controversial.

Methods: In an electronic search of candidate studies on the outcomes of stress echocardiography and stress radionuclide perfusion imaging, the prevalence and predictors of coronary artery disease in patients with a calcium score of zero were studied. The variables associated with the presence of CAD in this population were: hypertension, dyslipidemia and age >55 years. [table]

Conclusions: The absence of coronary artery calcification does not exclude the presence of coronary artery disease, but the prevalence of obstructive disease is very low. In this population, the independent predictors of CAD in the setting of a calcium score were dyslipidemia and age above 55 years.

Purpose: Coronary plaque calcification is a marker of atheroma burden. However, calcium scoring alone is not predictive of cardiac events and its clinical significance is controversial.

Methods: In an electronic search of candidate studies on the outcomes of stress echocardiography and stress radionuclide perfusion imaging, the prevalence and predictors of coronary artery disease in patients with a calcium score of zero were studied. The variables associated with the presence of CAD in this population were: hypertension, dyslipidemia and age >55 years. [table]

Conclusions: The absence of coronary artery calcification does not exclude the presence of coronary artery disease, but the prevalence of obstructive disease is very low. In this population, the independent predictors of CAD in the setting of a calcium score were dyslipidemia and age above 55 years.

Purpose: Coronary plaque calcification is a marker of atheroma burden. However, calcium scoring alone is not predictive of cardiac events and its clinical significance is controversial.

Methods: In an electronic search of candidate studies on the outcomes of stress echocardiography and stress radionuclide perfusion imaging, the prevalence and predictors of coronary artery disease in patients with a calcium score of zero were studied. The variables associated with the presence of CAD in this population were: hypertension, dyslipidemia and age >55 years. [table]

Conclusions: The absence of coronary artery calcification does not exclude the presence of coronary artery disease, but the prevalence of obstructive disease is very low. In this population, the independent predictors of CAD in the setting of a calcium score were dyslipidemia and age above 55 years.

Purpose: Coronary plaque calcification is a marker of atheroma burden. However, calcium scoring alone is not predictive of cardiac events and its clinical significance is controversial.

Methods: In an electronic search of candidate studies on the outcomes of stress echocardiography and stress radionuclide perfusion imaging, the prevalence and predictors of coronary artery disease in patients with a calcium score of zero were studied. The variables associated with the presence of CAD in this population were: hypertension, dyslipidemia and age >55 years. [table]

Conclusions: The absence of coronary artery calcification does not exclude the presence of coronary artery disease, but the prevalence of obstructive disease is very low. In this population, the independent predictors of CAD in the setting of a calcium score were dyslipidemia and age above 55 years.
Cardiovascular information systems influence the doctors’ selection of materials and devices, leading to significant savings in invasive cardiology

N. Klein1, M. Neef1, T. Lüsterhöver2, A. Hamed1, D. Pfeifer1, D. Thiele2,3,4
1University Hospitals Leipzig, Department of Cardiology and Angiology, Leipzig, Germany; 2Philips Healthcare, Eindhoven, Netherlands; 3University for applied sciences - Biomedical Engineering, Aachen, Germany;

Up to 50% of all costs for invasive cardiology patients are incurred in the cath lab. These costs can be split into fixed costs (such as, cath lab staff), fixed material costs (like scissors, and so on), and variable material costs (implants, single use devices, such as stents, and consumables, like balloons). This study aimed to significantly reduce the variable costs for different procedures in the cath lab.

Methods: We collected data with a cardiovascular information system (Philips CVIS®). We collected a baseline data set from April 1st, 2009 to March 30th, 2011. We then integrated a tool into CVIS to present the costs of finished procedures and give real-time feedback to the doctor. Medical reasons were always the primary influence on the choice of device, but the cath lab staff were trained and informed on device prices. The first observation ran from August 1st to September 30th, 2011. After adjustment training, a second observation ran from October 1st to November 30th, 2011.

Results: Results are shown in the table. The real-time feedback of costs also led to the following errors in 2% of procedures.

Table 1. Savings during observation period in % of baseline

Conclusion: Combined with an intensive cooperation with the purchasing department, informing and teaching staff in the cath lab about the prices of devices used, using a CVIS to provide real-time feedback, can

• significantly reduce costs for diagnostic and interventional, angi and electro-physiology procedures.
• help avoid coding errors that would otherwise result in lost reimbursement.

Regional differences in the utilisation of coronary angiography as initial investigation for the evaluation of patients with suspected coronary artery disease

I. Kosa1, I. Vassanyi2, A. Nemes3, E. Belicza4, G.Y. Kozmann2
1Cardiac Rehabilitation Centre of Military Hospital, Balatonfüred, Hungary; 2Research & Development Center of Health Informatics, Univ. Pannonia, Veszprém, Hungary; 3University of Szeged, Faculty of Medicine, 2nd Dept of Internal Medicine & Cardiology Center, Szeged, Hungary; 4Semmelweis University for applied sciences - Biomedical Engineering, Aachen, Germany

Introduction: Despite diagnostic algorithm of patients with suspected coronary artery disease (CAD) is well defined, a considerable number of such cases reach the diagnostic coronary angiography as initial investigation for the evaluation of patients with suspected CAD. The increasing number of this procedure is coupled with an increasing proportion of elderly subjects. The fact that the increase of age is not followed by increased mortality risk of involved patients suggests that one factor for greater incidence in some areas is the declined stringency in patient selection.

Methods: The system called DOILR (Dosimetry On Line for Interventional Radiology) has been implemented in five interventional cardiology laboratories with the capability to export patient dose reports by e-mail at the end of each procedure. The information contained in the data base of DOILR is used to correct of coding errors in 2% of procedures.

Results: During 2011, 3328 procedures were over 100 events in the database, which represents about 60% of all the activity in this room. The system allows the identification of the procedures with high cumulative skin dose values, and the possible inclusion in the existing clinical follow-up protocol. Simultaneously, the automatic feeding of the database allows the analysis of the trends in the different parameters registered: kerma area product (KAP), cumulative skin dose, fluoroscopy time, number of series and frames per study, KAP per frame and per second.

Use and misuse of multivariable approaches in interventional cardiology studies on drug-eluting stents: a systematic review

F. D’Ascenzo1, E. Cavallero1, G. Biordi Zoccai2, C. Morelli1, P. Omede1, M. Bollati1, D. Castagnoli1, M.G. Modena3, F. Gaia1, I. Sheilbani1, Division of Cardiology, University of Turin, Turin, Italy; 2University for applied sciences - Biomedical Engineering, Aachen, Germany; 3Regia Emilia, Modena, Italy

Purpose: Randomized clinical trials (RCTs) provide the most compelling clinical evidence, but they often require important resource and logistical efforts. By contrast, large, cost-free registries may be easily accessed to gather observational, real world data. However, observational studies require complex statistical analyses that often lead to flawed results because of inaccurate methods, especially from a statistic point of view. We aimed to appraise the performance of current multivariable approaches in the estimation of cardiac events after Drug Eluting Stent (DES) implantation.

Methods: Pertinent studies published in the literature were searched, selected, abstracted and appraised for quality and validity features. 6 studies using a logistic regression, 17 studies using a Cox proportional hazard analysis had a different follow up, with less than 10 events for covariates, yielding an overall low or moderate risk of bias. 16 studies using a propensity score without matching were included. The most frequent method for variable selection was logistic regression, with underlying difference in follow-up and less than 10 events for covariate in most of them.

Results: Calibration appraisal was not reported in the majority of the studies whereas discrimination appraisal was more frequently performed. Amongst the 17 studies using a propensity score, matching was usually performed with a nearest-neighbor–matching algorithm yet without appraisal of calibration or discrimination in most of the studies. Balance was evaluated in 46% of the studies, being obtained for all variables in 48% of them.

Conclusions: Better use and methodological appraisal of multivariable analysis is needed in order to improve the reliability of non-randomized studies and their impact on research and clinical practice.
P1620 From sound to ultrasound: a novel approach of computer-based pediatric cardiology teaching for medical students

I. Germanakis1, S. Stittich2, R. Geiger2, U. Salzer Muhar2. 1University Hospital of Heraklion, Heraklion, Greece; 2University Erlangen-Nuernberg, Pediatric Cardiology Dpt, Erlangen, Germany; 4Medical University, Dept of Pediatric Cardiology, Vienna, Austria; 5Heinrich-Heine University, Dept of Pediatric Cardiology, Dusseldorf, Germany

Purpose: To validate a multimedia-based paediatric cardiology teaching course for medical students, based on stepwise presentation of basic principles of clinical evaluation (sound: “virtual” cardiac auscultation) up to the final diagnostic tools (ultrasound: echocardiographic evaluation).

Methods: 30 medical students (21 female, 8 male, median age 24.8 yrs, of them 27 were undergraduates) of 5 European Institutions (3 countries) participated in a two week Erasmus Intensive Program (European Commission’s Life-long Learning Programmes). Teaching included theoretical and practical (virtual and hands-on) exercise, provided by 6 academic paediatric cardiologists and further teachers. Virtual cardiac auscultation was based on reproduction of digitally stored phonocardiograms, corresponding to a wide spectrum of congenital heart disease associated echocardiographic examinations. Hands-on experience included supervised evaluation of school aged children by conventional auscultation and echocardiographic examination by using portable echocardiographic systems. The teaching outcomes and the quality of the course were assessed by various questionnaires.

Results: The average total score of students was 78.8 (median=79.9), range 58-98.7. The increasing order students showed an excellent performance in auscultation theoretical test (92.4), echocardiography video interpretation test (83.4), paediatric cardiology theoretical test (82.7) and an acceptable performance in auscultation practical skills test (57.7). By using a 5-degree scale (1=not at all, 5=very much) students validated the course overall with a mean value of 4.48 (Table 1). Responses and performance were independent of country or Institution of students.

Table 1: Quality assessment of the course by participating students

<table>
<thead>
<tr>
<th>Quality assessment variable</th>
<th>Mean Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic content</td>
<td>4.32</td>
</tr>
<tr>
<td>Helpfulness</td>
<td>4.52</td>
</tr>
<tr>
<td>Enthusiasm</td>
<td>4.39</td>
</tr>
<tr>
<td>Number of hours taught</td>
<td>2.84</td>
</tr>
<tr>
<td>Total combined score</td>
<td>4.48</td>
</tr>
</tbody>
</table>

Conclusions: Modern computer-based intensive teaching when followed by hands-on practice, is a very effective means of pediatric cardiology teaching, highly appreciated by medical students.

P1621 Auscultational detection of coronary stenosis in humans: an angiographic validation study

R.F. Wilson1, E. Caldwell1, B. Guo1. 1University of Minnesota, Minneapolis, United States of America; 2AUM Cardiovascular, Northfield, MN, United States of America

Stenotic coronary arterial lesions cause turbulence and emit acoustical waves. We evaluated the accuracy of a new device that detects and analyses acoustical pressure waves from the chest wall (CADence device) to detect the presence of a coronary stenosis.

Device description: The device consists of a diaphragm, which activates a pressure transducer that records longitudinal waves in the acoustic range (20-20,000 Hz) from the anterior chest wall and stores them in digital format. After down-load, several frequency domains in the acoustic wave range associated with post-stenotic turbulence were examined using multiple spectral analysis techniques.

The presence of increased intensity in these domain regions led to classification as disease ‘present’ or ‘absent’.

Methods: Recordings were obtained from 191 patients immediately prior to elective cardiac surgery. Patients with the cardiac surgery were excluded. Recordings from up to 6 anterior chest positions were recorded during a breath hold. The acoustical recordings and coronary angiograms were analyzed blindly. An experienced angiographer reviewed each angiogram and graded the most severe diameter stenosis in each of 16 coronary segments. The acoustical recordings were analyzed by a digital processing technician blinded to the angiographic results and each recording was graded as disease “present” or “absent”.

Results: Analyzable recordings were obtained from 154/191 patients (81%). Ambient background noise was the most common reason for an unacceptable recording. 77 of the 154 patients with analyzable recordings had significant CAD (~50% stenosis in any arterial segment). 20%, 19%, and 11% had 1, 2 and 3 vessel disease.

The degree of stenosis that resulted in the maximal overall accuracy for detection of a stenotic lesion was ~50% stenosis. The area under the ROC curve for detection of a 50% stenosis was 0.73 (p<0.0001). The sensitivity and specificity for detection of a coronary stenosis ~50% in any vessel were 68 and 0.77 (NPV 0.71 and PPV 0.70). The sensitivity for predicting >50% stenosis in 1, 2 and 3 vessel coronary disease was 0.70, 0.61, and 0.77. The accuracy of detecting LAD lesions was similar to that of circumflex or RCA lesions.

Conclusions: These data suggest that the acoustical detection of coronary artery stenosis using the CADence device is feasible. In this first generation device, the diagnostic accuracy approached that reported for other non-invasive diagnostic tests. Its complete lack of risk and potential widespread applicability make it a device a potential game changer in the detection of significant coronary stenosis.

P1622 Aortic elasticity and carotid artery mechanics in Takayasu

I. Germanakis1, S. Yurdakul1, F. Alibaz Oner2, Y. Tayyareci2, H. Direskeneli2, S. Aytekin1, Florence Nightingale Hospital, Istanbul, Turkey; 3Marmara University, Department of Rheumatology, Istanbul, Turkey

Impairment in Aortic Elastic Properties and Mechanics of Carotid Artery System in Patients With Takayasu’s Arteritis

Background: Takayasu’s arteritis (TA) is a chronic inflammatory vasculitis of the aorta and its major branches. Increased arterial stiffness is known to be a predictor of cardiovascular mortality. Impairment of the elasticity in the involved arteries is an important feature of vascular injury in TA. In the present study we aimed to evaluate aortic and carotid artery elastic properties, to assess carotid arterial mechanics by using a novel strain imaging method, “velocity vector imaging” (VVI), in patients with TA.

Methods: We studied 33 patients with TA and 20 age and sex-matched controls. All the patients and healthy controls showed an excellent performance in auscultation theoretical test (92.4), echocardiography video interpretation test (83.4), paediatric cardiology theoretical test (82.7) and an acceptable performance in auscultation practical skills test (57.7). By using a 5-degree scale (1=not at all, 5=very much) students validated the course overall with a mean value of 4.48 (Table 1). Responses and performance were independent of country or Institution of students.

Table 1: Quality assessment of the course by participating students

<table>
<thead>
<tr>
<th>Quality assessment variable</th>
<th>Mean Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Academic content</td>
<td>4.32</td>
</tr>
<tr>
<td>Helpfulness</td>
<td>4.52</td>
</tr>
<tr>
<td>Enthusiasm</td>
<td>4.39</td>
</tr>
<tr>
<td>Number of hours taught</td>
<td>2.84</td>
</tr>
<tr>
<td>Total combined score</td>
<td>4.48</td>
</tr>
</tbody>
</table>

Conclusions: Modern computer-based intensive teaching when followed by hands-on practice, is a very effective means of pediatric cardiology teaching, highly appreciated by medical students.

P1623 Lung ultrasound to rule out congestive heart failure in the emergency department

L. Gargani1, P. Pang2, E. Davis2, A. Schumacher2, R. Sicari1, E. Picano1. 1CNR, Institute of Clinical Physiology, Pisa, Italy; 2Northwestern University, Feinberg School of Medicine, Department of Emergency Medicine, Chicago, United States of America

Purpose: Lung ultrasound (LUS) has emerged as a simple, reliable tool for the evaluation of pulmonary congestion, which is assessed by the sonographic sign known as B-lines (or ultrasound lung comets). Our aim was to determine the accuracy of LUS to rule out acute congestive heart failure in emergency room (ER) patients with acute dyspnea.

Methods: Two-hundred pts (55% female, mean age 61±17 yrs) admitted for acute dyspnea to ER were prospectively evaluated. They underwent a bedside LUS on admission by a portable device, according to a previously validated 28 scanning-site assessment. A positive LUS test was defined by >3 B-lines on >2 scanning sites bilaterally and/or by bilateral pleural effusion. All patients underwent a chest X-ray (CXR). Reviewers blinded to the LUS findings reviewed the medical records to confirm the aetiology of dyspnea.

Results: LUS was always performed in less than 5 minutes, with ~98% feasibility. Dyspnea due to cardiac pulmonary congestion was ruled in 51 patients (Group 1) and excluded in 149 patients (Group 2). Mean B-lines number was 71±47 in Group 1 and 22±41 in Group 2 (p<0.0001). A positive LUS test was found in 50/51 patients of Group 1 and in 31/149 patients of Group 2. Accuracy of LUS and CXR in detecting cardiac pulmonary congestion is shown in the table.

<table>
<thead>
<tr>
<th>Diagnostic method</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>LUS</td>
<td>99% (95% CI 99.0-100)</td>
<td>69% (95% CI 62.8-75)</td>
</tr>
<tr>
<td>Chest X-ray</td>
<td>83% (95% CI 80-86)</td>
<td>86% (95% CI 83.6-88)</td>
</tr>
</tbody>
</table>

Conclusions: Lung ultrasound is a quick, portable, and easy to perform test, which can be used safely by emergency physicians in their daily practice to rule out acute congestive heart failure.
under the curve of 0.86 (95% CI: 0.80-0.91) for B-lines to predict the cardiogenic origin of the dyspnoea, with a cut-off of 15 B-lines to maximize accuracy.

**Conclusions:** Sonographic B-lines are more sensitive than CXR for the evaluation of pulmonary congestion. In a dyspneic ER patient, the absence of bilaterally increased B-lines can reliably exclude the presence of cardiogenic pulmonary congestion with a 5-min bedside examination.

---

**P1624**

The use of chest x-ray as a diagnostic tool in acute aortic dissection: insights from the International Registry of Acute Aortic Dissection (IRAD)

E. Hofmann1, E. Kline-Rogers2, A.C. Braverman3, M. Voehringer4, P.G. Stepf1, V. Gourineni2, D.G. Montgomery2, E.M. Isselbacher4, K.A. Eagle1

1University Hospital Rostock, Rostock, Germany; 2University of Michigan, Ann Arbor, United States of America; 3Washington University in St. Louis, St. Louis, United States of America; 4Robert Bosch Hospital, Stuttgart, Germany; 5AP-HP - Hospital Bichat-Claude Bernard, Paris, France; 6Massachusetts General Hospital, Boston, United States of America

**Background:** Acute Aortic dissection is a life threatening disease requiring rapid diagnosis and treatment. As a diagnostic tool, chest x-rays (CXR) are simple, inexpensive, and easy to perform in an emergent setting. We compared aortic dissection patients with normal versus abnormal CXR findings to assess differences in symptoms and presentation.

**Methods:** Using data from the IRAD Registry, we evaluated 1110 Patients who presented from January 1996 to February 2011 with acute aortic dissections (Type A and Type B). Only CXRs from the tertiary hospital were analysed. Normal CXR was defined as lack of widening mediastinum, normal cardiac contour, normal aortic contour, no displacement of calcification of the aorta and no pleural effusion.

**Results:** Of 1110 patients analysed in IRAD, 227 (25.0%) had a normal CXR; 883 (75.0%) were abnormal. Of 615 Type A patients, 136 (22.1%) had normal CXR. These patients were more likely to have had a prior dissection (10.1% vs. 4.6%; p=0.009). Type B patients (495 total) with normal chest x-rays (141; 28.5%) were more likely to be younger than those with abnormal results (59.7 ± 14.5 vs. 64.4 ± 14.6; p<0.002) and were more likely to have an intracranic arterial dissection (5.1% vs. 12.1%; p=0.009) or migrating pain (22.1% vs. 14.0%; p=0.033). A widening of the aortic contour in patients with a CXR was observed in 60.4% of type A dissections and 50.7% of Type B dissections. Of the 1108 patients analysed, only 46.5% of Type A patients and 35.6% of Type B patients had evidence of widening of the aortic contour. And the patients were more likely to be younger than those with abnormal results (59.7 ± 14.5 vs. 64.4 ± 14.6; p<0.002).

**Conclusion:** CXR was abnormal in three-quarters of the IRAD population, with normal findings on CXR slightly more likely in Type B patients. Because normal CXR does not exclude acute Type A or Type B aortic dissection, it is important to characterize patients with these findings. Awareness of patient history and presenting symptoms associated with normal CXR in acute aortic dissection patients may help clinicians to better identify dissections in the absence of abnormal CXR findings.

---

**P1626**

Does pre-operative left ventricular shape play a role in systolic function after mitral valve repair?

F. Mattessant1, G. Tamborini2, P. Grimari3, M. Murat1, F. Alaman1, M. Zarobini1, L. Fusini, E.G. Cairo3, R.M. Lang3, M. Pepi2, Centro Cardiologico Monzino IRCCS, Milan, Italy; 1Department of Biomedical Engineering, Politecnico di Milano, Milan, Italy; 2The University of Chicago Medical Center, Chicago, United States of America

**Background:** Early mitral valve (MV) repair is known to result in functional benefits and morphological reverse remodeling of the left ventricle (LV). Our aim was to investigate whether in patients showing a depressed post-op LV function, the LV had already remodeled toward a less physiologic condition associated with volume overload. 55 patients (60±1yrs) with organic MV prolapse and ejection fraction (EF) <55% undergoing MV repair were enrolled. Based on pre/post EF change, patients were divided in 2 groups, MV_A (EFloss<10%), and MV_B (EFloss>10%). Transthoracic 3D echo was performed before and 6 months after surgery. Also, 40 normal subjects (NL) and 40 patients with dilated cardiomyopathy (DCM), age-matched, were studied for comparison. End-diastolic (EDV) and end-systolic (ESV) volumes, EF, and LV 3D shape indexes of sphericity (S) and connacity (Cn) were computed (perfect sphere/cone index=100%). Parameters were compared at each time point, and versus NL and DCM.

**Results:** MV repair was successful in all cases; 23 patients were assigned to MV_A, 32 to MV_B. Results are shown in the Table. Compared to NL, MV groups showed slightly enlarged EDV and higher EF, significant in MV_A, with similar ESV: compared to DCM the LV was significantly less dilated, with a higher EF. From the morphological perspective, pre-op LV was more spherical and less conical compared to NL, but not as much remodeled as DCM. No pre-op differences in LV volumes were found between MV groups, while MV_A was more spherical. Compared to pre-surgery, volumes and ED S decreased, while Cn increased, resulting in shape indexes similar to NL, but still slightly different. The decrease in EF observed in MV_A was associated with a post-operative ESV S higher than in MV_B.

---

**NEW SOFTWARE AND TOOLS FOR CARDIAC IMAGING**

**P1625**

A novel method for assessing diseased myocardium: tracer arrival time evaluation

N. Zarinabadi Nooralipour1, N. Chiribiri1, G. Hautvast2, M. Breeuwer1, E. Nager1, King’s College London, Division of Imaging Sciences, London, United Kingdom; 3Philips Healthcare, Imaging Systems – MR, best, Netherlands

Dynamic contrast-enhanced cardiovascular magnetic resonance imaging (DCE-CMR) is today the most popular method to assess perfusion in the myocardium and detect ischemia. This technique is mostly used to determine quantitative parameters such as peak of tissue impulse response curve to estimate perfusion. But perfusion quantification is challenging and suffers from several limitations including saturation effects associated. In this study a novel method for assessing diseased myocardium has been presented which is based on estimation of the tracer arrival time into the myocardium (tOnset) using DCE-CMR data.

Data were obtained from a patient during adenosine-induced hyperemia and have been analyzed using a software, which uses second derivative test on voxel level to identify the optimal tOnset. The relative tOnset which is the difference between the tracer arrival time in LV and tOnset has been calculated and used as parameter to assess the diseased myocardium.

Figure 1 shows estimated relative tracer arrival time for a 48-year-old male with one valve regurgitation in a voxel-wise bull’s-eye map (b) along with the perfusion map obtained using Fermi deconvolution method(a). The abnormalities in the LAD territories have been identified by the tracer arrival time map. Figure 2 shows a histogram of estimated tracer arrival time for the above patient. Most of the tOnset values are distributed around 30, except the tOnset values of the diseased voxels which are distributed around 45.

This method allows for the evaluation of areas of diseased myocardium by estimating the time point of tracer arrival at particular voxel. As a result a further post-processing step to establish perfusion indices is negated, thus minimizing errors and reducing processing time.

---

**P1627**

Inter-vendor discordance of strain: picture or processing?

K. Negishi1, S. Lucas1, T. Negishi1, J. Hamilton2, T. Manwick1, 1Cleveland Clinic, Department of Cardiovascular Medicine, Cleveland, United States of America; 2Epsilon Imaging, Ann Arbor, United States of America

**Purpose:** Previous reports have shown global longitudinal strain (GLS) to vary between vendors. We sought whether this reflects differences of analysis software or image characteristics.

**Method:** Three apical views were acquired using two machines (IE33, Philips; Vivid E9, GE Medical) in 45 consecutive patients (54±14y, 26 men) on the same day. Speckle tracking analysis was performed by two vendor specific (EchoPAC PC, GE Medical; QLAB, Philips) and two vendor-non-specific software (Cardiac Performance Analysis, Tomtec; EchoInsight, Epsilon). Bland-Altman plots were used for comparison. Echocardiographic images were used for a series of comparisons between combinations of echo machines and software (Table 1).

**Results:** Of 45 pts, 15 had heart failure/cardiomyopathy. 6 had coronary artery
A new 3D patient specific morphing tool enabling clinical application of non-invasive cardiac activation imaging

P.M. Van Dam1, A.W.M. Van Der Graaf2, M.J.W. Gotte2. 1Cortius Holding B.V., Amersfoort, Netherlands; 2Haga Teaching Hospital, The Hague, Netherlands

Purpose: Patient specific heart models are required to accurately determine cardiac electrical activation. However, no accurate computer tool exists to create patient specific computer heart models from Cardiovascular Magnetic Resonance (CMR) images.

Methods: New software was developed capable of morphing patient specific heart and thorax models from CMR or Computed Tomography (CT) images. We used a new mathematical morphing approach to translate all significant cardiac and thoracic anatomical structures into 3D models (figure 1).

Results: Twelve adult patient specific models have been created from CMR and CT (6 male, 6 female, 2 normal, 8 arrhythmia patients and 2 CRT patients). On average only 10-20 short axis and 2-4 long axis images were needed to make an accurate heart model. Between the reference imaging modality and the computer model, wall thickness variance was 1.1±0.9 mm (mean ± standard deviation) and the boundary variance for thorax and lungs was 2.0±1.5 mm. Consequently, the computer based morphing tool quantitatively approximates individual heart and thorax anatomy.

Conclusion: The accurate models created by the morphing software can be used to non-invasively determine cardiac electrical activation. Also, this new interactive technique links patient-specific cardiac anatomy to ECG waveforms. Combination of these techniques enables monitoring of the long-term effects of cardiac pacing and anti-arrhythmic medication, evaluation of congenital heart disease, and could be potentially attractive for quantitative non-imaging assessment of left ventricular contractile reserve, of potential interest in the stress lab and for home monitoring systems in cardiac heart failure.

Table 1

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Machine</th>
<th>Strain analysis software</th>
<th>Spearman's rho</th>
<th>P-value vs. (Expt 2)</th>
<th>Bias</th>
<th>SD</th>
<th>LOA (=1.96SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Different</td>
<td>Different (both vendor specific)</td>
<td>0.346</td>
<td>0.008</td>
<td>-2.0</td>
<td>6.0</td>
<td>11.7</td>
</tr>
<tr>
<td>2</td>
<td>Different</td>
<td>Same (vendor non-specific 1)</td>
<td>0.736</td>
<td>N/A</td>
<td>0.0</td>
<td>2.1</td>
<td>4.1</td>
</tr>
<tr>
<td>3</td>
<td>Different</td>
<td>Same (vendor non-specific 2)</td>
<td>0.637</td>
<td>0.396</td>
<td>-0.5</td>
<td>2.1</td>
<td>4.1</td>
</tr>
<tr>
<td>4</td>
<td>Same (Vendor 1)</td>
<td>Different (one vendor non-specific 1)</td>
<td>0.733</td>
<td>0.976</td>
<td>-2.4</td>
<td>3.2</td>
<td>6.5</td>
</tr>
<tr>
<td>5</td>
<td>Same (Vendor 1)</td>
<td>Different (one vendor non-specific 2)</td>
<td>0.725</td>
<td>0.912</td>
<td>1.0</td>
<td>2.2</td>
<td>4.4</td>
</tr>
<tr>
<td>6</td>
<td>Same (Vendor 1)</td>
<td>Different (both vendor non-specific)</td>
<td>0.704</td>
<td>0.764</td>
<td>3.8</td>
<td>2.3</td>
<td>4.6</td>
</tr>
<tr>
<td>7</td>
<td>Same (Vendor 2)</td>
<td>Different (one vendor non-specific 1)</td>
<td>0.309</td>
<td>0.604</td>
<td>-0.3</td>
<td>5.4</td>
<td>10.6</td>
</tr>
<tr>
<td>8</td>
<td>Same (Vendor 2)</td>
<td>Different (one vendor non-specific 2)</td>
<td>0.328</td>
<td>0.006</td>
<td>3.0</td>
<td>5.3</td>
<td>10.4</td>
</tr>
<tr>
<td>9</td>
<td>Same (Vendor 2)</td>
<td>Different (both vendor non-specific)</td>
<td>0.636</td>
<td>0.384</td>
<td>3.3</td>
<td>2.3</td>
<td>4.6</td>
</tr>
</tbody>
</table>

Expt, Experiment; SD, standard deviation; LOA, limits of agreement.

Conclusion: Force-frequency relation assessment with this new non-invasive, operator-independent force sensor is extendable to daily physiological exercise and could be potentially attractive for quantitative non-imaging assessment of left ventricular contractile reserve, of potential interest in the stress lab and for home monitoring systems in cardiac heart failure.

A new force sensor for imaging-independent assessment of force-frequency relationship in the stress echo lab: clinical validation

T. Bombardini, F. Faita, E. Picano. Institute of Clinical Physiology of CNR, Pisa, Italy

Background: The force-frequency relation (FFR) can be obtained in the stress echo lab, where the force is computed as the systolic pressure/end-systolic volume index ratio, and measured for increasing heart rates during stress. Ideally, the noninvasive, imaging-independent, objective assessment of FFR would greatly enhance its practical appeal.

Aims: To evaluate the feasibility of FFR measurement by a precordial cutaneous sensor and to compare the standard stress echo results vs this operator-independent FFR sensor.

Methods: The transcutaneous force sensor was positioned in the precordial region in 147 consecutive consecutive referred for exercise (n = 100), dipiridamole (n = 41), or pacing (n = 6) stress. The force was measured as the myocadial vibration amplitude in the isovolumic contraction period. FFR was computed as the curve of force variation as a function of heart rate. Standard echocardiographic FFR measurements were simultaneously performed.

Results: A consistent FFR was obtained in all patients. The sensor (see Figure, left panel) FFR slope and shape mirrored the more technically demanding and time-consuming echo (see Figure, right panel). The best cut-off value of the sensor-built FFR was 15.5 g x 10−3 (Sensitivity = 0.85, Specificity = 0.77). Variations (rest-stress) in force measured in FFR (R = 0.6).

Conclusions: Force-frequency relation assessment with this new non-invasive, operator-independent force sensor is extendable to daily physiological exercise and could be potentially attractive for quantitative non-imaging assessment of left ventricular contractile reserve, of potential interest in the stress lab and for home monitoring systems in cardiac heart failure.

Cardiovascular hemodynamics in the stress echo lab with open-source software

T. Bombardini, D. Ciri, E. Picano. Institute of Clinical Physiology of CNR, Pisa, Italy

Background: Stress echocardiographic evaluation of volumes is ideally suited for the quantitative calculation of a set of parameters allowing a complete characterization of cardiovascular hemodynamics of established pathophysiological and potential clinical relevance, including cardiac output, systemic vascular resistance, left ventricular elastance, arterial elastance, and ventricular arterial coupling. However, this is a tedious and time-consuming procedure.

Aims: 1) to build a web-based computing software program for self-instruction and calculation of hemodynamic parameters in the stress-echo lab. 2) to test the software with skilled echocardiographers 3) to distribute the software to the cardiological community.

Methods: A website with the informatics infrastructure was built (at cc-trainer.it.cnr.it). Ten skilled echocardiographers (American Society of Echocardiography class III) were asked to calculate hemodynamic parameters by using the...
personal knowledge (Mode 1) and by using the dedicated software called CC-trainer (Mode 2). After testing, the software was offered free on the web.

**Results:** The software was inserted in a dedicated web domain. After linking in, the cardiologist is asked to fill in the rest and stress data set. In a few seconds the program completes baseline and peak stress data, providing both numerical and graphical display of results (see Figure). The computation time of manual Mode 1 (55-63 min) was substantially reduced with software-assisted Mode 2 (≤3.05 min, p < 0.05 vs Mode 1).

**Conclusions:** Cardiovascular hemodynamics are important but their calculation remains time-consuming and demanding. However, they can be made simple, rapid and easy in the echo lab with a user-friendly, open-source program fed by simple raw echo data.

FROM THE DISTANCE – TELECARDIOLOGY

**P1631**

Telemonitoring of cardiac resynchronization therapy devices facilitates patients’ management and thus reduces mortality

M. Mazurek, E. Jedrzejczyk-Patet, A. Liberska, J. Boidol, A. Wozniak, R. Lenarczyk, J. Kowalczyk, P. Pruszkowska, O. Kowalski, Z. Kalarus. Medical University of Silesia, 1st Dept. of Cardiology, Silesia, Poland; 2M. Bufalini Hospital, Department of Cardiology, Baggiovara, Italy; 6Hospital of Parma, Department of Cardiology, Parma, Italy

**Aim:** To assess the usefulness of a daily monitoring of cardiac resynchronization therapy devices (CRT-D) with the use of telemonitoring.

**Methods:** Study population consisted of 137 patients (pts) implanted with CRT-D and monitored remotely on a daily basis via telemonitoring. 81% of devices were implanted in a primary prevention of sudden cardiac death (SCD). The ischemic etiology accounted for 62.7% of cases. Atrial fibrillation (AF) was present in 62 patients (45%). All tele-transmissions were screened for the percentage of CRT pacing and other data between January 2011 (baseline) and January 2012 (one year of follow-up). In line with the ESC guidelines, in which low CRT pacing was defined as <95% despite optimal medical therapy all patients were divided into two groups: 1) optimal CRT and 2) low CRT.

**Results:** Improvement in CRT pacing (Table 1) after one year of follow-up was achieved by every-day monitoring of the percentage of biventricular stimulation and thus immediate pharmacotherapy optimization (i.e. maximizing doses of betablocker, digoxin, amiodarone) as well as ablation procedure. Up to 42% (n=43) pts from the optimal CRT group in 2012 were in the low CRT group in 2011. The a-v node ablation was performed in 21.4% (n=9) of pts with low CRT in 2011 who improved and were classified into optimal CRT group in 2012. Independent risk factors for low CRT pacing were as follows: 1) atrial fibrillation (HR 7.82); 2) ventricle heart rate exceeding the upper tracking rate (HR 4.41); and 3) multiple premature ventricular contractions – PVCs<110/h (HR 3.9, all P<0.05). There were no significant differences in VT/VF episodes, number of adequate and inadequate shocks between low CRT and optimal CRT groups (P=NS).

**Table 1**

<table>
<thead>
<tr>
<th>Baseline (January 2011)</th>
<th>Optimal (&lt;95%) CRT pacing group</th>
<th>Low (&lt;95%) CRT pacing group</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>One year follow-up (January 2012)</td>
<td>43.2% (m=59)</td>
<td>56.8% (m=78)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean percentage of CRT pacing</td>
<td>74.4% (n=102)</td>
<td>25.5% (n=65)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Presence of AF</td>
<td>98.4%</td>
<td>89.1%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Mortality</td>
<td>60% (n=41)</td>
<td>90% (n=23)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

**Conclusions:** Every-day monitoring of the percentage of CRT pacing via tele-monitoring seems to reduce mortality by facilitating an early detection of low CRT pacing and thus allowing the immediate therapy modification.

**P1632**

Second-opinion stress tele-echocardiography for the Adonhers (aged donor heart rescue by stress echo) project

T. Bombardini1, D. Cini1, S. Ghersdetti1, R. Del Bene1, T. Grimaldi1, S. Sansosti1, W. Serra1, R. Sicari1, E. Picano1. 1Institute of Clinical Physiology of CNR, Pisa, Italy; 2M. Bufalini Hospital, Department of Cardiology, Cesena, Italy; 3Careggi University Hospital, Florence, Italy; 4Reggio Emilia Hospital, Department of Cardiology, Reggio Emilia, Italy; 5Baggiovara Hospital, Department of Cardiology, Baggiovara, Italy; 6Hospital of Parma, Department of Cardiology, Parma, Italy

**Aim:** To verify feasibility of a “second opinion” of digitally transferred images of stress echos to reduce mortality in aged donor hearts for heart transplant.

**Background:** To resolve the current shortage of donor hearts, we established the Adonhers protocol. An upward shift of the donor age cut-off limit (from the present 55 to 65 years) is acceptable if a stress echo screening on the candidate donor heart is normal.

**Aims:** To verify feasibility of a “second opinion” of digitally transferred images of stress echos to reduce mortality in aged donor hearts for heart transplant.

**Methods:** The informatics infrastructure was created for a core lab reading with a second opinion from the stress echo lab. Starting January 2010, real older donor stress echos were sent via internet to the central core echo lab, for a second opinion before heart transplant.

**Results:** Simulation protocol: n = 30 stress echo quad screen cine loops and reports were sent to the core echo lab; images were readable and the second opinion evaluation was feasible in all cases (100% feasibility). Transplant protocol: 19 older donor (age 54±10 years, 13 male) stress echos were sent via internet to the central core echo lab. The second opinion was feasible in 16/19 cases (84% feasibility); one case had low-quality cineloops, two cases had incorrect quad screen image upload. Second opinion answer delay was 37±48 min. Agreement between conventional and tele-echocardiographic interpretations was present in all 16 cases. Twelve hearts had normal stress echo response and 10 were successfully transplanted; 2 were not transplanted due to absence of recipient match. Four hearts had abnormal response and were dismissed.

**Conclusions:** Second-Opinion Stress Tele-Echocardiography can effectively be performed in a network aimed at safely expanding the heart donor pool for heart transplant.
Cost-effectiveness of the integration of home monitoring data with the hospital medical record

A. Garcia Quintana1, B. Vega Santana1, V. Feria Moreno1, E. Caballero Dorta1, F. Sosa Suarez2, M. Diaz Escoté1, J. R. Ramirez Rodriguez1, Y. Diaz3, C. Rios Diaz3, A. Medina Fernandez-Aceytuno4. 1University Hospital De Gran Canaria “Dr. Negrin”, Las Palmas de Gran Canaria, Spain; 2F.R Medical, Las Palmas de Gran Canaria, Spain.

Introduction: The electronic medical record (EMR) has become an essential tool for physicians. The integration of information from different sources is key, and until now accessing to every provider’s server was required for checking the patient’s data. Here we present a project of integration of home monitoring data with the EMR, so the patient and device information provided by the supplier goes directly to the hospital application for clinical follow up.

Objective: To determine the cost-effectiveness of the integration of information from the home monitoring system of ICDs with the EMRs of the hospital.

Material and Methods: The integration of the information provided by the Latitude System (BostonScientific) with the software for clinical follow up of pacemaker devices(Cardiotim) using the HLT protocol to send encrypted data, was made from July 2010 to February 2011. A close collaboration between cardiologist and the IT staff of the hospital was required. Until this moment 20 patients have been included, mean age 63.1 years (56-79), 13 males and 5 of them living on an island apart from the hospital (Lanzarote, CanaryIslands). Data about economic costs were obtained from the accounting service of the hospital.

Results: The cost of a medical visit for device follow up is 81.57€ and the movement of a patient from other island 150€/patient/day. Considering development expenditures of 10,000€, extrapolating this service to the population with an ICDs in our clinic (5,414), and estimating 24% of them live in another island, then we could obtain a saving of 38,338€ in the visits fees and 18,300€ in patients trips. In summary we could produce annual savings of 56,638€/year, considering that both the communicator and the service were provided by the supplier without additional cost to the ICDs price. The time expended in every clinical follow up visit is about 15 to 20 minutes per patient. With the data integration from Latitude to the EMR at least five minutes are saved without any typing mistakes. If you have 20 patients scheduled for every work day then 100 minutes are saved, which suppose more time for other duties or more patients per visit. Intangible benefits such as increased patients quality of life or the security provided by a closer monitoring should be regarded. Other benefit comes from the double data backup in the hospital and provider servers.

Conclusions: The integration of information from the telemonitoring of ICDs with the EMR is feasible and cost-effective.

Tele-cardiology for public emergency medical service: 7-year experience with 422.633 interventions

N.D. Brunetti1, L. De Gennaro2, G. Dellegrottaglie3, D. Amoruso3, G. Antonelli4, M. Di Blasi1. 1University of Foggia, Foggia, Italy; 2University of Torino, University Hospital, Monopoli, Italy; 3Cardio-on-line Europe S.R.L., Bari, Italy; 4Az. Ospedaliera Policlinico, Bari, Italy

Background: Tele-medical support is presently applied in several fields of medicine. Clinical evidence showed as pre-hospital ECG may shorten time to reperfusion in subjects with acute myocardial infarction, thus significantly affect- ing clinical outcomes of these patients.

Methods: A tele-medicine service presently supports the public free emergency medical service (EMS) “118” throughout whole Apulia, a 4-million inhabitants region in South-Eastern Italy. “118” is the Italian public free service responding to any kind of acute medical or surgical emergencies, whose aim is an immediate diagnosis of critical diseases in order to avoid emergency room delay-to-diagnosis. Patients are discharged from the ambulance and not transported at all in case of normal find- ings; direct admission to a critical care unit is arranged according to the level of care. Thanks to tele-cardiology support, “118” crews may record a complete 12-lead pre-hospital ECG with an apposite device, in any case of suspected heart dis- ease. The device does not allow the crew to directly see the ECG; the ECG is therefore sent by mobile phone support to a single regional tele-cardiology “hub” (Bari, Italy) to be evaluated by a cardiologist. The “118” control room, according to ECG and EMS crew report, then arranges for hospitalization when needed. Data from 2004 until early 2012 were hereby reported.

Results: 422,633 ECGs were recorded since 2004. Constantly growing trends of ECGs performed by “118” crews emphasize how tele-cardiology support is useful, truly on duty and frequently requested in every-day EMS practice (11,844 ECGs in 2005, 31,535 2006, 42,854 2007, 49,999 2008, 69,198 2009, 94,326 2010, 106,870 in 2011). Referring symptoms were dyspnea (9%), dizziness or fainting (2%), chest pain (25%), palpitations (7%), or other non-specific symp- toms. In 30,552 cases (7.2%) ECG showed a significant arrhythmia, in 23,777 (5.6%) signs suggestive for myocardial ischemia needing further examination (ECG mon- itoring, cardiac enzymeassay, coronary care or cath-lab admission).

Conclusions: Tele-cardiology may be useful in supporting a public EMS, improving the overall quality of medical assistance. A single tele-cardiology “hub” may easily support EMS in a 4-million inhabitants region.
Comparison between cryo and radiofrequency ablation in left atrial scar formation in patients with atrial fibrillation


Background: In patients suffering from atrial fibrillation the amount of post ablation scar formation as well as left atrial (LA) baseline fibrosis have an important impact on post procedural rhythm control success. Since most centers use radiofrequency (RF) technique not much is known about the effect of cryoballoon ablation on atrial scarning. Therefore the aim of this study was to determine whether there are differences between both methods affecting the postprocedural outcome using LA delayed enhancement cardiac magnetic resonance (LADE-CMR).

Method: A total of 28 patients (mean age 56.6±8.9 years) without any structural heart disease and a history of symptomatic paroxysmal atrial fibrillation at an average of 4.7±3.1 years underwent pulmonary vein isolation via RF (45%) or cryo ablation (55%). Every patient underwent a 3D navigated LA DE-CMR scan before ablation, as well as 24 hours and 3 months after the procedure. For determining the amount of DE we segmented the LA of each scan using a score with a threshold for fibrotic tissue detection compared to the blood pool signal plus two standard deviations.

Results: After pulmonary vein isolation we found a significant increase in LA DE in both ablation groups as well as left atrial (LA) baseline fibrosis. Assessment of arrhythmia recurrence at 3 months follow up was not statistically different in both groups. Average baseline fibrosis of included patients was 6.4±5.6%.

Conclusion: Our data present a trend towards more extended scar formation using Cryo balloon technique as compared to RF ablation. We could show that 3D navigated whole heart DE sequences are an excellent tool for studying scar formation.

Ischemic scar by contrast-enhanced cardiac magnetic resonance identifies non responders to cardiac resynchronization therapy in patients with right bundle branch block

A. Valle-Munoz1, J. Estornell-Erill2, M. Corbi-Pascual1, E. Lucas-Inarejos1, O. Fabregat-Andres1, L. Perez-Bosca1, P. Garcia-Gonzalez1, B. Bochard-Villarreal1, A. Quezada-Gorobio1, F. Ridecci Soriano1, 1Complejo Hospitalario Universitario, Albacete, Spain; 2ERESA-Consejo Hospital General Universitario, Valencia, Spain; 3Hospital General Universitario de Valencia, Valencia, Spain

Purpose: Among patients receiving cardiac resynchronization therapy (CRT), those with right bundle branch block (RBBB) benefits less than those with left bundle branch block (LBBB). Contrast enhanced MRI (CMR) allows to predict clinical response to CRT. Taking into account that in patients with left ventricular systolic dysfunction, RBBB is associated with a significantly greater scar burden by contrast-enhanced MRI than patients with LBBB we hypothesized that lack of response to CRT in patients with RBBB is related to the presence of ischemic scar.

Methods: We included 131 ischemic and nonischemic patients with left ventricular ejection fraction (LVEF) <35% receiving CRT. Late gadolinium enhanced (LGE)-MRI, we assessed the inadvertent effect to epicardial FP during routine AF ablation. We also investigated the impact of pre-existing left atrial (LA) tissue structural remodeling (LASM) assessed using LGE-MRI on the effect of FP ablation.

Results: Ablated FP area was wider in patients with successful AF ablation (22.8±12.3% vs. 15.9±10.5%, P<0.02). When assessed in conjunction with the extent of pre-existing LASRM, patients without recurrence had wider ablated FP area than patients with recurrence in patients with ≤20% LASRM (25.0±12.6% vs. 15.3±8.2%, P<0.02; Figure A). However this correlation did not hold up in patients with >20% LASRM (14.4±6.5% vs. 16.3±12.1%, P=0.70; Figure B).

Conclusion: Extensively ablating FP areas containing GP in routine PVAI seems to improve the outcome of AF ablation. Patients with low to moderate LASRM seem to benefit more from GP ablation than those with extensive LASRM.

Impact of the degree of left atrial tissue structural remodeling detected using LGE-MRI on the ablation of ganglionated plexi in patients with atrial fibrillation

K. Higuchi, M. Akkaya, M. Koopmann, J. Blauer, N. Burgon, K. Damal, R. Ranjan, E. Kholmovski, R. Macleod, N. Marrouche. University of Utah, Comprehensive Arrhythmia Research and Management Center, Salt Lake City, United States of America

Background: Affecting epicardial ganglionated plexi (GP), which is favorable for the prognosis after ablation of AF, is inevitable during pulmonary vein antrum isolation (PVAI) for patients with AF. GP is known to reside within epicardial fat pads (FPs).

Objectives: In this retrospective study, using late gadolinium enhancement (LGE)-MRI, we assessed the inadvertent effect to epicardial FP during routine AF ablation on the prognosis of AF after ablation. We also investigated the impact of pre-existing left atrial (LA) tissue structural remodeling (LASM) assessed using LGE-MRI on the effect of FP ablation.

Methods: We retrospectively investigated 60 patients who underwent LGE-MRI pre (to assess the extent of LASRM) and 3 month post AF ablation (to assess the extent of scar). FPs in well-known GP areas were segmented from T2 weighted MRI and projected on 3D LA image. Then the 3D LA image with FPs projection was merged with the 3D scar image on the LA visualized by LGE-MRI 3 month post ablation. The overlapped area of FPs and the scar were considered as the ablated FP (GP) areas.

Results: Ablated FP area was wider in patients with successful AF ablation (22.8±12.3% vs. 15.9±10.5%, P<0.02). When assessed in conjunction with the extent of pre-existing LASRM, patients without recurrence had wider ablated FP area than patients with recurrence in patients with ≤20% LASRM (25.0±12.6% vs. 15.3±8.2%, P<0.02; Figure A). However this correlation did not hold up in patients with >20% LASRM (14.4±6.5% vs. 16.3±12.1%, P=0.70; Figure B).

Conclusion: Extensively ablating FP areas containing GP in routine PVAI seems to improve the outcome of AF ablation. Patients with low to moderate LASRM seem to benefit more from GP ablation than those with extensive LASRM.
unreliable due to variable contrast and noise. We propose an automatic scar segmentation algorithm based on statistical clustering that is more robust to noise and contrast variability.

Methods: The proposed scar segmentation algorithm uses a k-means clustering of pixel intensities into tissue classes, with scar being the class with the highest mean intensity. We validated our algorithm against 34 ground truth scar segmentations, comparing several metrics for overlap of scar and an overall assessment of scar percentage. Each ground truth segmentation was produced as a statistical average of 5 manual expert segmentations. Figure 1 shows a single slice from an example segmentation overlaid on the LGE MRI.

Results: Automatic segmentation performed favorably compared to the experts, showing only 3% more variation from ground truth, as shown in Figure 1. We found a positive correlation between the quality of the automatic and expert segmentations (r²=0.48, p=0.0035), indicating the automatic method tends to track human performance. Intra-observer segmentation variability ranged from 4.8% - 11%, which is completely eliminated by the automatic approach.

Conclusions: The proposed algorithm dramatically improves the consistency of our scar segmentations and demonstrates accuracy that is comparable to expert manual segmentations.

Correlation between interatrial septal hypertrophy and interventricular septal hypertrophy and its impact on the outcomes of ablation in patients with atrial fibrillation

M. Akkaya, K. Higuchi, M. Koopman, N. Akoum, N. Burgon, K. Damal, N. Marrouche. University of Utah, Comprehensive Arrhythmia Research and Management Center, Salt Lake City, United States of America

Background: Left ventricular hypertrophy (LVH) is known to be associated with left atrial structural remodeling. LVH has shown to increase pressure in the left atrium (LA) consequently leading to LA dilatation. We hypothesized that the stress generated in the LA due to LVH may subsequently lead to an increase in the interatrial septal (IAS) thickness. The IAS is commonly targeted during atrial fibrillation (AF) ablation and an increase in LA thickness may affect the outcomes of AF ablation.

Methods: We included 429 AF patients who underwent an LGE-MRI prior to catheter ablation in this study. Interventricular septal (IVS) and IAS thickness were measured using cine MRI images. IAS was measured during both end-systole and end-diastole, while IVS was measured during end-diastole. Patients were then grouped into LVH (IVS > 12 mm; n=117) and no-LVH (IVS ≤ 12 mm; n=312) for further analysis.

Results: The mean age between two groups were comparable (65.7±11.4 vs. 64.6±12.5; P=0.394), with a male predominance in LVH group (78.7% vs. 58.2%; p<0.001). Mean IAS in systole was significantly higher in patients with LVH (7.66±1.32 mm) when compared to no-LVH patients (6.91±1.18 mm; P<0.001). Similarly IAS in diastole was also significantly higher in patients with LV (6.09±1.05 mm) than patients with no-LVH (5.60±1.00 mm; P<0.001). Patients with LVH experienced more AF recurrences (40.8% vs. 28.6% in no-LVH patients) over a 12-month follow-up period post ablation.

Conclusion: IAS hypertrophy is associated with an increase IAS thickness in patients with AF during. Increased IAS thickness may have significant implications for determining the ideal intensity and total duration of radiofrequency energy required to achieve a safe and successful AF ablation.

Intensity inhomogeneity correction in LGE-MRI of AF patients is important for accurate LA wall tissue characterization

A. Morris, J. Cates, D. Perry, N. Burgon, N. Marrouche, E. Kholmovski. University of Utah, Comprehensive Arrhythmia Research and Management Center, Salt Lake City, United States of America

Introduction: Late gadolinium enhancement MRI (LGE-MRI) to characterize structural remodeling in the left atrium (LA) has shown promise for the management of patients with atrial fibrillation (AF), including prediction of ablation outcomes. Tissue characterization, however, may be complicated by regional intensity inhomogeneity due to factors such as coil type and placement. We propose a localized intensity correction to produce a homogenous LA blood pool.

Methods: Under the assumption that the LA blood pool should exhibit uniform intensity with Gaussian noise and intensity inhomogeneity is slow varying, we estimate localized intensity variation in the LA by fitting a second-order polynomial to voxel values only within the LA endocardium. Intensity in the immediately-adjacent LA wall is then normalized with respect to this model.

Results: We applied the proposed correction to 8 patient LGE-MRI images and found a mean shift of 8.1 (±5.7) in the percentage of wall pixels classified as enhanced by an expert observer. Figure 1 compares a single uncorrected image (left) with its corrected version (right). The more uniform appearance of the corrected image is apparent, and its blood-pool intensity distribution (second row) has become more Gaussian. The panels at the bottom of the figure show how the spatial distribution of enhancement may also shift after correction.

Conclusions: Intensity inhomogeneity correction can dramatically alter the pattern and extent of enhancement of LA wall tissue and is therefore an important consideration for LGE-MRI in AF treatment.

18F-FDG PET/CT for characterization of vegetations on pacemaker and defibrillator leads found on transesophageal echocardiography


Purpose: A recent study reported that lead masses are seen on transesophageal echocardiography (TEE) in up to 14% of patients with a cardiovascular implantable electronic device (GIED). However, most were proven not to be sec-
Cardiac flow physiology during physical exercise studied using high-resolution perfusion magnetic resonance imaging

K.N. Asness1, T. Locke1, R. Williams2, J. Biglands2, N. Ali2, C. Hill1, I. Cardwell1, E. Nagel1, M. Hickey4, S. Redwood5, S. Piek1
1King’s College London, Cardiovascular Division, St. Thomas’ Hospital, London, United Kingdom; 2University of Leeds, Multidisciplinary Cardiovascular Research Centre, Leeds, United Kingdom; 3King’s College London, Division of Imaging Sciences, London, United Kingdom

Purpose: Exercise stress testing remains the most physiological method of inducing myocardial stress. Compatible ergometers together with high-resolution perfusion techniques have provided a potential method with which exercise physiology can be studied in the MRI environment. The purpose of this study was to quantitatively assess absolute myocardial blood flow as well as endocardial and epicardial segmental flow during rest and exercise stress.

Methods: Healthy volunteers without known cardiovascular disease gave informed consent for supine cycle ergometry on the MRI scanner table (Lode, Netherlands). Subjects underwent a standardised incremental exercise protocol. High-resolution perfusion cardiac MRI was performed on a 3Tesla Philips Achieva system using 0.04 mmol/kg Gd-DTPA (saturation recovery gradient echo, repetition time/echo time 2.7ms/0.96ms, flip angle 15°, Sx-k+1 SENSE acceleration, 11 interleaved training coils, spatial resolution 1.0×1.0×0.8 mm^3, 3 slices acquired at each RRI interval, 30 dynamic images).

Data were analysed with MASS® (Medis, Netherlands) and Matlab® (The MathWorks®, USA). Subendocardial and subepicardial myocardial blood flow (MBF) was calculated and the LV myocardium was divided into 6 segments per slice and its endocardial, epicardial and middle thirds. Transmural myocardial blood flow, as well as endocardial and epicardial MBF ratios were estimated using Fermi-function derived deconvolution. Data are presented as mean ± SEM.

Results: 18 subjects (mean age 36.4 years) completed rest and exercise scans. Resting transmural blood flow was 0.9±0.07 ml/g/min that increased to 2.1±0.2 ml/g/min during exercise (p<0.001). There was an endocardial/epicardial MBF ratio at rest of 1.48±0.1 which reduced to 1.16±0.05 during exercise (p=0.017).

Conclusions: High-resolution myocardial perfusion CMR is feasible and demonstrates changes in endocardial and epicardial myocardial blood flow during cycle ergometer stress. The loss of the endocardial/epicardial MBF blood flow ratio during cardiac stress has been shown in animal models but this is the first time it has been demonstrated in vivo in humans. It provides an ideal model to use for further research in disease processes as well as pharmacological modulation.
after PEA for CTEPH. We were able to demonstrate improved surrogate markers of PA pressure and resistance as early as 10 days after PEA in a large series of 65 patients.

**P1648** Normal regional pulse wave velocity predicts absence of aortic luminal growth in patients with Marfan syndrome: a comprehensive MRI-study

E.S.J. Kroner1, A.J.H. Scholte1, L.J.M. Kraft2, R.J. Van Der Geest2, B.J.M. Mulder1, Y. Hilhorst-Hofstee2, E.E. Van Der Wall1, A. De Roos3, J.H.C. Reiber1, J.J.M. Westenberg1, 1Erasmus Medical Center, Department of Cardiology, Leiden, Netherlands; 2Leiden University Medical Center, Department of Radiology, Leiden, Netherlands; 3Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands

Methods: Thirteen healthy volunteers (mean age 35±15 years, 11 male) regional PWV and aortic luminal areas were assessed by 1.5T MRI (Philips). Regional PWV in MFS patients was considered increased when exceeding age-related PWV (n≥26; mean age 50±10 years, 15 male) by two standard errors. At 2-year follow-up, the incidence of luminal growth for the five aortic segments (ascending aorta (S1), aortic arch (S2), thoracic descending aorta (S3), suprarenal abdominal aorta (S4) and subrenal abdominal aorta (S5)) was determined. A mean luminal diameter increase ≥1.5 mm was considered significant growth. The regional PWV at baseline was compared with cross-sectional luminal area growth from baseline to FU.

**Results:** Regional PWV at baseline was increased in 17 out of 102 segments (17%). Significant luminal growth at FU was reported in 14 segments (14%). The specificity of regional PWV-testing was ≥78% for all aortic segments.

**Figure 1**

**Conclusions:** The specificity of regional PWV-testing at baseline for prediction of luminal aortic growth during 2-year follow-up in patients with Marfan syndrome is ≥78% for all aortic segments, i.e. normal age-related regional PWV predicts in ≥78% of the cases the absence of luminal aortic growth.

M. Selwaness1, G. Van Den Bouwhuijsen1, G.C. Verwoert1, A. Dehghan1, M. Vemool1, A. Hofman1, A. Van Der Lugt1, J.J. Wentzel1, J.C.M. Witteman1, O.H. Franco1, 1Erasmus Medical Center, Department of Epidemiology, Rotterdam, Netherlands; 2Erasmus Medical Center, Department of Radiology, Rotterdam, Netherlands; 3Erasmus Medical Center, Thoraxcenter, Biomedical Engineering Department, Rotterdam, Netherlands

**Purpose:** Intra plaque hemorrhage (IPH) is a characteristic of the vulnerable plaque that has been associated with cardiovascular disease. Potential determinants of plaque vulnerability and in specific IPH remain unclear. We studied the factors associated with intra plaque hemorrhage in particular blood pressure parameters.

**Methods:** Within the framework of the Rotterdam Study, the carotid arteries of 1006 healthy participants 45 years and older with intima-media thickness (>2.5mm) on ultrasound were imaged with a 1.5-Tesla MRI scanner. IPH was defined as a hyperintense signal on a 3D-T1w GRE MR sequence. Generalized estimation equation analysis, adjusted for sex, age, wall thickness and cardiovascular risk factors including smoking, BMI, total cholesterol and diabetes, was used to assess the association between blood pressure parameters and IPH.

**Results:** MRI imaging of the carotid arteries revealed presence of IPH in 444 of 1866 (24%) plaques. Systolic blood pressure (SBP) and pulse pressure (PP) were significantly associated with IPH after adjustment for age and sex. After further adjustment for wall thickness and cardiovascular risk factors, PP yielded the strongest association, with an odds ratio (OR) per SD increase in PP of 1.22 (95% CI 1.07-1.40) and an OR per SD in SBP of 1.13 (95%CI 0.99-1.28). Only PP remained significant after additional adjustment for other blood pressure components.

**Conclusions:** Pulse pressure was the strongest determinant of IPH independent of cardiovascular risk factors and other blood pressure components. The association between pulsatile flow and IPH may provide novel insights into the development of the vulnerable plaque and future clinical practice.

P.1650 Pulse wave dynamics in the carotid artery: assessment with high field velocity-encoded magnetic resonance imaging

E.S.J. Kroner1, H.J. Lamb2, H.J. Siebelink1, E.E. Van Der Wall1, J. Van Der Grond3, M.A. Van Buchem2, A. De Roos2, J.J.M. Westenberg2, 1Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 2Leiden University Medical Center, Department of Radiology, Leiden, Netherlands; 3Erasmus Medical Center, Department of Cardiology, Rotterdam, Netherlands.

**Purpose:** It is hypothesized that aortic pulse wave reflection at the interface between a compliant aorta and stiffer carotid arteries limits the transmission of excess pulsatile energy. Vessel stiffness can be expressed by pulse wave velocity (PWV; propagation speed of the flow wave through the artery). Velocity-encoded (VE) MRI is well-validated for accurate PWV-assessment. The purpose of this study was to use 3T VE MRI to evaluate aortic and carotid PWV as well as pulsatility damping in the carotid artery.

**Methods:** Thirteen healthy volunteers (4 male, mean age 25±3 years) underwent 3T MRI (Philips) to assess PWV in the aortic arch and the left carotid artery based on the transit-time method and one-directional through-plane velocity-encoded (VE) MRI. At the two levels of carotid PWV assessment, maximal velocity Vmax, minimal velocity Vmin and mean velocity Vmean during the cardiac cycle were calculated. From these values, the pulsatility index (PI [Vmax – Vmin]/Vmean) and resistive index (RI [Vmax – Vmin]/Vmax) were calculated.

**Results:** PWV was 20% higher (p<0.001) in the carotid arteries (PWV = 5.8±1.0 m/s) as compared to the aorta (PWV = 4.8±0.7 m/s). PI was 72% reduced in the carotid artery while RI lowered 32%.

M. Selwaness1, G. Van Den Bouwhuijsen1, G.C. Verwoert1, A. Dehghan1, M. Vemool1, A. Hofman1, A. Van Der Lugt1, J.J. Wentzel1, J.C.M. Witteman1, O.H. Franco1, 1Erasmus Medical Center, Department of Epidemiology, Rotterdam, Netherlands; 2Erasmus Medical Center, Department of Radiology, Rotterdam, Netherlands; 3Erasmus Medical Center, Thoraxcenter, Biomedical Engineering Department, Rotterdam, Netherlands

**Purpose:** Intraluminal hemorrhage (IPH) is a characteristic of the vulnerable plaque that has been associated with cardiovascular disease. Potential determinants of plaque vulnerability and in specific IPH remain unclear. We studied the factors associated with intraplaque hemorrhage in particular blood pressure parameters.

**Methods:** Within the framework of the Rotterdam Study, the carotid arteries of 1006 healthy participants 45 years and older with intima-media thickness (>2.5mm) on ultrasound were imaged with a 1.5-Tesla MRI scanner. IPH was defined as a hyperintense signal on a 3D-T1w GRE MR sequence. Generalized estimation equation analysis, adjusted for sex, age, wall thickness and cardiovascular risk factors including smoking, BMI, total cholesterol and diabetes, was used to assess the association between blood pressure parameters and IPH.

**Results:** MRI imaging of the carotid arteries revealed presence of IPH in 444 of 1866 (24%) plaques. Systolic blood pressure (SBP) and pulse pressure (PP) were significantly associated with IPH after adjustment for age and sex. After further adjustment for wall thickness and cardiovascular risk factors, PP yielded the strongest association, with an odds ratio (OR) per SD increase in PP of 1.22 (95% CI 1.07-1.40) and an OR per SD in SBP of 1.13 (95%CI 0.99-1.28). Only PP remained significant after additional adjustment for other blood pressure components.

**Conclusions:** Pulse pressure was the strongest determinant of IPH independent of cardiovascular risk factors and other blood pressure components. The association between pulsatile flow and IPH may provide novel insights into the development of the vulnerable plaque and future clinical practice.

**P1651** Ultra high field magnetic resonance carotid vessel wall imaging: comparison between 7T and 3T

E.S.J. Kroner1, M.J. Versluis2, N.J. Brouwer1, E.E. Van Der Wall1, A. De Roos2, A.G. Webb2, H.J. Siebelink1, H.J. Lamb2, 1Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 2Leiden University Medical Center, Department of Radiology, Leiden, Netherlands.

**Purpose:** Magnetic Resonance Imaging (MRI) enables high-resolution carotid artery vessel-wall imaging, although clinical applications are currently hampered by suboptimal signal-to-noise (SNR) and contrast-to-noise-ratio (CNR). Vessel wall MRI is expected to benefit from higher magnetic field strength. The purpose...
of this study is to measure the SNR and CNR of 7T carotid MRI as compared to 3T, with similar in-plane spatial resolution and total scan time.

**Methods:** 18 volunteers (11 males, 7 females, mean age=29±7 yrs) underwent MRI-examinations at 7T (using a custom built surface transmit/receive coil of 15 cm diameter) and at 3T (using a commercial phased-array coil with two flexible oval elements, each 14 x 17 cm). MRI of the left carotid artery vessel-wall was performed at 7T with identical in-plane resolution as 3T MRI (0.46 x 0.46 mm²) providing transverse T1- and T2-weighted images. Blinded analysis of SNR and CNR for the two separate MRI sequences was assessed using Vessel Mass software and compared between 7T and 3T.

**Results:** At 7T, SNR and CNR are significantly higher as compared to 3T MR for both T1- and T2-weighted images, with gain factors ranging from 1.3 to 5.9.

**Conclusion:** Ultra high field 7T MR carotid vessel wall Imaging improves SNR and CNR, as compared to 3T. The improved SNR and CNR at 7T MRI may enable more detailed assessment of plaque morphology.

**P1652** Impact of cardiovascular risk factors on aortic pulse wave velocity: A comparison of healthy volunteers and patients after acute STEMI

G. Klug1, H.J. Festenitzer1, M. Kremer1, A. May2, L. Kautner1, N. Riegler1, M. Schocke2, W. Jaschke3, O. Pachinger4, M. Metzlter1

1Innsbruck Medical University; 2Department of Internal Medicine III, Cardiology, Innsbruck, Austria; 3Innsbruck Medical University, Department of Radiology, Innsbruck, Austria.

**Aims:** Aortic pulse wave velocity (aPWV, m/s) is associated with traditional cardiac risk factors and is an independent prognostic parameter for future cardiac events. The association of cardiac risk factors with aPWV in patients with STEMI is not yet evaluated.

**Methods:** 115 subjects were enrolled in this study (n=43 controls without significant CVD, n=72 STEMI patients within 7 days of index event). Aortic aPWV was determined with velocity encoded, phase contrast cardiac MRI (retrospectively ECG-gated, temporal resolution: 20ms). Medical history was obtained to determine pre-existing cardiovascular risk factors (hypertension, smoking, hypercholesterolemia, family history of CVD). Blood pressure (BP) and lipid profiles were determined and ESC SCORE was calculated to quantify total cardiovascular risk.

**Results:** In controls aPWV was correlated with age (r: 0.883, p<0.001), systolic BP (SBP; r: 0.530, p<0.002) and ESC SCORE (r: 0.683, p<0.001) but not with diastolic BP (DBP; p>0.05). In patients with recent STEMI aPWV correlated with age (r: 0.301, p<0.001) and ESC SCORE (r: 0.312, p<0.01) but not with DBP (p>0.05). In controls hypertension (5.0±1.4 vs 11.1±3.8 mmHg, p<0.001) and hypercholesterolemia (5.9±2.3 vs 10.9±3.8 mHg, p<0.001) were associated with higher aPWV, but smoking, diabetes and positive family history were not (all p>0.05). In contrast in STEMI patients subjects with hypertension and hypercholesterolemia did not show higher aPWV (all p>0.05). Smoking, diabetes and family history had no impact on aPWV in STEMI patients (all p>0.05).

**Conclusion:** We observed differences in the association of cardiac risk factors with aortic stiffness (aPWV) between healthy subjects and patients after acute STEMI. These results may reflect more aggressive treatment in STEMI patients with aortic stiffness (aPWV) between healthy subjects and patients after acute STEMI. These results may reflect more aggressive treatment in STEMI patients after acute STEMI.

**P1654** Mechanical properties of the aneurysmal sinuses of valsalva: regional and directional variations

D.P. Sokolis1, E.P. Kricharis1, K.M. Lampropoulos1, D.C. Iliopoulos2

1Laboratory of Biomechanics, Foundation of Biomedical Research, Athens, Greece; 2Athens Medical Center, Department of Cardiothoracic Surgery, Athens, Greece

**Purpose:** Information on the mechanical properties of the aneurysmal sinuses of Valsalva is non-available, although this could facilitate our understanding of the pathophysiology of aortic root rupture, which is a biomechanical phenomenon occurring when the strength of the root tissue is overcome by the hemodynamic loads exerted on the sinus wall. Consequently, the objective of the present study was to examine the material properties of the aneurysmal sinuses of Valsalva, as a function of region and direction.

**Methods:** Aneurysmal sinus specimens were obtained from 8 patients (ages 27-82 years, diameters 4.5-9.3 cm), undergoing elective surgery. These were cut into tissue strips that were allocated to groups according to region: Left (LCS) vs. Right (RCS) vs. Non-Coronary Sinus (NCS) and direction: circumferential (CIRC, n=LS=8, nRCS=11, nNCS=17) vs. longitudinal (LONG, nLS=8, nRCS=13, nNCS=17). The tissue strips were tested until failure (wall rupture) on a uniaxial tensile-testing apparatus; failure stress (index of tissue strength), failure strain (index of tissue extensibility), and peak elastic modulus (index of tissue stiffness) were calculated from the experimental data.

**Results:** The biomechanical indices of the LCS and RCS were similar, unlike those of the NCS. Failure stress did not vary in CIRC than LONG specimens from the LCS (92.2±33.2 vs. 70.6±43.7 N/cm², p>0.2) and RCS (79.5±18.7 vs. 72.1±26.1 N/cm², p>0.2), whereas the difference was significant at the NCS (143.6±29.7 vs. 40.5±6.3 N/cm², p<0.002). Similarly was observed for peak elastic modulus (278.5±91.0 vs. 219.6±52.6 N/cm², p<0.2 in LCS; 236.6±51.0 vs. 221.5±61.5 N/cm², p<0.2 in RCS; 534.4±124.0 vs. 120.1±16.4 N/cm², p<0.002 in NCS). Failure strain did not display significant directional variations (0.73±0.07 vs. 0.72±0.09, p=0.2 in LCS, 0.70±0.07 vs. 0.61±0.07, p=0.2 in RCS, 0.75±0.07 vs. 0.66±0.06, p=0.46 in NCS).

**Conclusions:** Our findings are in agreement with the clinical observation of aortic root aneurysm disruption and rupture predominantly occurring at the LCS or NCS. RCS was the weakest region in the CIRC axis and NCS was weakest in 18F-FDG PET uptake indicated increased metabolic activity in the wall of AAA, particularly in the shoulder regions. Both SUVs and TBRs were higher in the shoulder region as compared to the non-aneurysmal aorta; 2.08±0.39 vs 1.75±0.34 (p<0.05) and 1.91±0.34 vs 1.45±0.24 (p<0.05), respectively. Consistent with these findings, there was also USPIO uptake in the aortic wall on MRI scanning (Figure 1). Interestingly, there was accumulation of USPIO but not FDG in the intraluminal thrombus.
the LONG axis. The regional heterogeneity in material properties of the LCS and RCS vs. the NCS may be ascribed to the presence of coronary arteries in the former regions. The present biomechanical information may contribute to the development of more sophisticated criteria for estimation of the risk of complications than the transverse diameter used traditionally.

**P1656 Comprehensive CMR assessment after a transapical-transcatheter aortic valve implantation**

L. Biere,1 F. Pinard,2 S. Delepine,1 F. Routelle,1 N. Virot,2 J.-L. Corbaux,1 F. Prunier,1 J.-L. Debruy,3 S. Willetteau,1 A. Furber1

1University Hospital of Angers, UPRES 3860 (LPRM), Angers, France; 2UMR CNRS 6214-INSERM U771 faculté de médecine d’Angers, Angers, France; 3University Hospital of Angers, department of Anesthesia and Critical Care Medicine, Angers, France; 4University Hospital of Angers, department of Cardiovascular and Thoracic Surgery, Angers, France

**Objective:** To describe the time course of myocardial scarring after a transapical-transcatheter aortic valve implantation (TA-TAVI) with the Edwards SAPIENTM prosthesis in a 3-month follow-up study using cardiac magnetic resonance imaging (CMR).

**Methods:** In 13 TA-TAVI patients, CMR was performed at discharge and 3 months (3M). Cine-MRI was used for left ventricular (LV) functional assessment, and delayed enhancement imaging was employed for detecting the presence of myocardial scar. Special attention was given to any artifacts caused by the prosthesis, which were consequently defined using a three-grade artifact scale.

**Results:** We systematically reported the presence of small delayed hyperintensity relating to the apical segment with no variation found between discharge and 3M (3.2±1.7g vs. 2.9±1.0g). LV ejection fraction, end-diastolic, and end-systolic volumes did not significantly vary. A small area of apical akinesia was observed, with no improvement at follow-up. Unlike the Edwards SAPIEN XTTM prosthesis, the Edwards SAPIENTTM prosthesis was responsible for a larger signal void, thus also observed to be consistent for RN-cuspfusion patterns.

**Conclusions:** Bicuspid valves induced significantly altered AAo hemodynamics compared to tricuspid valves, which may help explain the heterogenic expression of BAV related aortopathy.

![Figure 1. Transmural or subendocardial hyperintensity](https://example.com/figure1.png)

**P1657 Bicuspid aortic valve: association of cusp morphology and aortic hemodynamics**

A. Barker1, M. Mark2, J. Buek3, R. Loreni1, J. Box1, S. Bauer1, J. Schulz-Menger1, F. Von Knebeldorf1,1 Albert-Ludwig University of Freiburg, Department of Radiology/Medical Physics, Freiburg, Germany; 2Northwestern University, Feinberg School of Medicine, Chicago, United States of America; 3Charité Medical Faculty, Experimental and Clinical Research Center, Working Group Cardiac MRI, Berlin, Germany

**Purpose:** Hemodynamics may play a contributing role to the progression of aortopathy in bicuspid aortic valve (BAV) disease. This study measured the wall shear stress (WSS) forces at the wall of the ascending aorta (AAo) in BAV patients.

**Methods:** 4D flow sensitive magnetic resonance imaging was used to examine the jetting, local wall shear stress (WSS), and hemodynamic characteristics in the AAo of 60 subjects. This included 15 BAV patients - 12 with fusion of the right and left (RL) coronary cusp (6 stenotic) and 3 with fusion of the right and non-coronary cusp (RN; 1 stenotic). The RL-BAV cohort was compared to healthy subjects (n=15), age-matched subjects (n=15), and age-AAO size-matched subjects (n=15). Steady-state free-precession cine images of the bicuspid cusps were coregistered with the 4D flow scans to visualize the impact of the valve morphology on aortic flow characteristics.

**Results:** The aortic flow jet propagated in a direction influenced by the type of aortic valve cusp fusion, eventually impinging at AAo wall. For the RL-BAV patients, the position of the jet/wall impingement at the right-atrial anterior position of the AAo correlated to regions of statistically elevated systolic and time averaged WSS (Fig. 1). WSS patterns in the RL-BAV AAo were significantly elevated compared to 0.3 N/m² compared to 0.4±0.3 N/m² in age/aorta size-matched subjects, p<0.001).

**Conclusions:** 3D speckle tracking might offer a new rapid method to quantify LV dysfunction in adult patient with TOF. Among various 3D strain measurements, global longitudinal strain seems the optimal parameter to detect LV dysfunction.

![Figure 1.](https://example.com/figure1.png)

**P1659 Impact of right ventricular restrictive physiology with pulmonary regurgitation on left ventricular myostructure.**

L. Zhong1, J.L. Tan1, T.T. Le1, R.S. Tan2, 1National Heart Centre Singapore (NHCS), Singapore, Singapore; 2Duke-NUS Graduate Medical School Singapore - National Heart Centre Singapore, Singapore, Singapore

**Background and aims:** In patients with repaired tetralogy of Fallot (rTOF), the relationship of right ventricular (RV) restrictive physiology with pulmonary regurgitation and left ventricular (LV) myostructure is unknown.

**Methods:** We studied consecutive patients with prior surgically repaired TOF who were referred for cardiac MR imaging, and compared with those of 10 normal subjects. Cine MR and velocity-encoded MR of the pulmonary trunk were performed. The presence of end-diastolic pulmonary forward flow (EUFF) is a marker of restrictive RV physiology in rTOF. Pulmonary regurgitant fractions (PRF) were derived from pulmonary flow tracing. The LV myostructure end-systolic strain (ε) is determined as: ε = ε = -1.3 ln[(1+3[LVESV]/Wv)²] (1+3[LVESV]/Wv)]², whereas LVESV,
Clinical impact of imaging in congenital heart disease

LVEDV and Vwall are LV end-systolic and -diastolic volumes and myocardial volume. 

Results: See table. In 35 TOF patients (27 ± 13 years old, median 5.50 years old after surgical closure), RVEDV correlated with PRF (r = 0.41, P < 0.05). TOF Patients had reduced +d(21 ±4%) vs ±5 ±3%, P < 0.01) than normal subjects. Patients with restrictive RV had significant higher PRF and smaller index LVEDV and index LVESV, but comparable +d than non-restrictive RV. 

**Table 1**

<table>
<thead>
<tr>
<th>Normal</th>
<th>Non-restrictive RV</th>
<th>Restrictive RV</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVEDV (cm²)</td>
<td>33.7 ± 11.4</td>
<td>22.5 ± 11.4</td>
<td>24.52 ± 10.77</td>
</tr>
<tr>
<td>RVESV (cm³)</td>
<td>19.25 ± 6.9</td>
<td>15.79 ± 6.7</td>
<td>16.01 ± 6.9</td>
</tr>
<tr>
<td>RVFAC (%)</td>
<td>42.0 ± 0.9</td>
<td>38.6 ± 0.4</td>
<td>38.4 ± 0.02</td>
</tr>
<tr>
<td>RVEDV (cm³)</td>
<td>0.1 ± 0.01</td>
<td>0.09 ± 0.01</td>
<td>0.08</td>
</tr>
<tr>
<td>RVFAC (cm²)</td>
<td>1.88 ± 0.06</td>
<td>1.43 ± 0.80</td>
<td>1.81 ± 0.05</td>
</tr>
</tbody>
</table>

Conclusions: This study demonstrates early and significant regression of RV volumes following PVR. This effect is seen as early as 1 month with continued benefit at 18 months. RV function is significantly reduced in the immediate post-operative period and shows a trend to late recovery.

**Table 1**

<table>
<thead>
<tr>
<th>Pre op</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVEDV (cm²)</td>
<td>33.7 ± 11.4</td>
<td>22.5 ± 11.4</td>
<td>24.52 ± 10.77</td>
<td>27.54 ± 10.67</td>
</tr>
<tr>
<td>RVESV (cm³)</td>
<td>19.25 ± 6.9</td>
<td>15.79 ± 6.7</td>
<td>16.01 ± 6.9</td>
<td>17.53 ± 23.3</td>
</tr>
<tr>
<td>RVFAC (%)</td>
<td>42.0 ± 0.9</td>
<td>38.6 ± 0.4</td>
<td>38.4 ± 0.02</td>
<td>44 ± 0.8</td>
</tr>
<tr>
<td>RVEDV (cm³)</td>
<td>0.1 ± 0.01</td>
<td>0.09 ± 0.01</td>
<td>0.08</td>
<td>0.09 ± 0.01</td>
</tr>
<tr>
<td>RVFAC (cm²)</td>
<td>1.88 ± 0.06</td>
<td>1.43 ± 0.80</td>
<td>1.81 ± 0.05</td>
<td>1.88 ± 0.06</td>
</tr>
</tbody>
</table>

**P1660**

Multiparametric assessment of the right ventricle by echocardiography in patients with repaired tetralogy of fallot undergoing pulmonary valve replacement: a comparative study with MRI

J.B. Selly, X. Inari, F. Rouberti, P. Mauriat, J.B. Thambo. University Hospital of Bordeaux - Hospital Haut Leveque, Department of Cardiology, Bordeaux-Pessac, France

Purpose: Evaluation of the right ventricle (RV) using transthoracic echocardiography is challenging in patients with congenital heart disease affecting the right ventricular outflow tract such as Tetralogy of Fallot (TOF). MRI is commonly used to determine the best timing for pulmonary valve replacement (PVR) but accessibility remains limited.

The objective of this study was to evaluate the feasibility and the accuracy of a multiparametric echocardiographic approach including 2D strain and 3D volumes and function assessment, in comparison with MRI.

Methods and results: We performed a complete echocardiographic study including 2D parameters (TAPSE, S’ TDI, T etralogy index, Fractional area change (FAC)), 3D parameters (RV end-diastolic area (RVEDA), RV end systolic area (RVESA), RV fractional area change (RVFAC), tricuspid annular plane systolic excursion (TAPSE), RV tissue Doppler imaging (TDI), and peak main pulmonary artery velocity (MPA).

Results: Results are displayed in Table 1.

**Table 1. Measured Echo parameters pre-op and on follow up**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Pre-op</th>
<th>1 month</th>
<th>3 months</th>
<th>6 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>RVEDA (cm³)</td>
<td>33.7 ± 11.4</td>
<td>22.5 ± 11.4</td>
<td>24.52 ± 10.77</td>
<td>27.54 ± 10.67</td>
<td>25.85 ± 11.81</td>
</tr>
<tr>
<td>RVESV (cm³)</td>
<td>19.25 ± 6.9</td>
<td>15.79 ± 6.7</td>
<td>16.01 ± 6.9</td>
<td>17.53 ± 23.3</td>
<td>16.88 ± 23.6</td>
</tr>
<tr>
<td>RVFAC (%)</td>
<td>42.0 ± 0.9</td>
<td>38.6 ± 0.4</td>
<td>38.4 ± 0.02</td>
<td>44 ± 0.8</td>
<td>38.5 ± 0.05</td>
</tr>
<tr>
<td>RVEDV (cm³)</td>
<td>0.1 ± 0.01</td>
<td>0.09 ± 0.01</td>
<td>0.08</td>
<td>0.09 ± 0.01</td>
<td>0.08</td>
</tr>
<tr>
<td>RVFAC (cm²)</td>
<td>1.88 ± 0.06</td>
<td>1.43 ± 0.80</td>
<td>1.81 ± 0.05</td>
<td>1.88 ± 0.06</td>
<td>1.82 ± 0.09</td>
</tr>
</tbody>
</table>

Conclusions: Our study demonstrates that patients with restrictive RV have significant smaller index LVEDV and have no effect on LV systolic strain compared to non-restrictive RV, although both are significantly reduced compared to normal.

**P1661**

Right ventricular dysfunction in patients with pulmonary atresia and intact ventricular septum

J. Radijovic,1 G. Ashrapdoo,1 V. A. Varkocz,1 E. Bollasshe,1 M. Ladouceur,1 E. Barre1, L. Colide1, A. Redheul1, L. Iserin1, E. Mousseaux1, IAP-HP - European Hospital Georges Pompidou, Paris, France; 2Inserm U878, AP-HP - European Hospital Georges Pompidou, Paris, France

Background: Patients with pulmonary atresia and intact ventricular septum (PAIVS) or critical pulmonary stenosis (PS) have restrictive right ventricular (RV) physiology as defined by the presence of an antegrade flow to pulmonary artery during atrial contraction. Although abnormal RV filling pattern is widely present in PAIVS/PS, little is known about parameters reflecting it, and their impact on cardiac function. The aim of our study was to describe by Cardiac Magnetic Resonance (CMR) imaging parameters of RV diastolic pressure in patients with PA/PS and biventricular repair.

Methods and results: Twenty-five patients (8 males, mean age 30.87 ± 10.99 years), and 25 normal subjects matched for age and sex (mean age 31 ± 9 years) were included. CMR was performed at 1.5 T by using SSFP sequences in axial and short axis views to estimate volumes of the right atrium and right ventricle. Phase contrast (PC) imaging was consecutively obtained in all subjects. Sixteen patients (64%) had an antegrade flow to pulmonary artery during atrial contraction, and none of the controls. There was a significant retrograde flow to inferior vena cava (IVC) during atrial contraction in patient group (100 ± 93 ms vs 17 ± 10 ms, p < 0.001). Right atrium (RA) was dilated, both in systole and diastole (23.9 ± 10.5 cm2 vs 13.2 ± 5.2 cm2, p < 0.001, and 18.7 ± 9.7 cm2 vs 8.5 ± 2.2 cm2, p < 0.001, respectively). Patients had shorter tricuspid E wave deceleration time (154 ± 67 ms vs 251 ± 91 ms, p < 0.001), as well as higher A wave (255.7 ± 118 vs 189 ± 54 ms, p < 0.001). Pulmonary regurgitation (PR) fraction was 53 ± 12%. Right ventricle was dilated both in diastole (111 ± 32 mm2/m2 and in systole (171 ± 56 mm2/m2), with reduced ejection fraction (50 ± 11%).

Conclusion: Our study confirms that majority of patients with PAIVS/PS have restrictive RV physiology with an antegrade flow to PA during atrial contraction. This study demonstrates early and significant regression of RV volumes following PVR. This effect is seen as early as 1 month with continued benefit at 18 months. RV function is significantly reduced in the immediate post-operative period and shows a trend to late recovery.

**P1663**

Impaired right ventricular contractile reserve later after surgical closure of isolated ventricular septal defect

T. Moller1, P.M. Fredskine2, H. Holmstrom3, E. Thaulow3,4.1 North-West Heart Hospital Trust: Department of Paediatrics, Tonsberg, Norway; 2University College of Health Sciences - Campus Kristiania, Oslo, Norway; 3Oslo University Hospital, Department of Pediatric Cardiology, Oslo, Norway

Purpose: Reduced aerobic exercise capacity and abnormally elevated right ventricular systolic pressure during exercise have previously been demonstrated in asymptomatic adolescents after surgical closure of isolated ventricular septal defect (VSD). The current study sought to determine contractile reserve in asymptomatic adults with post-operative VSD. Patients with post-operative VSD were recruited from the Vestfold region in Norway and a subgroup of patients were included in the current study.

Methods: Eleven asymptomatic patients (age 12 – 24 years, 5 females, median age at defect closure 61 months) and 22 healthy age- and gender-matched control subjects were studied by echocardiography at rest and during incremental bicycle exercise until a target heart rate of 160 bpm.

Results: Patients had lower tricuspid annular peak systolic excursion (TAPSE) (17.3 ± 3.9mm) at rest as compared to controls (22.3 ± 2.9, p = 0.002), Correspond-
ingly, the maximal TAPSE during exercise was reduced in the patient group (22.9±3.8 versus 31.4±4.1, p<0.001). Peak systolic tricuspid annular velocity (S') was similar at rest in both groups (patients 9.5±2.7, controls 9.7±1.6, p=0.305), whereas the patient group had lower maximum S' during exercise (12.4±2.6 versus 15.3±2.7, p<0.009). Isovolumetric right ventricular acceleration (IVA), measured in the tricuspid annulus, was reduced in the patient group both at pre-exercise (median 1.3 versus 1.8cm/sec/2, p=0.026, heart rate 92±6÷14.1) and during the highest evaluable exercise stage (median 2.9 versus 4.5cm/sec/2, p=0.014, heart rate 147±1÷85).

Conclusion: Asymptomatic adolescent patients with surgically closed isolated ventricular septal defect have impaired right ventricular contractile reserve.

Methods: Twenty-six patients (11 Fontan and 15 normal patients) underwent echocardiography with intravenous contrast agent (Sonovue®) administration. Dedicated software was used to perform particle image velocimetry (PIV) and to visualize intracavitary flow in the systemic ventricles of the patients. Vortex parameters including vortex depth, length, width, and sphericity index were measured. Vortex pulsatility parameters including relative strength, vortex relative strength, and vortex pulsation correlation were also measured.

Results: Vortex length (VL) was significantly lower in Fontan patients (0.54±0.102 versus 0.65±0.125, P=0.024). Vortex width (VW) was higher (0.36±0.093 versus 0.27±0.044, p=0.014) and sphericity index (SI) was lower (1.56±0.439 versus 2.42±0.626, p=0.001) in the normal group. Relative strength (RS) (0.756±0.517 versus 1.90±0.471, p=0.009) and vortex relative strength (VRS) (0.190±0.133 versus 0.433±0.141, p=0.001), were significantly lower in the Fontan patients group.

Conclusions: Fontan patients had aberrant flow patterns as compared to normal hearts in terms of position, shape, sphericity and direction of the main vortices. Whether vortex characteristics are related with clinical outcome is subject to further investigation.

Methods: Twenty-three patients with a fenestration extracardiac conduit prospectively underwent investigation by cardiac magnetic resonance (CMR), echocardiography, and invasive manometry under the same general anesthetic 12±4 months after Fontan surgery. Fenestration flow was determined using phase contrast CMR either by subtracting flow in the Fontan pathway above the fenestration from Fontan flow below the fenestration or by direct measurement (12 patients, Figure).

Results: Measured and calculated fenestration flows showed an excellent agreement (r=0.92, p<0.0001, Figure). Fenestration flow constituted a mean of 31±12% (range 8-50%) of ventricular preload. It was associated with a lower Qp/Qs (r=-0.64, p=0.001) and oxygen saturation (r=-0.74, p=0.001). Fenestration flow volume correlated with pulmonary vascular resistance (r=0.45, p=0.044) and markers of ventricular diastolic function (early diastolic strain rate r=0.57, p=0.008 and ventricular untwist rate r=0.54, p=0.02). In 14 patients (61%) all of the net inferior vena cava flow and part of the superior vena cava flow were diverted into the systemic atrium and did not reach the lungs. The magnitude of contribution of fenestration flow to ventricular preload was the most important predictor of ability to close the fenestration.

Conclusion: Fenestration flow can be measured accurately with CMR. The amount of fenestration flow is related both to the pulmonary vascular resistance and systemic ventricular diastolic ventricular function, and may be used to predict hemodynamic suitability for fenestration closure.

Introduction: Myocardial ischemia may represent an important risk factor for sudden cardiac death and infarction in patients with congenital or acquired heart disease.

Purpose: In order to avoid ionising radiation inherent to PET and SPECT imag-

Clinical impact of imaging in congenital heart disease 261
ing, we utilized advanced magnetic resonance imaging (MRI) methods to assess myocardial blood flow and viability.

**Methods:** MRI first-pass perfusion imaging (0.03 mmol/kg Gd-DTPA; TR/TSE=2.61,1.020) was performed in 18 patients with suspected ischemia (age: 0.3–21 years; transposition of the great arteries post arterial switch operation n=12, anomalous origin of the left coronary artery (ALCAPA) pre operation n=2, post operation n=3, Kawasaki syndrome n=2, aberrant coronary artery n=1). Myocardial blood flow (ml/min) was calculated in 6 LV segments per slice (2.3 slices/pt). Quantitative blood flow at rest and stress (Adenosin 140 μg/kg/min) was derived from signal intensity curves with model independent deconvolution. Late enhancement studies (Gd 0.1 mmol/kg) using T1 weighted inversion recovery sequences were performed to detect myocardial scarring. Furthermore cine MRI and 3D perfusion imaging was performed to assess ventricular function and coronary anatomy. All CMR results were compared to conventional x-ray guided coronary angiography.

**Results:** Myocardial blood flow was significantly reduced at stress due to an occlusion of the left coronary (n=3) or circumflex artery (n=1) artery and a hypoplastic left anterior descending artery in one. Another pt showed subendocardial ischemia but normal coronary arteries. Scar tissue was detected in the antero-septal region of two patients. MR-perfusion imaging during hyperemia showed severe myocardial ischaemia in the antero-septal wall of the LV in the patient with aberrant LCA. Late enhancement imaging showed viable myocardium in the corresponding region. Therefore this patient and one TGA pt received minimal invasive direct coronar artery bypass (MIDCAB) surgery for revascularisation using the left mammary artery. Post operative MRI showed normal myocardial perfusion and function and in both pts. Two ALCAPA pts received corrective coronary surgery. The Kawasaki pts did not require any intervention other than medical therapy. Good agreement was found between MR-perfusion and viability imaging, wall motion analysis and invasive coronary angiography.

**Conclusions:** In children with congenital or acquired coronary artery disease stress-induced perfusion defects and scar tissue can be detected with MRI in order to guide further therapy such as surgical revascularisation.

**Variations of coronary anatomy assessed by non-invasive computed tomography coronary angiography in infants with transposition of the great arteries after arterial switch operation**

C.E. Velthuis1, S.L.M.A. Beeres1, D.N. Kalkman2, M.G. Hazekamp2, J.J. Baas1, K.M. van der Graaf1, M.R.M. Jongbloed1,1 Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands; 2 Leiden University Medical Center, Department of Cardiothoracic Surgery, Leiden, Netherlands.

**Purpose:** In the current study the occurrence of coronary anatomy variations in adult patients with congenital transposition of the great arteries (TGA) corrected by arterial switch operation (ASO) was assessed with the use of non-invasive computed tomography coronary angiography (CTA).

**Methods:** The study population consisted of 23 adult patients (age 21±3 years) with TGA corrected by ASO in whom CTA was performed. Coronary anatomy on CTA was assessed according to the Leiden Classification. In addition, the presence of coronary artery stenoses was evaluated and the angle at which the coronary artery originated from the neo-aorta was measured. An angle of <30° was defined as a sharp angle coronary origin. In addition, patients were clinically evaluated at the outpatient clinic and echocardiography was performed.

**Results:** On CTA post-operative coronary anatomy was 1R-2LCx in 18 patients (78%), 1RxC-2L in 4 patients (17%) and in one patient 2RxCx (4%). In one patient significant coronary artery ostial stenoses (stenoses of >50%) was observed. Remarkably, an interarterial coronary course was observed in 5 patients (22%) (example case in Figure 1) and another 6 patients (26%) had a sharp angle coronary origin. During a clinical follow-up patients with interarterial coronary course reported more cardiac complaints and had slightly lower left ventricular ejection fraction on echo.

**Conclusions:** In the present study CTA demonstrates that a potential malignant coronary artery pattern is frequently observed in adult patients with TGA corrected by ASO.
Leftward bulging of atrial septum is induced by nitroglycerine and exaggerated during the strain phase of valsava.

**Background:** Leftward bulging of the interatrial septum (LBA) is a requirement for detection of patent foramen ovale (PFO) during contrast echocardiography. On release of Valsalva strain contrast free blood from inferior vena cava often sweeps contrast away from foramen ovale. We examined the effect of nitroglycerine on LBA during rest and Valsalva strain.

**Methods:** Patients with obstructive sleep apnea had been screened for PFO with contrast TEE. The interatrial septal motion was at least 10 mm in thirteen patients and they were chosen for this retrospective analyses. Video recordings from periods during the exam without contrast injections exams were visually analyzed for the presence/absence of LBA defined as a leftward shift and leftward convexity of the septum. A beat was defined as LBA when there was any period of LBA during the heart cycle. Periods of resting respiration and during Valsalva strain before and after nitroglycerine spray with foot down bed tilt were analyzed. The analysis was made by two observers, blinded to each other. Discrepancies were then settled in consensus.

**Results:** We studied 1,772 beats distributed to 146 periods. After nitroglycerin the systolic blood pressure decreased from 132±17 to 136±1.7 mmHg (P=0.006). The proportion of LBA increased significantly during resting respiration from 21±22% to 83±6% (P<0.001). After Valsalva strain from 48±17% to 80±17% (P=0.001). After nitroglycerin LBA occurred in at least three beats during all 37 studied Valsalva strain periods and the first LBA during Valsalva strain period occurred after 4±2 beats.

**Conclusion:** Nitroglycerine administration induces LBA both in resting respiration and in Valsalva strain. During Valsalva strain nitroglycerine induce some LBA in 100% of strain periods. Nitroglycerine reduces left atrial pressure more than right atrial pressure. Nitroglycerine administration may increase sensitivity for PFO detection and the strain period of Valsalva is an alternative to the Valsalva release period for detection of patent foramen ovale.

---

Assessment of left atrial mechanics after percutaneous closure of patent foramen ovale.

**Purpose:** Evaluation of left atrial (LA) size and function using conventional and more recent echocardiographic parameters is potentially feasible in the routine clinical setting. However, the influence of the few sutures placed in the left atrial function after percutaneous closure of patent foramen ovale (PFO) has not been thoroughly studied.

**Methods:** Over a period of 40 months, 50 patients (pts) with PFO were referred to our centre for clinically indicated percutaneous PFO closure. Among them 25 pts (mean age 40.7±12 years) were enrolled in our study due to cerebrovascular events and transient ischemic attacks. Transthoracic echocardiogram was performed in all pts before the procedure, at 3 and 6 months after the intervention. Pulsed LA volume were measured and volumetric indices were derived accordingly. Strain and strain rate were calculated in all 25 pts for the lateral, anterior and inferior LA walls. Peak strain and strain rate values were measured during the contractile, reservoir and conduit LA phases. A transesophageal echocardiogram was also undertaken at the 6-month follow-up to verify complete closure of the defect.

**Results:** All patients completed the procedure uneventfully and at 6-month follow-up the closure appeared intact. For the LA lateral wall, the total 3 values were correlated with the LA volumetric indices (LA active emptying fraction: LA AEF; LA passive filling fraction: LA PEF). After 3 months a decrease in the strain rate of the anterior wall of LA was observed (from 2.1±0.22 to 1.66±0.26; P=0.045), while LA AEF was greater compared to baseline from 31±0.1±6 to 34±0.1±6; P=0.004.

**Conclusion:** Closure of patent foramen ovale with a PFO occluder results in altered LA function. In specific, the anterior atrial wall, where the device is placed, is the more affected. However, total LA systolic function improves probably due to the fact that the device provides a more rigid surface, which enables a more forceful atrial contraction. Strain and strain rate represent a promising tool in the evaluation and follow-up of patients who have undergone PFO closure.
Effect of advanced therapy on right ventricular function in patients with congenital heart disease and severe pulmonary hypertension

M.G. Ageletak, L. Griffiths, V.S. Mahadevan. Manchester Royal Infirmary, Manchester Heart Centre, Manchester, United Kingdom

Purpose: To retrospectively analyze the effect of bosentan on echocardiographic right ventricular parameters in this group of patients. Prospectively collected data from adult patients with PAH-CHD initiated on bosentan over a period of 2.5 years were analyzed. Baseline echocardiographic parameters including right atrial (RA) volume, right ventricular (RV) wall thickness, TAPSE, RV flow velocities, right ventricular myocardial performance index (RV MPI) were analyzed prior to therapy initiation (baseline) an at the last follow-up. All patients were on a dose of 125mg bd. Patients also had assessment of exercise tolerance using continuous 6 minute walk distance (6MWD) testing. Complete data were available and analyzed from 14 patients with PAH-CHD (4 with Down syndrome, 11 female) who had received bosentan for a mean duration of therapy 17.5±7 months. Three of the patients were also on concomitant sildenafil treatment.

Methods: A significant average improvement in 6MWD (46 m as compared to baseline, p=0.047), on mean follow up was observed. No evidence of drop in systemic saturations were observed. The echocardiographic parameters for the assessment of right heart function are given in Table 1 as mean values ± standard error of the mean. Statistical analysis was performed using paired t tests and Wilcoxon non-parametric test.

Results: There was evidence of a trend in reduction of RV thickness on follow up but did not reach statistical significance. There was no major change in other RV functional parameters. Bosentan does not appear to significantly change right ventricular echocardiographic parameters in PAH-CHD patients. However a larger study is necessary to assess this in further detail.

Efficacy of exercise training in pulmonary arterial hypertension in grown-up congenital heart disease

T. Becker-Grueng1, N. Ehlken1, M. Gorenflo2, A. Hager1, M. Halank1, M. Lichtenblau1, F. Reichenberger1, R. Specht1, E. Grueng1, 1Department of Pulmonary Hypertension, Thoraxklinik at the University of Heidelberg, Heidelberg, Germany; 2Department of Pediatric Cardiology and Congenital Heart Diseases, University of Heidelberg, Heidelberg, Germany; 3Department of Pediatric Cardiology and Congenital Heart Diseases, Technische Universität München, Munich, Germany; 4Department of Pneumology, Technical University of Dresden, Dresden, Germany; 5Department of Pneumology, University of Giessen and Marburg, Giessen, Germany; 6Pulmonary Hypertension Program, University Hospital, Zurich, Switzerland

Objective: This prospective study was to assess the efficacy of exercise training as add-on to medical therapy in patients with pulmonary arterial hypertension associated with congenital heart disease (CHD-APAH).

Methods: Patients with invasively confirmed CHD-APAH received in-hospital exercise training for 3 weeks and continued at home. Efficacy parameters were evaluated at baseline, after 3 weeks and 15 weeks. Medical treatment remained unchanged during 15 weeks after baseline. The survival rate was assessed in a follow-up period of 21±14 months.

Results: Twenty consecutive patients (16 female, 4 male, mean pulmonary arterial pressure 60±23 mmHg, 9 patients were operated, 10 ASD, 11 VSD, 1 PFO, 2 PDA, 10 Eisenmenger syndrome) were included. Patients significantly improved the mean distance walked in 6 minutes compared to baseline by 63±47 meters after 3 weeks (p=0.001) and by 67±59 meters after 15 weeks (p=0.001). Qual- ity of life score (p=0.050), peak oxygen uptake (p=0.002) and maximal workload (p=0.003) improved significantly by exercise training after 15 weeks. The 1- and 2-year survival rates were 100%. In one patient lung transplantation was performed 1 year after exercise training.

Conclusion: Exercise training as add-on to medical therapy may be effective in patients with CHD-APAH, improving quality of life, work capacity and further prognostic relevant parameters. It was also associated with an excellent long-term survival. Further randomized controlled studies are needed to confirm these results.

Contemporary therapy in pediatric pulmonary hypertension (PH)-results from the global registry tracking outcomes and practice in pediatric pulmonary hypertension (TOPP)

T. Humpl1, R.J. Bars2, R. Kronma2, R.M.F. Berger4, D. Moore4, M.S. Fasnacht Bolliat3, M. Zik3, M. Buehlig3, I. Schulze-Neick5. Hospital for Sick Children, Division of Cardiology, Toronto, Canada; 3Columbia University, New York, United States of America; 4University of Washington, Seattle, United States of America; 5University Children's Hospital, University Hospital Groningen, Groningen, Netherlands; 6Vanderbilt University, Nashville, United States of America; 7University Children's Hospital, Department of Cardiology, Zurich, Switzerland; 8The Children's Memorial Health Institute, Warsaw, Poland; 9Children's University Hospital of Geneva, Geneva, Switzerland; 10Great Ormond Street Hospital for Children, London, United Kingdom

Purpose: The global registry TOPP collects data on demographics, clinical status and outcomes in pediatric PH. One of the primary objectives was to describe current medical therapy. Treatment decisions were made by site clinicians without TOPP involvement.

Methods: 31 sites from 19 countries enrolled patients (diagnosis of/after January 2001, enrollment 2008-2010, age 3 months - 18 years at confirmatory right heart catheterization). PH was defined as: mPAP >25 mmHg, PCWP <15 mmHg and mPAP/PCWP >3 units x m². PH targeted therapy (PHTT) included prostacyclin and its analogs (PGls), endothelin receptor antagonists (ERAIs) and phosphodiesterase inhibitors type 5 (PDE5Is). Calcium channel blockers (CCBs) were considered as PHTT in responders to acute vasodilator testing. Supportive therapy included antiocoagulation, oxygen, diuretics and/or digitalis.

Results: Of the 456 patients enrolled, 362 (79%) met all entrance criteria with...
Does the pulmonary vascular resistance predict outcome in the modern era?

M. Marla1, C. Jameson1, A. Bell2, R. Tullah1. 1University Hospitals Bristol NHS Foundation Trust, Bristol Royal Hospital for Children, Bristol, United Kingdom; 2Evelina Children’s Hospital, London, United Kingdom

Background: Paediatric pulmonary hypertension (PH) is common in congenital heart disease. The gold standard investigation is cardiac catheterization for calculation of pulmonary vascular resistance (PVR). Since 1958 there has been little information about the changing link with outcome, which is likely to have improved with modern surgical and intensive care and advanced pulmonary vasodilator therapy (DFT).

Aims: To determine the outcome of decision-making after cardiac catheterisation in the modern era.

Methods: All children undergoing PVR study from 1996-2011 were prospectively included. The entry criteria was a tricuspid regurgitant velocity of >2.8m/s with clinical or echocardiographic evidence of a raised PVR. Catheterization followed the standard protocol by one operator (measurement at baseline, in 10ppm Nitric oxide, 20ppm NO and then 20ppm NO +100% oxygen, with measured oxygen consumption). Outcome measures included survival, need for medication, persistence or resolution of PH as defined by echocardiography.

Results: 176 studies were performed on 169 children. The median (range) age was 380 (21-10038) days. 103 had PH associated with un-operated congenital heart disease (aPAH-CHD). Of these, 54 had Down syndrome and 7 had tetralogy of Fallot. 58 had idiopathic pulmonary arterial hypertension and 6 had other conditions, such as hepato-pulmonary syndrome (some children having more than one condition). The mean PVR at baseline was 9.4±4.2mmHg, falling to 5.3±2.3mmHg at 20ppmNO and 2.0±1.1mmHg at 100ppmNO oxygen. 9 had severe pulmonary arterial hypertension with a PVR >15mmHg. 34 had pulmonary vein stenosis and 72/103 had AVSD or VSD. There were 35 who were postoperative with CHD (of whom 14 had Down syndrome), 24 children had chronic lung disease, 5 had idiopathic pulmonary arterial hypertension and 6 had other conditions, such as hepato-pulmonary syndrome (some children having more than one condition). The mean PVR at baseline was 9.4±4.2mmHg, falling to 5.3±2.3mmHg at 20ppmNO and 2.0±1.1mmHg at 100ppmNO oxygen. 9 had severe pulmonary arterial hypertension with a PVR >15mmHg. 34 had pulmonary vein stenosis and 72/103 had AVSD or VSD. There were 35 who were postoperative with CHD (of whom 14 had Down syndrome), 24 children had chronic lung disease, 5 had idiopathic pulmonary arterial hypertension and 6 had other conditions, such as hepato-pulmonary syndrome (some children having more than one condition). The mean PVR at baseline was 9.4±4.2mmHg, falling to 5.3±2.3mmHg at 20ppmNO and 2.0±1.1mmHg at 100ppmNO oxygen. 9 had severe pulmonary arterial hypertension with a PVR >15mmHg.

In GI the PAP ranged between 16-63mmHg (mean 32.8±9.2). In GI, 20-140mmHg (mean 42.1±26.4) and in the control group 12-25 mmHg (mean 20.4±4.9mmHg). PAP was raised in 40% of infants in GI (mean 44.8±9.4) while the rest had a normal PAP in GI. In 55% of the patients (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) and a non significant difference between GI and GII (P=0.137). Follow- ing treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9).

Conclusion: A dosing regimen consisting of a dose of 10 mg for children up to 20 kg, and 20 mg above 20 kg is predicted to result in a sufficiently high responder rate on VO2peak in children between 7-17 years. This recommended dose regimen applied to children between 1-17 years is also predicted to result in a VO2peak response similar to or better than that seen at the labeled adult dose of 20 mg TID and showed a favourable B/R for long term survival.

Effect of bronchopneumonia on pulmonary artery pressure in infants with and without left to right cardiac shunts

A. Kotby1, M.A. Shaheen1, W.M. Elgindy1, M. Khalifa2. 1Ain Shams University, Children’s Hospital., Cairo, Egypt; 2Ain Shams University, Cairo, Egypt

Purpose: To study the effect of acute bronchopneumonia on the pulmonary artery pressure (PAP) in infants with and without left to right cardiac shunts and follow up the rate of decline of the raised PAP if present.

Methods: 60 infants (mean age of 5.2±2.6 month) were divided into 3 groups: GI: included 20 infants with bronchopneumonia, GII: 20 infants with left to right cardiac shunts (VSD: 11, ASD: 6, PDA: 1 and ASD and VSD: 2) and bronchopneumonia, and GIII: were 20 healthy normal controls. Patients were subjected to full clinical examination, pulse oximetry, X ray, ECG, and echocardiographic evaluation.

Results: PAP was measured using the tricuspid regurgite peak velocity. Pulmonary artery systolic peak velocity equivalent to right ventricular systolic pressure was FVSP= 4v2 + RAPv, the systolic regurgitant tricuspid flow velocity and RAP is right atrial pressure. PAP was estimated at admission and one month later following complete resolution of the bronchopneumonia.

In GI the PAP ranged between 16-63mmHg (mean 32.8±11.5), in GI: 20-140mmHg (mean 42.1±26.4) and in the control group 12-25 mmHg (mean 20.4±4.9mmHg). PAP was raised in 40% of infants in GI (mean 44.8±9.4) while the rest had a normal PAP in GI. In 55% of the patients (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001) but a non significant difference between GI and GII (P=0.137). Following treatment with sildenafil, children who did not have a normal PAP in GI 55% had an increased PAP (mean 55.9±26.9). There was a highly significant increase in the mean PAP in GI & GII than control (P<0.001).
heart failure occurred more commonly in the conventional treatment arm compared with propranolol treated arm (27.5% vs. 5%; respectively; p = 0.015). Two patients in the conventional treatment arm and in 1 patient in propranolol arm died. No episodes of bradyarhythmia or bronchospasm were reported with propranolol treatment.

Conclusions: The addition of propranolol was well tolerated by infants with VSD and heart failure. Addition of beta-blocker over and above the conventional treatment leads to symptomatic improvements and reduces worsening of heart failure. However, there was no difference in the death, hospitalization or need for surgery.

Result: Eighty-eight adult patients (68.4% male, mean age 34±10 years) were randomized (valsartan n=44, placebo n=44). Two patients (valsartan n=1, placebo n=1) died during follow-up and eight withdrew consent, leaving 76 patients (valsartan n=38, placebo n=38) for analysis. Overall, there was no change between baseline and follow-up in RV EF in either the valsartan (ΔRV EF: -0.28%, p=0.79) or the placebo group (1.00%, p=0.23). V'O2peak declined in both groups to a similar extent (ΔV'O2peak: valsartan -2.6 ml/kg/min, p=0.02, placebo -2.6 ml/kg/min, p=0.01). However, in symptomatic patients (valsartan n=8, placebo n=14) valsartan had a significant beneficial effect of 4.7% on RV EF (p=0.02). In this subgroup, valsartan protected against further deterioration of VO2 peak, but this effect was not significant.

Conclusions: Valsartan has a beneficial effect on RV EF in symptomatic patients with a systemic right ventricle. Moreover, deterioration of VO2peak was less in the valsartan group than in the placebo group.

P1685 Bosentan treatment in mildly impaired Fontan patients: a randomized controlled trial

M.J. Schuurij1, J.C. Vis1, B.J. Bouma1, A.P.J. Van Dijk2, J.P. Van Melle1, P.G. Pieper3, H.W. Vliegen4, G.T. Sieswerda5, B.J.M. Mulder1, 1Academic Medical Center, Department of Cardiology, Amsterdam, Netherlands; 2Radboud University Nijmegen Medical Centre, Department of Cardiology, Nijmegen, Netherlands; 3University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; 4Leiden University Medical Center, Department of Cardiology, Leiden, 5University Medical Center Utrecht, Department of Cardiology, Utrecht, Netherlands

Purpose: Low pulmonary vascular resistance (PVR) is crucial to patients with a Fontan circulation for survival. In Fontan patients, PVR is elevated in patients with Fontan circulation. We aimed to determine whether an endothelin-1 receptor antagonist improves exercise capacity in Fontan patients.

Methods: The study was a prospective, multicenter randomized open label trial. One group received bosentan for six months. The other group did not receive study medication for the first three months, followed by treatment with bosentan for six months. Primary endpoint was exercise capacity (peak V'O2) and secondary endpoints were Short Questionnaire to Assess Health (SQUASH) score, NYHA class, NT-pro-BNP levels and SF-36 quality of life (QoL).

Results: Forty-two participating patients (median age 29 range 18 - 56 years), 52% male, 92% NYHA II-III were included from four referral centers. Ten patients were not motivated to finish the study Analysis of all patients who finished the study at six months of treatment showed that mean peak V'O2, median SQUASH score, NYHA class, median NT-pro-BNP level and QoL remained unchanged as compared to baseline. Symptomatic patients (NYHA II-III) were no different in endpoints as compared to asymptomatic patients (NYHA I). Seven patients reported mild adverse effects.

Peak exercise capacity: Fontan patients treated for six months with bosentan

Conclusion: In our ongoing study with relatively mildly impaired Fontan patients, bosentan was not beneficial in our current analysis. Results from all visits are available within a few months.

P1686 Cardiac transplantation in adult Congenital Heart Disease

M. Brown, K.W. Chee, S.C. Mckenzie, D.G. Platts, G. Javorsky. The Prince Charles Hospital, Brisbane, Australia

Background: Patients with complex congenital heart disease (CHD) are surviving into adulthood due to increased success of surgical procedures and specialist grown-up CHD units. Deterioration in adult CHD patients may require cardiac transplantation which has been associated with increased mortality in this subgroup of patients.

Method: We performed a retrospective analysis of CHD patients who underwent heart transplantation at our institution (1990 to 2012). We evaluated diagnosis, aetiology, surgical methods, perioperative issues and outcomes. Results: 2.4% (8/327) cardiac transplants were performed for adult CHD (7 heart, 1 heart-lung). Mean age = 30.1 years (range 9 - 45). Diagnosis: Tetralogy of Fallot = 3; Transposition of Great Vessels with truncus arteriosus = 2; Tricuspid Atresia = 1; double outlet hypoplastic right ventricle with pulmonary stenosis and VSD = 1; VSD, ASD and PDA = 1. Prior cardiothoracic surgery episodes = 2.25 (range 1-5). Bypass time = 280 minutes (98-579). Red blood cell transfusions = 20.6

Reference text: Eplerenone in systemic right ventricle, a randomized placebo-controlled clinical trial: the EDEVES study

D. Subira, S. Puigcastel, M. Estruch1, A. Mas1, M.A. Pijana, R. Serra1, J. Ordonez1, I. Ferrera-Gonzalez1, M.T. Subirana2, J. Casalsalada1, 1Hospital Universitari Vall d’Hebron, Barcelona, Spain; 2Hospital de la Santa Creu i Sant Pau, Department of Cardiology, Barcelona, Spain; 3Hospital de la Santa Creu i Sant Pau, Department of Biochemistry, Barcelona, Spain

Background: There is still no proven pharmacological strategy for the treatment of the failing systemic right ventricle (SRV). However, there is growing evidence that myocardial fibrosis may play a role in its pathophysiology.

Methods: We conducted a collaborative bicenter, double-blind, placebo-controlled clinical trial to assess the effects of eplerenone 50mg during 12 months on VO2peak, measured by cardiac magnetic resonance and neurohormonal and collagen turnover biomarker (CTB) levels.

Results: Twenty six patients with atrial switch repair for transposition of the great arteries were included in the trial. Plasma endothelin-1 levels were in NYHA class 3 patients suggesting this good baseline situation, levels of N-terminal pro-brain natriuretic peptide (NT-proBNP: 188.3±125.7 pg/mL), C-terminal propeptide of type I procollagen (CICP: 267.8±184.1 ng/mL), C-terminal telopeptide of type I collagen (ICTP: 4.59±2.6 μg/L), the CTB profile with a good baseline as expected.

Conclusion: Eplerenone showed an improvement of the CTB profile suggesting that reduction of myocardial fibrosis may play a role in its pathophysiology.
A simple risk score predicting clinical right ventricular failure after congenital cardiac surgery in adults

M.J. Schuring1, C. Gulik1, B.J. Bouna1, D.R. Koelbergen2, M.G. Hazekamp3, W.K. Lagrand4, B.J.M. Mulder5, 1Academic Medical Center, Department of Cardiology, Amsterdam, Netherlands; 2Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands

Background: Right ventricular (RV) failure is a life-threatening syndrome characterized by edema, hypotension and in worse cases shock or multi organ failure. Congenital heart disease (CHD) patients often undergo right-sided surgery, and contribution of the RV to their cardiac pump function is essential. We aimed to identify determinants of RV failure after cardiac surgery and to determine prognosis of CHD patients.

Methods: Adults with CHD operated between January 2001 and January 2011 in the Medical Center were studied. Clinical characteristics, laboratory tests, surgical data and intensive care unit outcome were obtained from medical records. The diagnosis of clinical RV failure was made by careful review of the medical records by two independent physicians. Determinants of clinical RV failure were identified by logistic regression analysis.

Results: Data of 412 consecutive patients (median age 36 (range 18–74) years, 56% male) were studied. Eighteen patients were diagnosed with clinical RV failure (4.4%), of which six patients died. A risk score incorporating significant determinants of multivariate analysis identified low-, medium- and high-risk subgroups, with a risk score of 1 or more episodes 3R rejection = 83%. Post transplant complications were stage II or III chronic kidney disease n=2, chronic myopathy and/oedema at 10 years n=1. All survivors had a LVEF greater than 50% at last review. Mean follow up = 8.3 years (range 0.17 years).

Conclusions: In CHD patients the use of a simple risk score based on multiple risk factors of multivariate analysis identified low-, medium- and high-risk subgroups, with a risk score of 1 or more episodes 3R rejection = 83%. Post transplant complications were stage II or III chronic kidney disease n=2, chronic myopathy and/oedema at 10 years n=1. All survivors had a LVEF greater than 50% at last review. Mean follow up = 8.3 years (range 0.17 years).
were collected from the medical records. Logistic regression analysis was performed to identify determinants of residual PAH.

**Results:** Of all 630 patients from a tertiary referral center with a history of a left-to-right shunt, 405 patients had undergone closure of this shunt (median age 35 years, 44% male). The prevalence of residual PAH in this group was found to be 8.4% (n=34). In patients with impaired exercise capacity (NYHA class ≥ II) and age above 40 years the prevalence of PAH was 52% (n=13). In multivariate analysis, age above 40 years and impaired exercise capacity were significant determinants of residual PAH (OR 11.5, 95%CI 4.4 – 30). Furthermore, patients aged 25 years or older at the time of closure were at increased risk for residual PAH (OR 4.0, 95%CI 2.0 – 8.2). No association was found with type of defect.

**Conclusion:** A considerable amount of patients with a closed left-to-right shunt have residual PAH. Patients at highest risk for residual PAH were those with impaired exercise capacity, age above 40 and those in whom closure was performed above 25 years of age.

**Figure 1. The variation of Ea, Ees and Ea/Ees**

**Conclusion:** Continuous increase in Ea values and deterioration of the contractility-afterload mismatch may indicate the onset of PLE after the Fontan operation.
Higher baseline LVOT gradient was associated with an impaired freedom from intervention (HR 2.9 (1.9-4.7)).

Conclusions: DSS progresses slowly in adulthood. However, patients with associated congenital anomalies are at risk for faster disease progression and should be monitored cautiously.

P1694 Natural history of the bicuspid aortic valve: long term prevalence and predictors of clinical outcome

V. Leen riffetti, M. Bobbo, R. Piazza, E. Leibali, P. Roccario, M. Cinelle, R. Mimo, E. Cervesato, G.L. Nicolosi, Santa Maria degli Angeli Hospital, Department of Cardiology, Pordenone, Italy

Purpose: Aim of our retrospective study was to describe the long term natural clinical history of a population with bicuspid aortic valve (BAV).

Materials and methods: Standard for inclusion was the presence of BAV at ultrasound examination. We collected history and echocardiographic data at enrollment, mid-term and last follow-up. We considered aortic valve replacement, aortic surgery and death as clinical end points and focused on prevalence, determinants and evolution of complications (stenosis, regurgitation, dilation, aneurysm, dissection and endocarditis). Predictors for the progression of the disease and predictors of outcome were determined by logistic regression.

Results: Our study included 392 out of 7194 patients (0.4%) consecutively referred for echocardiographic examination to our Department in the period between 09/1986 to 09/2011. Mean duration of follow-up was 10.4±5.4 years. At baseline 35% of patients were ≤30 years of age, 40% were >30 years of age at first examination was 27±19 years. BAV was associated with other congenital cardiac malformation in 36 cases (12%); aortic coarctation in 22 of them. Natural history: aortic valve (31.8%) were hypertensive. Prevalence of complications at baseline was: 15 patients (6.4%) with at least moderate aortic stenosis, 57 patients (24.6%) with at least moderate aortic regurgitation, 113 patients (37.4%) with aortic dilation (defined as an aortic ratio ≥1.1 calculated on the basis of the expected aortic diameter using Roman’s formula) and 19 patients (6.2%) with aortic aneurysm (aortic ratio >1.5). We found significant association at baseline between systemic hypertension and the complications of the disease, and between baseline aortic aneurysm at least moderate degree and aortic dilation/aneurysm at baseline. There was a trend toward significance for age and at least moderate aortic regurgitation as predictors of late outcome, while aortic aneurysm at baseline was confirmed to be a strong predictor of late outcome (odds ratio [OR]: 2.98; 95% confidence interval [CI], 2.98-156; P < .001). Sixty four patients (21.2%) underwent aortic valve replacement and/or aortic surgery during follow-up. Eight patients died (5 due to cardiovascular causes); mean age at death was 62±24 years.

Conclusions: BAV has a prevalence of 0.4% in our echocardiographic community. Different from other reports, our series was composed mostly by young patients. Indication to surgery was more frequently related to aortic regurgitation and aortic aneurysm. Long term follow-up showed low cardiovascular mortality (1.6%) and high prevalence of complication leading to surgery (21.5%).

P1695 Repair ventricular dilation in pulmonary regurgitation after repair of Tetralogy Of Fallot: how fast does it progress?

F. Bonassini1, S. Navarin2, C.J. Kellenberger3, M. Greutmann1, M. Mocetti1, E. Valsangiacomo Bucheli1, 1University Hospital Zurich, Cardiovascular Center, Department of Cardiology, Zurich, Switzerland; 2University Children’s Hospital, Department of Cardiology, Zurich, Switzerland; 3University Children’s Hospital, Zurich, Switzerland

Purpose: Repair of tetralogy of Fallot (TOF) is generally performed in the first year of life with low morbidity and mortality. Progressive pulmonary regurgitation (PR) is the most common long-term sequela after TOF repair. Severe PR may lead to right ventricular (RV) dilation, RV dysfunction and ventricular arrhythmias. Pulmonary valve replacement is thus advocated in patients with progressive RV dilation and/or dysfunction as measured by serial cardiac imaging. In this cardiac magnetic resonance (CMR) study we sought to assess the rate of progression of RV dilatation and to determine associated factors.

Methods: Our study included 302 out of 7194 patients (0.4%) consecutively referred for echocardiographic examination to our Department in the period between 09/1986 to 09/2011. Mean duration of follow-up was 10.4±5.4 years. At baseline 35% of patients were ≤30 years of age, 40% were >30 years of age at first examination was 27±19 years. BAV was associated with other congenital cardiac malformation in 36 cases (12%); aortic coarctation in 22 of them. Natural history: aortic valve (31.8%) were hypertensive. Prevalence of complications at baseline was: 15 patients (6.4%) with at least moderate aortic stenosis, 57 patients (24.6%) with at least moderate aortic regurgitation, 113 patients (37.4%) with aortic dilation (defined as an aortic ratio ≥1.1 calculated on the basis of the expected aortic diameter using Roman’s formula) and 19 patients (6.2%) with aortic aneurysm (aortic ratio >1.5). We found significant association at baseline between systemic hypertension and the complications of the disease, and between baseline aortic aneurysm at least moderate degree and aortic dilation/aneurysm at baseline. There was a trend toward significance for age and at least moderate aortic regurgitation as predictors of late outcome, while aortic aneurysm at baseline was confirmed to be a strong predictor of late outcome (odds ratio [OR]: 2.98; 95% confidence interval [CI], 2.98-156; P < .001). Sixty four patients (21.2%) underwent aortic valve replacement and/or aortic surgery during follow-up. Eight patients died (5 due to cardiovascular causes); mean age at death was 62±24 years.

Conclusions: BAV has a prevalence of 0.4% in our echocardiographic community. Different from other reports, our series was composed mostly by young patients. Indication to surgery was more frequently related to aortic regurgitation and aortic aneurysm. Long term follow-up showed low cardiovascular mortality (1.6%) and high prevalence of complication leading to surgery (21.5%).

P1696 Increased risk for aortic dilation in adults with isolated BAV as compared to coarctation patients with BAV

P. Luijendijk1, H.A.C.M. De Bruin-Bon1, S.M. Boekholdt1, J.W.J. Vriend2, H.W. Vliegen3, B.J.M. Mulder1, B.J. Bouma2

1Academic Medical Center, Amsterdam, Netherlands; 2Hagaziekenhuis, The Hague, Netherlands; 3Leiden University Medical Center, Department of Cardiology, Leiden, Netherlands

Purpose: The association between aortic coarctation (CoA) and bicuspid aortic valve (BAV) is well known. Aortic dilation is common in CoA patients, especially in CoA patients with BAV (CoA–BAV). However the risk for aortic dilation in CoA-BAV compared to isolated BAV patients is not well established. The aim of our study was to compare the risk for aortic dilatation in CoA-BAV versus isolated BAV patients.

Methods: Echocardiograms of 85 consecutive adult CoA-BAV and 85 BAV patients were included. Mean aortic diameter was 32.3±6.2 mm for CoA-BAV and 38.4±5.7 mm for the isolated BAV group (P<0.001). Mean aortic root diameters were 31.6±5.5 mm in CoA-BAV and 39.0±5.8 mm in the isolated BAV group (P<0.004). Ascending aortic dilation was found in 18 (21%) CoA-BAV and in 46 (58%) isolated BAV patients (P<0.001). Aortic root dilation was found in 16 (46%) CoA-BAV and in 14 (40%) isolated BAV patients (P=0.54). As was present in 21 (21%) CoA-BAV and in 33 (44%) isolated BAV patients (P<0.03), whereas ARF was found in 7 (8%) versus 33 (41%) patients respectively (P<0.001). Left coronary cusp fusion was most common in both CoA-BAV and isolated BAV (80% versus 76%). No significant difference was found in the coronary cusp fusion types between both groups. Aneurysm was found in 58 (76%) CoA-BAV versus 74 (93%) isolated BAV patients (P<0.001).

Conclusion: The risk for ascending aortic dilatation is higher in isolated BAV patients as compared to CoA patients with BAV. Although the prevalence of a rave was higher in BAV patients, no association was found between ascending aortic dilatation and the aortic valve morphological characteristics. These findings suggest that prior coarctation repair might be protective for aortic dilation.
and reduced handgrip strength, and are most pronounced in patients with classic end-to-side anastomoses.

**P1698 Outcomes of transcatheter closure of atrial septal defect with a fenestrated Amplatzer Septal Occluder**

J.-K. Wang, M.T. Lin, S.N. Chiu, C.A. Chen, M.H. Wu. National Taiwan University Hospital, Taipei, Taiwan

**Purpose:** In patients with atrial septal defect (ASD) complicated with moderate-to-severe pulmonary hypertension or heart failure, complete closure of the defect may carry significant risks. A fenestration was generally created in the occluder for gradual reduction of shunt. However, the follow-up results were seldom reported.

**Methods:** During a 10.5-year period, 44 patients (10 males) with ages ranging from 7 to 81 years underwent transcatheter closure of ASD with a fenestrated device. Of them, 39 patients had pulmonary hypertension, 4 had heart failure and 1 had pulmonary atresia intact ventricular septum with a right atrial pressure above 15 mm Hg after balloon test occlusion. A fenestration was created about 1/3 to 1/4 of the diameter of the Amplatzer septal occluder. The techniques of device deployment are similar to those reported.

**Results:** Of the 44 patients, the mean pulmonary artery systolic pressure was 66±19 mmHg and mean Qp/Qs ratio was 2.7±1.4. The mean device diameter used was 30±6 mm. Implantation was initially successful in all 44 patients. Immediately after implantation, shunt flow across the fenestration was observed in all 44 patients. However, 1 developed embolization of the device several hours later. The patient was sent for emergent surgery. All patients were available for at least one surgical or percutaneous intervention throughout adulthood (605 surgeries and 244 percutaneous interventions). In 678 patients with TOF, NYHA class I had elevated hsTnT levels and 5 (96%) patients had elevated NT-pro-BNP (P<NS). Compared to patients with normal hsTnT, patients with elevated hsTnT had higher NT-pro-BNP (567±842 pg/mL vs 1428±884 pg/mL, p<0.01) and hscRP levels (0.3±0.4 vs 4.2±10.7, p<0.03). Four out of 6 patients (67%) with moderate-to-severe dysphonia of systemic ventricle had elevated hsTnT levels vs 4 out of 37 (11%) with normal or mildly impaired ventricular function (P<0.008). All (100%) patients with moderate-to-severe dysfunction of systemic ventricle and 26 out of 36 (72%) with normal or mildly impaired ventricular function had elevated NT-pro-BNP levels. Four out of 9 (44%) patients with moderate-to-severe dysfunction of subpulmonary ventricle had elevated hsTnT levels vs 3 out of 10 (30%) with normal or mildly impaired ventricular function (P<0.03). All (100%) patients with moderate-to-severe dysfunction of subpulmonary ventricle and 8 out of 30 (27%) patients with normal or mildly impaired subpulmonary ventricular function had elevated NT-pro-BNP levels (P<NS). On multivariate model hsTnT but not NT-pro-BNP predicted significant systolic ventricular dysfunction (Exp (B) 11.0, 95% CI 1.5-81.6, P=0.01).

**Conclusions:** Transcatheter closure of ASD in patients with moderate-to-severe pulmonary hypertension or heart failure using a fenestrated device is safe and effective.

**P1700 High-sensitivity troponin T concentrations in adult congenital heart disease**

P. Szymanski, J. Rybicka, M. Liczynska, A. Klisiewicz, P. Hoffman. National Institute of Cardiology, Warsaw, Poland

**Background:** Patients with congenital heart disease (CHD), especially patients with complex and cyanotic lesions are by definition classified as at least stadium B or C chronic heart failure. There are no reports on the utility of high sensitivity troponin (hsTnT) assays in adults with CHD.

**Methods:** We assessed hsTnT in a series of 43 patients (mean age 34±14 years, 22 female) including 16 with simple and 27 with complex CHD (23 cyanotic heart disease), admitted to a tertiary adult CHD referral center. Nine patients were in NYHA class I, 13 in NYHA class II and 21 in NYHA class III. All patients underwent routine clinical and echocardiographic evaluation and had hsTnT, NT-pro-BNP and hscRP measurements; hsTnT levels were measured in healthy controls.

**Results:** Out of 43 CHD patients 8 (17%) had elevated (≥0.003 pg/mL) hsTnT levels (range 0.004-0.021 ng/mL); 32 (74%) patients had elevated NT-pro-BNP concentrations (≥1.25 pg/mL). All controls had hsTnT ≤0.003 pg/mL. None (0%) out of 9 patients in NYHA I class had elevated hsTnT levels and 5 (96%) patients had elevated NT-pro-BNP (P<NS). Compared to normal hsTnT, patients with elevated hsTnT had higher NT-pro-BNP (567±842 pg/mL vs 1428±884 pg/mL, p<0.01) and hscRP levels (0.3±0.4 vs 4.2±10.7, p<0.03). Four out of 6 patients (67%) with moderate-to-severe dysphonia of systemic ventricle had elevated hsTnT levels vs 4 out of 37 (11%) with normal or mildly impaired ventricular function (P<0.008). All (100%) patients with moderate-to-severe dysfunction of systemic ventricle and 26 out of 36 (72%) with normal or mildly impaired ventricular function had elevated NT-pro-BNP levels. Four out of 9 (44%) patients with moderate-to-severe dysfunction of subpulmonary ventricle had elevated hsTnT levels vs 3 out of 10 (30%) with normal or mildly impaired ventricular function (P<0.03). All (100%) patients with moderate-to-severe dysfunction of subpulmonary ventricle and 8 out of 30 (27%) patients with normal or mildly impaired subpulmonary ventricular function had elevated NT-pro-BNP levels (P<NS). On multivariate model hsTnT but not NT-pro-BNP predicted significant systolic ventricular dysfunction (Exp (B) 11.0, 95% CI 1.5-81.6, P=0.01).

**Conclusions:** In this pilot series hsTnT levels were elevated in a substantial number of CHD patients, especially with significant dysfunction of the systemic and subpulmonary ventricles, suggesting and ongoing myocardial injury in these patients. Compared to NT-pro-BNP, hsTnT was a less sensitive but more specific, independent predictor of ventricular dysfunction in adult CHD.

**THE ROLE OF BIOMARKERS IN CONGENITAL HEART DISEASE**

**P1701 Brain natriuretic peptide in patients with tetralogy of fallot -a systematic review**

J.A. Eindovhine, A.E. Van Den Bosch, P.R. Jansen, E. Boersma, J.W. Roos-Hesselink. Erasmus Medical Center, Thoraxcenter, Department of Cardiology, Rotterdam, The Netherlands

**Purpose:** Brain natriuretic peptide (BNP) and N-terminal-pro-brain natriuretic peptide (NT-proBNP) are well-established markers for heart failure in the general population. However, the value of BNP and NT-proBNP as a diagnostic and prognostic marker for patients with surgically corrected Tetralogy of Fallot (TOF) is still unclear.

**Methods:** A systematic review was conducted including all articles focusing on TOF. Data on BNP measurement, patient characteristics and cardiac functional parameters were extracted.

**Results:** A total of 770 patients from 20 articles were included. Both symptomatic and asymptomatic patients after surgically corrected TOF revealed higher BNP levels compared to age and gender matched controls. The severity of pulmonary valve regurgitation (PVR) and right ventricular end-diastolic volume (RVEDD) correlated positively with BNP values. Negative correlations between BNP and exercise capacity were observed. Three small studies with longitudinal data, describing a total of 77 patients, showed a significant decrease of BNP levels 6 months or longer after pulmonary valve replacement compared to BNP levels before the intervention.

**Conclusion:** This systematic review shows higher plasma BNP levels in patients with TOF compared to controls. The observed significant correlations between

---

**Figure 1. BNP/NT-proBNP values and age per study**

---
Brain natriuretic peptide (BNP) and N-terminal probrain natriuretic peptide (NT-proBNP) are well-established markers for heart failure in acquired heart disease. However, the value of BNP and NT-proBNP as a diagnostic and prognostic marker for patients with univentricular hearts and Fontan Physiology is still uncertain. Methods: A systematic review was conducted including all articles focusing on Fontan physiology. Data on BNP measurement, patient characteristics and cardiac functional parameters were extracted. Results: A total of 1165 patients from 16 articles were included. Patients with a classic Fontan had significantly higher BNP levels than the patients treated with the currently used Fontan approach. Young patients after the first palliative operation had higher BNP levels than patients after the bidirectional Glenn procedure (BDG) or Fontan with a total cavopulmonary connection (TCPG). The BNP levels after TCPG were comparable to those of healthy controls. A strong correlation between BNP and severity of heart failure was observed in symptomatic patients. The dominant pulmonary venous drainage was 100.0%, tricuspid valve atresia with the atrialization of the aorta- 88.9%, subaortal aortic stenosis - 100.0%, partial anomalous pulmonary venous drainage - 100.0%, right atrial isomerism - 100.0%. The correlation of BNP and those with non-highly elevated BNP. Second, cardiac performances influencing high-levels of BNP were determined. Pursue: The number of patients with high-levels of BNP was twenty-five. Birth weight (2.8 kg vs 2.8 kg), age (37.1 months vs 47.1 months) and cardiovascular ratio (60% vs 59%) were not significantly different between two groups. Conclusions: Our study showed heart failure worsened all the more in patients with BNP levels 100pmol/l over. This study also revealed that a variety of RV overload were related to high levels of BNP. But all the left-sided factors were not associated with high levels of BNP significantly.

Methods:
- Combination of traditional and emerging biomarkers will be used.
- The role of biomarkers in CHD / Atherosclerosis

Introduction: Coronary restenosis is one of the major complications after coronary stent implantation. The main mechanism for developing restenosis after vascular injury is an exceeding neointimal hyperplasia. Although the histological composition of the neointimal hyperplasia is well characterized, the molecular regulation remains poorly understood. The eNOS/Caveolin interaction represents an important regulatory system for the integrity of the endothelial function and plays an essential role in initial stage of atherosclerotic plaque development. The relevance of Caveolin-1 in atherosclerosis is discussed conversely as co-operating proatherogenetic properties by regulation of pro-proliferative genes on one side and anti-atherogenetic properties by regulation of protective lipoprotein metabolism on the other side. Furthermore, there is strong evidence for negative regulatory influence of Caveolin-1 on endothelial nitric oxide synthase (eNOS), which plays an important role for physiological endothelial function. All these studies focused selectively on Caveolin-1 or eNOS. Therefore we sought to investigate the interaction between Caveolin-1 and eNOS in the development of atherosclerosis using a vascular injury model in Cav-1−/−, eNOS−/− and double Cav-1/eNOS−/− mice. Methods: In C57/B16 (WT), Cav-1−/−, eNOS−/− and Cav/eNOS−/− mice a mechanical injury of the femoral artery was performed using an intraluminal wire. The development of the atherosclerotic lesions sections were examined with Elastic van Giesen staining and digital microscopic images was taken to quantify the intima-media ratio and lumen-vessel wall ratio. For differentiation of intra-neuronal cells Galexin-3 and alpha-Smooth muscle actin (SMA)-staining were used.

Figure 1. BNP/NT-proBNP values and age per study

Conclusion: This systematic review shows that BNP levels differ among Fontan patients in accordance with the performed surgical procedures and increase in symptomatic patients with heart failure. BNP levels decreased after BDG and interestingly, normalized completely after TCPG reflecting the reduced volume load of the ventricle. However, as individual BNP values differ widely, conclusions should be drawn with caution. Sequential BNP measurement in large, prospective studies is warranted.

Brain natriuretic peptide in patients with Fontan physiology - a systematic review -

Brain natriuretic peptide (BNP) and N-terminal probrain natriuretic peptide (NT-proBNP) were used. We found that BNP and NT-proBNP as a diagnostic and prognostic marker for patients with univentricular hearts and Fontan Physiology is still uncertain. We compared the clinical behavior between patients with high-levels of BNP and those with non-highly elevated BNP. Second, cardiac performances influencing high-levels of BNP were determined. Pursue: The number of patients with high-levels of BNP was twenty-five. Birth weight (2.8 kg vs 2.8 kg), age (37.1 months vs 47.1 months) and cardiovascular ratio (60% vs 59%) were not significantly different between two groups. Conclusions: Our study showed heart failure worsened all the more in patients with BNP levels 100pmol/l over. This study also revealed that a variety of RV overload were related to high levels of BNP. But all the left-sided factors were not associated with high levels of BNP significantly.

Methods:
- Combination of traditional and emerging biomarkers will be used.
- The role of biomarkers in CHD / Atherosclerosis

Introduction: Coronary restenosis is one of the major complications after coronary stent implantation. The main mechanism for developing restenosis after vascular injury is an exceeding neointimal hyperplasia. Although the histological composition of the neointimal hyperplasia is well characterized, the molecular regulation remains poorly understood. The eNOS/Caveolin interaction represents an important regulatory system for the integrity of the endothelial function and plays an essential role in initial stage of atherosclerotic plaque development. The relevance of Caveolin-1 in atherosclerosis is discussed conversely as co-operating proatherogenetic properties by regulation of pro-proliferative genes on one side and anti-atherogenetic properties by regulation of protective lipoprotein metabolism on the other side. Furthermore, there is strong evidence for negative regulatory influence of Caveolin-1 on endothelial nitric oxide synthase (eNOS), which plays an important role for physiological endothelial function. All these studies focused selectively on Caveolin-1 or eNOS. Therefore we sought to investigate the interaction between Caveolin-1 and eNOS in the development of atherosclerosis using a vascular injury model in Cav-1−/−, eNOS−/− and double Cav-1/eNOS−/− mice. Methods: In C57/B16 (WT), Cav-1−/−, eNOS−/− and Cav/eNOS−/− mice a mechanical injury of the femoral artery was performed using an intraluminal wire. The development of the atherosclerotic lesions sections were examined with Elastic van Giesen staining and digital microscopic images was taken to quantify the intima-media ratio and lumen-vessel wall ratio. For differentiation of intra-neuronal cells Galexin-3 and alpha-Smooth muscle actin (SMA)-staining were used.
Results: After 42 days a significant reduction of the IMR in eNOS(-/-) mice compared to C57/B16 was observed, whereas Cav-1(-/-) mice showed significantly higher IMR. Double Cav-1(-/-)eNOS(-/-) mice lacked significant differences in IMR compared to WT. The contribution of SMA positive cells to IMR was determined by flowcytometry and was significantly higher in Cav-1(-/-)eNOS(-/-) mice compared to WT. No significant differences in mononuclear cells were observed in the atherosclerotic lesions.

Conclusions: The eNOS-Cav1 interaction plays a pivotal role in the development of atherosclerosis. The exclusive loss of Cav1-1 leads to significant increase of atherosclerotic lesions, which may be reverted in the absence of eNOS.

The downstream mechanisms triggered by Cav1-1 and eNOS in the plaque development needs to be addressed in further studies.

P1706

Carotid intima-media thickness as a predictor of multi-territory arterial stenoses, while CIMT progression with risk of future CV events in patients with symptomatic carotid artery obstruction

L. Wrotniak1, A. Kablak-Zembicka1, T. Przewlocki1, P. Plantenaxe1, J. Gaccon1, A. Roslakiewica1, L. Teilek1, P. Podolec1, J. Jagiellonian University Medical College, John Paul II Hospital, Dept of Cardiac & Vascular Disease, Krakow, Poland; E. Szczeklik Hospital, Dept of Invasive Cardiology, Tarnow, Poland

Subclinical artery occlusive disease (SAS) is frequently an overt manifestation of atherosclerosis. The study aimed to assess the prevalence of concomitant to SAS significant stenoses in other major vascular locations, as well as possible associations between carotid intima-media thickness (CIMT) and internal carotid artery stenosis (ICAS) with cardiovascular (CV) risk.

Mean degree and size of ICAS were determined in 218 patients (116M), aged 62±8.4 years with symptomatic SAS before PTA. Of those, CIMT measurement was repeated in 108 randomly chosen patients in the mean follow-up time of 36.5±26 months. The difference between follow-up CIMT and baseline CIMT (ΔCIMT) was observed. Incidences of CV death, myocardial infarction and ischemic stroke (CV/MIs) were noted. Coronary (CAD), renal (RAS) and lower extremities (PAOD) were verified.

Baseline CIMT value and ICA atherosclerotic plaques were significantly related to the presence of CAD (p<0.01), PAOD (p<0.001), RAS (p<0.05), CAD severity (p<0.001) and the overall number of arterial territories with lumen reduction >=50% by means of ultrasonography, CT or angiography.

Results: Normal baseline CIMT value (-1.1mm) was observed in 28 (12.8%), thickening (CIMT between 1.0-1.3mm) in 50 (22.9%), disseminated atherosclerotic plaques but ICAS ≥50% in 51 (23.4%), and ICAS ≥50% in 40 (18.9) subjects with SAS.

Isolated SAS was found in 46 (21%) subjects, while 1 concomitant arterial territory involvement was found in 83 (38.1), 2 in 55 (25.2%) and 3 or 4 other arterial territories involved in 34 (15.6%) subjects.

Baseline CIMT value and ICA atherosclerotic plaques were significantly related to the presence of CAD (p<0.01), PAOD (p<0.005), RAS (p<0.05), CAD severity (p<0.001) and the overall number of arterial territories with lumen reduction >=50% (p<0.001), CIMT value (t=1.16, CI 1.05-1.28, p=0.005) and ICAS (t=1.54, CI 1.39-1.7, p=0.001) occurred an independent marker of multi-territorial arterial stenoses.

During mean follow-up period of 56.5±36 months, CV/MIs occurred in 27 (12.4%) subjects. In patients with CV/MIs CIMT was observed, as compared to those with no CV event (ΔCIMT = +0.199±0.57 vs. +0.008±0.26mm, p=0.039). Also, CV/MIs was more prevalent in patients with increased level of ICAS. Progression of atherosclerotic plaques underwent afterwards (mean number of territories: 1.8±1.1 vs. 1.3±1.1, p=0.042). Multivariate regression analysis identified 2 independent risk factors of CV/MIs development: significant CAD (t=1.32; CI 1.11-1.58, p=0.003) and CIMT progression (R=0.22; CI 1.02-1.46, p=0.003).

Conclusions: CIMT and ICAS stenosity are independently associated with multi-territorial arterial stenoses, while CIMT progression with risk of future CV events in patients with symptomatic SAS.

P1707

Inhibition of soluble adenyl cyclase prevents oxysterols-induced apoptosis of rat aortic smooth muscle

A. Appukuttan, S. Kumar, H.P. Reusch, Y. Ladiio. Ruhr-University Bochum, Dept. of Clinical Pharmacology, Bochum, Germany

Smooth muscle cells (SMC) apoptosis has been found to contribute in atherosclerotic plaques instability. Within several stress factors promoting SMC apoptosis in advanced plaques oxysterol play a substantial role. Nevertheless, the underlying cellular mechanisms of the oxysterols-induced apoptosis in SMC are still poorly understood. Previously (J Biol Chem, 2009, 284:14768-14778) we found that type 10 soluble adenyl cyclase (sAC) controls the intrinsic pathway of apoptosis in advanced plaques, promoting the early apoptosis in SMC. In the present study we proved a potential contribution of sAC in oxysterols-induced apoptosis. For this purpose rat aortic SMC were treated with 25-hydroxycholesterol (30 μM) or 7-ketocholesterol (20 μM) (two major oxidation products of cholesterol) found in human atherosclerotic plaques. Apoptosis was analysed by TUNEL staining and caspase-3/9 cleavage. Apoptosis of SMC induced by treatment with oxysterols was significantly suppressed by pharmacological inhibition of sAC with the selective sAC inhibitor KN745 (30 μM, Cayman) or by SAc knockdown (shRNA-transfection). Anal-
CAD vs. HC (p=0.003), whilst mMMPs were only increased in NSTEMI (p=0.043). No significant differences were found for pMPs or eMPs (Table).

In NSTEMI patients, positive correlations were found between mMMPs, pMPs and age (p<0.05). Anti-MMP and monocyte counts (p=0.013), monocyte expression of CD163, CD34, CD204 (all p<0.05) and EPC counts (p=0.052, p<0.001).

Demographic data and counts of MP

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>pMP</th>
<th>mMMP</th>
<th>eMP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median</td>
<td>60</td>
<td>3.2</td>
<td>21.9</td>
</tr>
<tr>
<td>Min-Max</td>
<td>40-70</td>
<td>0.2-3</td>
<td>1.9-4.5</td>
</tr>
</tbody>
</table>

Results: *p<0.05 vs. HC (Mann-Whitney test).

Conclusions: Atherosclerotic CAD is associated with up-regulation of small-sized apoptotic MPVs and mMMPs are increased in NSTEMI. Levels of apoptotic Anti-MMPs correlate with monocyte expression of pro-reparative receptors and EPC counts, with possible implications for the regulation of cardiovascular repair in advanced CAD.

---

**P1710**

**Dendritic cells affect both inflammatory and immunosuppressive processes in human atherosclerotic plaques**


Introduction: Atherosclerosis is associated with a complex inflammatory process in the vessel wall, which can result in plaque instability. Dendritic cells (DC), which are characterized by their ability to induce a T-cell specific immune response, play a crucial role in plaque inflammation. Apart from that, DCs also have been shown to be involved in immunosuppressive processes, by interacting with regulatory T-cells, which in turn inhibit DC maturation as well as the proliferation of T-lymphocytes. The aim of our study was to investigate the existence of a possible correlation between the emergence of DCs and regulatory T-cells in atherosclerotic plaques.

Materials and methods: Cross-sections of 30 human carotid endarterectomy specimens were immunohistochemically analysed for the presence of activated DCs (Fascin), regulatory T-cells (FOXP3+), T-lymphocytes (CD3) and COX-2 expressing cells, which are generally increased in the course of inflammation. Classification of atherosclerotic specimens into stable and vulnerable plaques was performed using Trichrome staining.

Results: Plaques were grouped into stable or vulnerable based on their morphological characteristics (lipid content, thickness of the fibrous cap). As compared with stable plaques, vulnerable lesions were characterized by increased levels of COX-2 positive cells, especially in the plaque shoulders and the fibrous cap, indicating an increased inflammatory process in those regions. In stable plaques, the numbers of activated DCs were significantly decreased at the plaque shoulder regions, which was associated with a reduction of recruited COX-2 positive T-lymphocytes. On the contrary, the numbers of regulatory T-cells were increased in stable as compared to vulnerable plaques. Nearly all of the investigated plaques (stable and vulnerable plaques) showed a negative correlation between activated DCs and regulatory T-cells and number of regulatory T-cells.

Conclusion: Raised numbers of COX-2 positive cells indicate an increased inflammatory state in vulnerable as compared to stable plaques. The negative correlation between activated DCs and regulatory T-cells suggests an increased differentiation of naïve T lymphocytes into regulatory T-cells in the absence of mature DCs, which might contribute to an enhanced plaque stability.

---

**P1711**

**Incremental effect of hypercholesterolemia on coronary plaque progression and high-risk composition compared to standard low local endothelial shear stress (ESS)**

K.C. Koskinas1, Y.S. Chatzizisis1, M.I. Papadakis1, A.B. Baker2, A.U. Coskun3, M. Jones1, A. Antoniadis1, E.R. Edelman4, C.L. Feldman1, P.H. Stone1. Brigham and Women’s Hospital, Boston, United States of America; 2Massachusetts Institute of Technology, Cambridge, United States of America; 3Erciyes University School of Medicine, Department of Cardiology, Kayseri, Turkey; 4Siyami Ersek Thoracic and Cardiovascular Surgery Center, Department of Cardiology. Istanbul, Turkey; 5Beth Israel Deaconess Medical Center, Boston, United States of America

Purpose: The relative contribution of systemic risk factors and local low ESS to atherosclerosis is well documented, yet their interrelating effect in-vivo is largely unknown. We investigated the combined impact of different levels of hypercholesterolemia and local ESS on subsequent plaque progression and histological composition.

Methods: Diabetic, hyperlipidemic pigs were grouped into a higher - total cholesterol (TC) (852±32mg/dl, n=4) and a lower-TC group (658±34 mg/dl; n=5), 3-vascular coronary angiography and IVUS were performed in-vivo at 3-5 time points over 36 weeks. 3D-reconstructed arteries were divided into 3-mm segments. ESS was calculated using computational fluid dynamics. Segments were stratified according to systemic TC and local ESS. Change of plaque volume (ΔPV) was measured between consecutive time-points. Arteries were harvested, and segments were analyzed using histopathology and RT-PCR. Gene expression of the LDL receptor (LDL-R), lectin-like oxidized LDL receptor-1 (LOX-1), and monocyte chemoattractant protein-1 (MCP-1) were assessed.

Results: ΔPV over time was greater in low-ESS segments (<1.2Pa) from higher-TC vs. lower-TC animals. At follow-up, low-ESS segments from higher-TC animals (n=22; 19%) had the greatest mRNA levels of LDL-R, LOX-1, and MCP-1, and the greatest lipid content and inflammation – greater even than segments from lower-TC animals with similarly low ESS (<1.2Pa) (Figure).

Figure 1. ESS, TC, and coronary plaque histology

Conclusions: The combination of higher TC and low local ESS leads to the most marked plaque progression and high-risk phenotype in the natural history of CAD. Local risk factors (low ESS) and systemic risk factors (hypercholesterolemia) synergistically exacerbate local plaque development and progression towards inflamed, high-risk lesions.

---

**P1712**

**Prognostic value of uric acid in patients with stemi undergoing primary angioplasty: two year follow-up**

M.G. Kayal1, H. Uyar2, M. Apak1, M. Eren1, M. Ergen1, N. Kalay1, D. Eck1, O. Sahin1, A. Oguzhan1, C.M. Gibson2, A. Kaya1, Y.S. Chatzizisis1, M.I. Papadakis1, A.B. Baker2, A.U. Coskun3, A. Antoniadis1, E.R. Edelman4, C.L. Feldman1, P.H. Stone1. Brigham and Women’s Hospital, Boston, United States of America

Objective: Elevated uric acid levels have been associated with cardiovascular disease in epidemiological studies. The relationship between uric acid levels and long-term outcomes of STEMI patients undergoing primary percutaneous coronary intervention (PCI) is not available.

Methods: Data from 2,249 consecutive patients with STEMI who underwent primary PCI were evaluated. Patients were divided in two groups as either high or low uric acid using an upper limit of normal value of 6 mg/dl for female and 7 mg/dl for male in our central laboratory.

Results: There were 1,643 patients (mean age 55.9±11.6 and 85% male) in the low uric acid group and 606 patients (mean age 60.5±12.6 and 76% male) in the high uric acid group. Serum uric acid levels were 8.0±1.5 in the high uric acid group and 5.2±1.0 in the low uric acid group (p<0.001). The in-hospital mortality rate was significantly higher in patients with high uric acid levels (9% vs. 2%, p<0.001) as was the rate of adverse outcomes in patients with high uric acid. The mean follow-up time was 24.3 months. Cardiovascular mortality, re-infarction, target vessel revascularization, heart failure, and MACE were all significantly higher in high uric acid group (Figure). In a multivariate analyzes, high plasma uric acid levels were an independent predictor of MACE during the in-hospital (odds ratio (OR) 2.03, <0.05% confidence interval (CI) 1.25-3.75; p=0.006) and long-term follow-up period (OR 1.64, <0.05% CI 1.05-2.56; p=0.03).

Conclusion: High uric acid levels on admission are independently associated with both in-hospital as well as long-term adverse outcomes among patients with STEMI undergoing primary PCI.
Decrease in regulatory T-cells and increase in pro-inflammatory cells in unstable compared to stable atherosclerotic lesions

I. Rothm1, I. Atlakova1, K. Schubert1, D. Kretzschmar1, R. Pistul1, J. Zorow1, T. Kroenert2, H.-R. Figulla1, A. Yilmaz1, J. Krannert2, Saalfeld, Gefässchirurgie, Saalfeld, Germany

Background: Dendritic cells (DCs), T-cells, and macrophages are involved in the complex mechanisms of atherosclerosis. However, the role of regulatory T-cells (Tregs) in atherosclerosis is not completely understood. Therefore, we investigated in our present study the frequency of regulatory T-cells in unstable compared to stable carotid plaques and compared it to other inflammatory cells such as cytotoxic T-cells, TH-cells, as dendritic cells (DCs).

Methods: Advanced atherosclerotic lesions were obtained by thomboendarterectomy (TEA), and they were classified as unstable (n=13) according to the size of their lipid core (<40%), their thickness of the fibrous cap (<100μm), and the presence of neovascularisation, and they were compared with stable plaques (n=9) which did not fulfil the above criteria. The plaque specimens were immunostained using primary antibodies which are specific for T-cells (CD3), activated T-cells (CD25), cytotoxic T-cells (CD8), TH-cells (CD4), Tregs (FoxP3), DCs (CD11c), and mature DCs (CD13). The results were compared for stable versus unstable plaques and their frequency was correlated with each other.

Results: Compared to stable plaques, we found in unstable plaques significantly high levels of CD4+ CD25+ Treg cells (2.9-fold, p<0.01), CD8+ cytotoxic T-cells (p=0.02), CD4+ T-helper cells (4.1-fold, p=0.03), CD25+ activated T-cells (16.1-fold, p=0.03), CD209+ DCs (2.9-fold, p=0.01), and CD83+ DCs (5.0-fold, p=0.01). In contrast, there was a significantly lower frequency of FoxP3+ Tregs in unstable than in stable plaques (0.3%±0.03, p=0.01).

Conclusions: Comparing the emergence of different inflammatory cells with each other, we could show a significant correlation between DCs and different T-cell subtypes, e.g. CD209+DC (n=0.5, p=0.02), CD209+CD8 (n=0.67, p=0.01), CD209+CD4 (n=0.65, p=0.01), CD83-CD4 (n=0.67, p=0.01), and between different T-cell subtypes compared to one another, e.g. CD8-CD3 (n=0.70, p=0.001), and CD8-CD4 (n=0.37, p=0.007).

Also, we were able to show a significant inverse correlation between DCs and Tregs, e.g. CD209-FoxP3 (r=0.49, p=0.04), and a trend towards an inverse correlation between DC-CD8-FoxP3 (r=0.42, p=0.08).

Hypoadiponectinemia is associated with severity of coronary atherosclerosis and poor long-term outcome in patients with angiographically documented coronary artery disease


Purpose: Adiponectin (APN) is an adipocytokine with cardioprotective effects. Patients with plasma APN levels <4.0μg/ml have a 2-fold increased prevalence of coronary artery disease (CAD), but the prognostic role of APN levels is unknown. We evaluated the relationship between APN levels, CAD severity and long-term prognosis.

Methods: Consecutive patients were enrolled from inpatients who underwent coronary angiography or percutaneous coronary intervention (PCI) for stable CAD or acute coronary syndrome (ACS) at our Institution. Venous blood was drawn after an overnight fast and APN levels were evaluated by a ELISA assay. In a subgroup of CAD or ACS patients, transcoronary (Aorta/Coronary Sinus) APN levels were measured. Patients were divided into 2 groups according to the plasma APN levels below (low APN) or above (control group) the value of 4.0μg/ml. Major adverse cardiac events (MACE) were considered death, acute myocardial infarction and coronary angiography or percutaneous coronary intervention (PCI) for stable CAD.

Results: A total of 311 patients completed a follow-up of 18.4±6.8 years, with 254 patients in the APN group (69% male, mean age 62±10.3) and 59 patients in the control group (78% male, mean age 64±8). No difference were observed between groups except for a higher rate of diabetes (29,4% vs 10,7%; p<0.001), and cumulative exposure to antiretroviral therapy (1.61±0.23 vs 1.09±0.31; p<0.01). Thirty-four consecutive patients with significant carotid artery stenosis (78% male, mean age 44 years) receiving ART underwent cardiac computed tomography (1.39±0.43 vs 1.09±0.22P<0.001), and CD83+ DCs (5.0-fold, p=0.03). Plaques with ulcerated surface had higher ΔT compared to plaques with irregular and regular (2.08±0.14 vs 1.37±0.09°C; p=0.01). Heterogeneous plaques had higher ΔT compared to homogenous (1.78±0.41 vs 1.09±0.31°C; p<0.001). Specimens with thin fibrous cap had higher ΔT (1.69±0.42 vs 0.98±1.20°C; p<0.001). Specimens with intense expression of VEGF had higher ΔT compared to specimens with low (1.67±0.41 vs 0.95±0.20°C, p=0.01).

Conclusions: Increased thermal heterogeneity detected in carotid arteries by microwave radiometry correlates with ultrasound and immunohistochemical findings. Further studies are needed to validate this method for the non-invasive assessment of carotid plaques.
Early inhibitory drug effect on the expression of pro-inflammatory and pro-oxidant genes in coronary regions of low endothelial shear stress: an in vivo study in diabetic hyperlipidemic juvenile swine

1Cardiovascular Division, Brigham and Women’s Hospital, Harvard Medical School, Boston, United States of America; 2Department of Biomedical Engineering, University of Texas, Austin, United States of America; 3Department of Mechanical and Industrial Engineering, Northeastern University, Boston, United States of America; 4Harvard-MIT Division of Health Sciences and Technology, Massachusetts Institute of Technology, Cambridge, United States of America

Purpose: Low endothelial shear stress (ESS) activates pro-inflammatory pathways and critically determines the localization of atherosclerosis. Angiotensin receptor blockers and statins exhibit pleiotropic effects with anti-inflammatory actions in advanced plaques. However, the effect of drugs on the earliest pathobiologic manifestations of atherosclerosis is not well known. We tested the hypothesis that angiotensin receptor blockers and statins exert a vasculoprotective effect in coronary regions exposed to low ESS in a porcine model of human-like atherosclerosis.

Methods: Twelve diabetic/hyperlipidic swine (age: 3 mo) were grouped into controls (n=4), and those treated with V (320 mg; n=4) or V/S (320 mg; n=4). 3D coronary artery reconstruction by angiography & intravascular ultrasound was performed in vivo at baseline and 8 (follow-up) weeks post-induction. Baseline local ESS was calculated by computational fluid dynamics and normal 5 mm segments with local ESS ≤1.2 Pa; n=60) or higher (>1.2 Pa; n=89) ESS were identified. Coronary arteries were harvested at follow-up. qRT-PCR was used for assessing the expression of pro-atherogenic, anti-inflammatory and pro-oxidant genes

Results: The upregulation of sterol regulatory element-binding protein 1 (SREBP1), intercellular adhesion molecule-1 (ICAM-1), monocyte chemotactic protein-1 (MCP-1) and lipopolysaccharide-associated phospholipase-A2 (LpPLA2) in low ESS segments was inhibited in the V and V/S groups compared to controls (Figure; *p<0.05). V/S also suppressed the upregulation of NADPH oxidase (gp91phox) expression.

Conclusions: V and V/S attenuate the pro-atherogenic effects of low ESS within only 8 weeks. These results suggest a drug-induced mechanism of regional atherosclerosis early in the natural history of coronary artery disease.

Low levels of pro-apoptotic molecules Bax and Bim account for apoptosis resistance in CD4+CD28null T cells in patients with acute coronary syndrome

I.E. Dumitru, R.F. Antunes, J.C. Jaski, St. George’s University of London, United Kingdom

Purpose: The immune system, and in particular T cells, have a pivotal role in atherosclerosis. Patients with acute coronary syndrome (ACS) have higher numbers of a subset of T lymphocytes, the CD4+CD28null T cells. Compared to stable angina patients and healthy individuals, CD4+CD28null T cells have been shown to participate in plaque instability and recurrence of acute coronary events via production of inflammatory cytokines and lysis of endothelial and vascular smooth muscle cells. However, the mechanisms that lead to the accumulation of CD4+CD28null T cells in ACS are not understood. We have recently shown that CD4+CD28null T cells from ACS patients upregulate constitutive receptors OX40 and 4-1BB, which enables these cells to produce inflammatory cytokines and express molecules involved in cytoxicity production and cytoktic function. OX40 and 4-1BB are known to regulate the homeostasis of the T cell compartment via apoptosis. Our aim was to investigate apoptosis pathways and sensitivity of CD4+CD28null T cells from ACS patients to identify alterations that could explain the accumulation of these cells in ACS.

Methods: The expression of death receptors (Fas and ligands (Fasl)), as well as the levels of anti-apoptotic (Bcl-2, Bcl-XL survivin) and pro-apoptotic (Bax, Bim) proteins was quantified using flow cytometry in CD4+CD28null T cells from patients with ACS. Apoptosis sensitivity of CD4+CD28null T cells was measured using Annexin V and 7-AAD staining and via detection of activated caspases-3.

Results: We show that CD4+CD28null T cells from ACS patients express significantly lower levels of the death receptor Fas compared to conventional CD4+CD28 T cells. Furthermore, the pro-apoptotic proteins Bax and Bim were significantly decreased in CD4+CD28null T cells compared to their CD28+ counterparts. Interestingly, CD4+CD28null T cells failed to upregulate Bim and Bax following activation, in stark contrast to CD4+CD28 T cells. No differences were found in the levels of anti-apoptotic proteins between the two T cell subsets.

Conclusions: We identified defects in the death receptor Fas and the pro-apoptotic proteins Bim and Bax in CD4+CD28null T cells from ACS patients, which suggest that these cells are resistant to apoptosis. These findings could open the way for novel therapies aimed at targeted induction of apoptosis in CD4+CD28null T cells to stabilise atherosclerotic lesions.
Infusion of lin-/sca-1+ and endothelial progenitor cells improves proinflammatory and oxidative stress factors in atherosclerotic mice

A. Briasoulis, D. Tousoulis, P. Kourkoulis, G. Vogiatzi, A. Valatsou, N. Papageorgiou, A. Pantopoulou, C. Antoniades, D. Perrea, C. Stefanidis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Background: The impact of direct infusion or indirect mobilization of progenitor cells on atherosclerotic plaque development and progression is not clear. We sought to investigate the effects of lin-/sca-1+ cells (P), endothelial progenitor cells (E) and G-CSF (G) administration on the inflammatory and oxidative component of atherogenesis.

Methods: Apolipoprotein-E deficient mice were induced with 0.1 mg OCH/kg in PBS. G-CSF (100 mcg/kg/day) and/or progenitor cells were infused in the left carotid artery. The inflammatory/oxidative component of cell infiltration was assessed 7 days post-treatment.

Results: The administration of both G-CSF and progenitor cells significantly decreased the levels of sICAM-1 and sVCAM-1: G: p<0.001, P: p<0.003, E: p=0.01), IL-6 (G: p=0.003, P: p=0.001, E: p=0.05), IL-6 (G: p=0.003, P: p=0.003, E: p=0.01), ox-LDL (G: p=0.02, P: p=0.018, E: p=0.05) and lipid Perox (G: p=0.006, P: p=0.002, E: p=0.05) 6 days after the initiation of treatment. No significant effects of lin-/sca-1+ cells, ECPS and G-CSF on TNF-α and MMP-9 levels were observed. The effects of all treatments on the levels of pro-inflammatory molecules and oxidative stress parameters 7 days post-treatment were not significant. Interestingly, the levels of sICAM-1 and sVCAM-1 increased 7 days post-treatment. No significant difference between the G-CSF and progenitor cell groups was observed.

Conclusions: Direct infusion of progenitor cells and indirect mobilization of hematopoietic progenitor cells significantly decreased the levels of proinflammatory and oxidative stress factors. Treatment with hematopoietic progenitors, ECPS or G-CSF may exert a beneficial effect on vascular inflammation and endothelial dysfunction.

VASCULAR INFLAMMATION AND SIGNALING

Notch ligand, delta-like 4, blockade inhibits lesion formation after vascular injury

D. Fukuda1, H. Yagita2, M. Akawa1. 1 Brigham and Women’s Hospital, Department of Medicine, Cardiovascular Division, Boston, United States of America; 2 Juntendo University, Faculty of Medicine, Tokyo, Japan

Purpose: Excessive neointimal hyperplasia after vascular injury contributes to restenosis, which remains as a major limitation of the coronary angioplasty. Monocytes/macrophages play crucial roles in this disease process through the promotion of inflammation. The Notch pathway regulates embryonic development and contributes to physiological and pathological processes in adult tissues. We previously showed that Notch signaling triggered by delta-like 4 (DLL4), one of the Notch ligand, promotes inflammatory responses in human macrophages in vitro. The role of DLL4 in the neointimal hyperplasia, however, remains unknown. In this study we tested the hypothesis that inhibition of DLL4 prevents lesion formation after vascular injury.

Methods: We induced wire-mediated vascular injury to C57BL/6 mice. To block DLL4-mediated Notch signaling in vivo, we administered well-characterized anti-DLL4 neutralizing antibody (DLL4-Ab) twice a week and harvested mice at one week or four weeks after surgery. To investigate potential roles of DLL4 in macrophage-dependent inflammation, we performed loss-of-function and gain-of-function experiments.

The CD3-CD56-CD16+ subset was significantly higher in the intracoronary blood of AngII-PBS compared to PBS-PBS and the increase was significantly enhanced in AngII-OCH compared to AngII-PBS by 1.5, 1.9, and 2.2-folds (P<0.05 for each), respectively. Real-time PCR showed that AngII enhanced the expression levels of HIC-class II, RANTES, and IFN-γ within the aorta in AngII-OCH compared to AngII-PBS by 8.2 and 5.4-folds (P<0.05 for each), respectively. In situ zymography revealed that AngII increased MMP activity in media and adventitia of the aortic aneurysm in AngII-OCH compared to AngII-PBS.

Conclusions: IKT cells are involved in the development of experimental abdominal aortic aneurysm and dissection via activating macrophages and T lymphocytes and up-regulating MMP activity within the vascular tissue.
experiments using the murine macrophage like cell line RAW264.7, and transmembrane co-culture system with vascular smooth muscle cells.

**Results:** DiI4 RNA expression in injured femoral arteries increased (P < 0.05) after vascular injury. Immunohistochemistry in the lesions co-localized DiI4 expression and Notch activation as gauged by accumulation of a cleaved product of Notch1 receptor. DiI4-Aβ treatment attenuated lesion formation compared with control (P < 0.01) at four weeks after injury (N=10). At one week after surgery, Ab treatment reduced macrophage accumulation in necrotic (P < 0.05). DiI4-Aβ treatment reduced pro-inflammatory molecules IL-1β, MCP-1, and MMP-9 in femoral arteries at this time point (P < 0.05) and also IL-1β expression in macrophages in the spleen, a reservoir of this cell type (P < 0.05). Loss-of-function and gain-of-function in vitro experiments demonstrated that DiI4 induces polarization shift of RAW264.7 cells towards pro-inflammatory state as determined by increased expression of IL-1β, iNOS, and MMP-9 and reduction of IL-10. Furthermore, a co-culture experiment with RAW264.7 cells overexpressing DiI4 promotes MCP-1 expression in vascular smooth muscle cells.

**Conclusions:** These results suggest that DiI4 promotes inflammatory responses in macrophages, leading to excessive lesion formation after vascular injury. DiI4 can be a potential therapeutic target for neointimal hyperplasia.

---

**A link between inflammation, extracellular matrix and cardiovascular disease: An atherosclerotic plaque rupture in ST-elevation myocardial infarction**

K. Distelmaier, A. Mangold, C. Adbrecht, I.M. Lang. Medical University of Vienna, Vienna, Austria

Atherosclerotic plaque rupture with subsequent mural thrombus formation is considered as the event compromising epicardial flow in ST-elevation myocardial infarction (STEMI). Although the crucial role of metalloproteinases (MMPs) in coronary plaque rupture is well investigated, the trigger for enhanced MMP synthesis and activation has not been understood yet. The cell surface glycoprotein expression of EMMPRIN (extracellular MMP inducer) may be the trigger for enhanced MMP synthesis and coronary plaque rupture in STEMI.

Proteomic shotgun analyses as well as western blots showed an accumulation of EMMPRIN (extracellular matrix MMP inducer) mRNA and protein in the cell wall to be the trigger for enhanced MMP synthesis and coronary plaque rupture in STEMI.

The enrichment of soluble EMMPRIN correlates with local MMP-9 activity. In vitro stimulation of PMNs, isolated from STEMI patients, with complement component C5a showed an upregulation of EMMPRIN by RT-PCR.

Our data suggest that EMMPRIN represents a crucial link between local inflammatory processes, enhanced MMP synthesis and coronary plaque rupture.

---

**Platelet serotonin promotes the efficient recruitment of neutrophils to sites of acute inflammation**

D. Duerschmeid1, G.L. Suiland 2, H. Herr1, C. Carbo2, D. Demers2, A. Brill1, S.M. Cifuni2, S. Cicko3, M. Idzk03, C. Bod1. 1University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany; 2Immune Disease Institute, Children's Hospital, Harvard Medical School, Boston, United States of America; 3University Medical Center, Department of Cardiology/Cardiology, Freiburg, Germany

**Objectives:** The majority of peripheral serotonin is stored in the granules of circulating platelets, which release it upon activation at sites of inflammation. We asked whether this affects neutrophil behavior in inflammatory responses.

**Methods:** Complete blood cell counts were determined in C57BL/6 (WT) mice and trypsinpan hydroxylase (Tph) I-deficient mice, which do not produce non-neuronal serotonin. Platelet serotonin depletion was induced by long-term treatment with fluoxetine. Laser-capture-endothelial interactions were visualized by intravital microscopy in mesenteric venules. Sterile peritonitis was induced with thioglycollate and extravasated cells harvested. Aseptic wounds were punched into dorsal skin and myeloperoxidase deposition was measured. Acute lung inflammation was induced by inhalation of lipopolysaccharide (LPS). Survival after intraperitoneal injection of 20 mg/kg E. coli LPS was monitored.

**Results:** Absence of non-neuronal serotonin in Tph1-/- mice was associated with an increased leukocyte count as compared to WT (9.1 ± 2 versus 6.1 ± 1.03 x 10⁶ /μl, P < 0.0001, n=18). Neutrophil surface expression of L-selectin was reduced in Tph1-/- mice and soluble L-selectin increased. Despite elevated leukocyte count, 30% fewer leukocytes rolled on unstimulated venous endothelium of Tph1-/- mice compared to WT (P < 0.001, n=8-9). The velocity of rolling leukocytes was significantly higher in Tph1-/- mice than in WT (P < 0.001). Leukocyte adhesion to LPS injection was significantly reduced in Tph1-/- as compared to WT (P < 0.007, n=10). Blocking serotonin uptake into platelets by fluoxetine reduced serotonin in WT mice by >80%. Fluoxetine-treated mice also showed reduced leukocyte rolling and adhesion. Four hours after inflammatory stimulation, neutrophil extravasation into skin wounds, inflamed lung and peritoneum were significantly reduced in Tph1-/- mice as compared to WT (P < 0.05, n=10). We identified that the serotonin receptor subtypes 5-HT1A and 5-HT1B are present on neutrophils but serotonin did not induce in vitro neutrophil chemotaxis. Survival after LPS-induced endotoxic shock was better in Tph1-/- mice than in WT mice (p < 0.005, n=14).

**Conclusion:** Absence of non-neuronal serotonin impairs the recruitment of neutrophils to sites of acute inflammation and protects from endotoxic shock. Leukocyte rolling and adhesion were decreased in Tph1-/- and fluoxetine-treated mice, indicating a role of platelet serotonin in early leukocyte-endothelial interactions.

---

**Vascular dysfunction and skin inflammation are mechanistically interconnected by IL17A and IL-6 signaling in a mouse model of psoriasis**

S. Karbach1, A. Crawford3, M. Oelze1, A. Dabber1, A. Nikolaev1, S. Rose-John1, P. Wenzel2, E. Stebitz1, T. Muenzel1, A. Waisman1.

1University Medical Center of the Johannes Gutenberg University Mainz, Mainz, Germany; 2Institute of Biochemistry University Medical Center Kiel, Kiel, Germany

**Introduction:** Abnormal production of inflammatory mediators, especially the IL-23/IL-17A axis, plays a decisive role in the pathogenesis of psoriasis and other autoimmune diseases. IL-17 has as well been described to promote endothelial dysfunction, axis and cardiovascular disease. However, there is not yet been an experimental approach to address the correlation between IL-17A-endothelial dysfunction and psoriasis.

**Methods and Results:** Mice with a c-Inducibleoverexpression of IL-17A cross-breeding the Cre recombinase under transcriptional control of K14 in keratinocytes (K14-IL-17Aind+) were compared with the IL-17Aind+ controls. IL-6 and IL-17A were increased in the serum of K14-IL-17Aind+ mice and of patients suffering from an acute episode of psoriasis (measured by ELISA). K14-IL-17Aind+ (conditionally overexpress IL-17A in the skin and dermivascular tissue) showed an overt skin inflammation including dermal infiltration of effector T cells, formation of neutrophil microabscesses and hyperkeratosis resembling human psoriasis. FACS analyses K14-IL-17Aind+ mice showed vascular endothelial and smooth muscle dysfunction (assessed by aortic ringrelaxation studies), increased blood pressure (measured by tail cuff method) as well as increased vascular protein forming in the blood as well as increased NADPH oxidase activity the heart membrane fraction (measured by chemiluminescence) at the age of 3 months. Aortic NOX-2, iNOS and HO-1 expression (assessed by Westernblot, immunohistochemistry and mRNA-RT-PCR) and aortic infiltration of MPO+ neutrophil granulocytes (assessed by fluorescence-immunohistochemistry and facs) was increased in K14-IL-17Aind+ compared to controls providing a possible mechanism for vascular dysfunction in psoriasis. Skin disease and endothelial dysfunction were improved by blocking IL-6, indicating a mechanistic role for IL-6 downstream of IL-17A in comparison, animals which are completely lacking the IL-17A-Receptor (IL-17RΔe) were partially protected from angiotensin II-induced vascular dysfunction andadventitial stress as well as from chemically induced psoriasis, highlighting the importance of this cytokine in both diseases.

**Conclusions:** Vascular dysfunction experimental psoriasis seems to be mediated by IL-17-driven inflammation. With the K14-IL-17Aind+ we provide a novel mouse model to study.

---

**Tacrolimus limits myocardial infarction in mini-pig model by ligating the left anterior descending coronary artery (LAD)**

S. Chu1, J.L. Sheu2, T.H. Tsai1, Y.L. Chen1, H.K. Yip1. Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Cardiology, Kaohsiung, Taiwan; 2Kaohsiung Chang Gung Memorial Hospital, Chang Gung University, College of Medicine, Cardiovascular Surgery, Kaohsiung, Taiwan

**Purpose:** This study hypothesize that tacrolimus therapy limited left ventricular (LV) infarct and remodeling through suppressing inflammatory response, oxidative stress and regulating the mitogen-activated protein kinase (MAPK) and Akt signaling pathways in an acute myocardial infarction (AMI) mini-pig model by ligating the left anterior descending coronary artery (LAD).

**Methods:** Twelve male mini-pigs were equally randomized into AMI treated by saline (3.0 mL, AMIIS), and AMI treated by tacrolimus (0.5mg) (AMIT). Thirty minutes after the procedure, intra-LAD injections were performed just beyond the ligation. The animals were sacrificed by dye 14 after AMI induction.

**Results:** Inflammatory biomarkers at transcription or protein levels [matrix metalloproteinase (MMP-9), plasminogen activator inhibitor-1, tumor necrotic factor (TNF-α), nuclear factor (NF)-κB] and cellular level (CD40+ cells) were significantly higher in AMIS than in AMIT animals. Fibroseformation biomarkers at protein level (α-smooth muscle actin, transforming growth factor-β) and extent of Sirius red staining were significantly elevated in AMIS compared to those in AMIT animals (all p < 0.03). Anti-oxidant biomarkers at protein or transcription levels (heme oxygenase, redox protein, glutathione reductase, glutathione peroxidase) were higher in AMIS than in AMIT animals (all p < 0.01). Protein expressions of ERK1, p38 MAPK, and Akt were increased in AMIS than in AMIT animals (all p < 0.001). Significantly aggravated LV infarction and remodeling were noted.

---

**Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790 by guest on 11 March 2019**
in AMIS than in AMIT animals, whereas LV ejection fraction was reduced in AMIS than in AMIT animals (all *p* < 0.001).

**Conclusions:** Intra-cytoplasmic administration of tacrolimus attenuated inflammation and MAPK signaling, limited infarct size, and preserved LV function.

**Background:** High-mobility groupbox1 (HMGB1) facilitates gene transcription as an architectural nuclear protein but may also be secreted, thereby mediating inflammatory and immune responses. HMGB1 has recently been identified in human atherosclerotic lesions and is involved in HMGB1 induced reduction of HMGB1 in macrophages. In ApoE-/- mice, activated platelet-secreted in early stages of atherogenesis, therefore we hypothesized an interaction between HMGB1 and platelets. A recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot and Immunofluorescence microscopy, and flow cytometry. HMGB1 expression in human coronary artery thrombosis was studied by immunohistochemistry.

**Results:** Recombinant HMGB1 (20 μg/mL) bound to thrombin-activated human platelets (mean fluorescence intensity MFI 2.49 vs 25.01, *p* = 0.0079). RAGE was one of the known receptors for HMGB1. We identified RAGE in platelets by RT-PCR with mRNA extracted from highly purified platelets. Binding of recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot and immunofluorescence microscopy, and flow cytometry. HMGB1 expression in human coronary artery thrombosis was studied by immunohistochemistry.

**Methods:** Binding of recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot. Its expression is elevated upon TRAP-6-induced platelet activation. IL-17 significantly enhanced the PAR-1-mediated GP Ib/IIa activation, which is highly expressed in platelet-rich coronary artery thrombi.

**Results:** Recombinant HMGB1 (20 μg/mL) bound to thrombin-activated human platelets (mean fluorescence intensity MFI 2.49 vs 25.01, *p* = 0.0079). RAGE was one of the known receptors for HMGB1. We identified RAGE in platelets by RT-PCR with mRNA extracted from highly purified platelets. Binding of recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot. Its expression is elevated upon TRAP-6-induced platelet activation. IL-17 significantly enhanced the PAR-1-mediated GP Ib/IIa activation, which is highly expressed in platelet-rich coronary artery thrombi.

**Background:** High-mobility groupbox1 (HMGB1) facilitates gene transcription as an architectural nuclear protein but may also be secreted, thereby mediating inflammatory and immune responses. HMGB1 has recently been identified in human atherosclerotic lesions and is involved in HMGB1 induced reduction of HMGB1 in macrophages. In ApoE-/- mice, activated platelet-secreted in early stages of atherogenesis, therefore we hypothesized an interaction between HMGB1 and platelets. A recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot and Immunofluorescence microscopy, and flow cytometry. HMGB1 expression in human coronary artery thrombosis was studied by immunohistochemistry.

**Results:** Recombinant HMGB1 (20 μg/mL) bound to thrombin-activated human platelets (mean fluorescence intensity MFI 2.49 vs 25.01, *p* = 0.0079). RAGE was one of the known receptors for HMGB1. We identified RAGE in platelets by RT-PCR with mRNA extracted from highly purified platelets. Binding of recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot. Its expression is elevated upon TRAP-6-induced platelet activation. IL-17 significantly enhanced the PAR-1-mediated GP Ib/IIa activation, which is highly expressed in platelet-rich coronary artery thrombi.

**Methods:** Binding of recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot. Its expression is elevated upon TRAP-6-induced platelet activation. IL-17 significantly enhanced the PAR-1-mediated GP Ib/IIa activation, which is highly expressed in platelet-rich coronary artery thrombi.

**Results:** Recombinant HMGB1 (20 μg/mL) bound to thrombin-activated human platelets (mean fluorescence intensity MFI 2.49 vs 25.01, *p* = 0.0079). RAGE was one of the known receptors for HMGB1. We identified RAGE in platelets by RT-PCR with mRNA extracted from highly purified platelets. Binding of recombinant HMGB1 to platelets was examined in diluted human and mouse whole blood by flow cytometry. Expression of the HMGB1 receptor on platelets was confirmed by Western blot. Its expression is elevated upon TRAP-6-induced platelet activation. IL-17 significantly enhanced the PAR-1-mediated GP Ib/IIa activation, which is highly expressed in platelet-rich coronary artery thrombi.
The addition of bevacizumab in the adjuvant chemotherapy of cancer patients increases the incidence of major cardiovascular events: a prospective study

A. Michelonga1, K. Tountzou1, A. Synetos1, E. Tsiamis1, F. Zagouri2, A. Biamis2, M.A. Dimopoulos2, S. Kyvelou1, D. Tousoulis1, C. Stefanadis1. 1University of Athens Medical School, 1st Department of Cardiology, Athens, Greece; 2University of Athens, Faculty of Medicine, Department of Clinical Therapeutics, Athens, Greece

Purpose: The anti-angiogenic agent of bevacizumab is used widely in the treatment of various types of malignancies. A little number of retrospective trials has investigated the effect of bevacizumab on the cardiovascular system. We evaluated prospectively the incidence of major cardiovascular events and the predictors of adverse outcomes in patients treated with bevacizumab.

Methods: One hundred and forty seven cancer patients were divided into two groups, according the treatment selected by oncologists. Group 1 (76 patients) received conventional chemotherapeutic scheme with bevacizumab and group 2 (71 patients) similar chemotherapeutic schemes without bevacizumab. Baseline evaluation before the initiation of the therapy included recording of risk factors for coronary artery disease, previous medication and their electrocardiogram. All patients were prospectively followed up at 6 and 18 months and the incidence of the following events was recorded: death, cardiac event, myocardial infarction and deep vein thrombosis.

Results: The two groups had similar baseline demographic characteristics. Total mortality had no difference between the two groups (28.94% versus 33.80%, p=0.52). On the contrary, cardiovascular events were significantly higher in the bevacizumab group compared to the control group (9.21% versus 1.40%, p=0.03). A number of cardiovascular events that were recorded in bevacizumab and did not cause death. Moreover, patients treated with bevacizumab had higher incidence of deep vein thrombosis (5.26% versus 2.81%, p=0.05). Multivariante analysis using Cox proportional hazards with forward stepwise logistic regression analysis identified left bundle branch block on the baseline ECG, as well as the use of bevacizumab as the only independent predictors of cardiovascular events.

Conclusions: The addition of bevacizumab in the conventional chemotherapeutische scheme for the treatment of metastatic breast or colorectal cancer, significantly increases the incidence of major cardiovascular events. Left bundle branch block and the use of bevacizumab provides better risk stratification.

Angiogenesis II promotes skeletal muscle angiogenesis induced by exercise training: role of microRNAs-27a and 27b

T. Fernandes1, N.D. Da Silva Junior1, U.P.R. Soci1, E.C. De Carmon1, G.F.A. Molta1, V. Cacholdero1, V. Laherne1, E.M. Oliveira2, F. Zagouri2, A. Biamis2, M.A. Dimopoulos2, S. Kyvelou1, D. Tousoulis1, C. Stefanadis1. 1University of Sao Paulo (USP), School of Physical Education and Sport, Sao Paulo, Brazil; 2Complutense University of Madrid, Department of Physiology, Madrid, Spain

Purpose: Exercise training (ET) promotes skeletal muscle angiogenesis related to high performance. MicroRNAs (miRNAs) are an emerging class of non coding small RNAs that regulate gene expression posttranscriptionally by targeting miRNAs. miRNAs-27a and -27b target the angiogenin-converting enzyme (ACE). We investigated the effects of ET on soleus miRNAs-27a and 27b expression and whether they regulate the skeletal muscle renin angiotensin system (RAS) in ET-induced angiogenesis.

Methods: Wistar rats (n=30) were assigned to 3 groups: Sedentary (S), Trained 1 (T1) and Trained 2 (T2). T1: swimming training consisted of 60 min, 1x/day/10 weeks, with 5% body weight workload. T2 the same as T1 until 8th week, in the 9th week they trained 2x/day, and in the 10th week 3x/day. Blood pressure (BP) and heart rate (HR) were evaluated by direct measurement and angiogenesis by soleus capillary-to-fiber ratio. Soleus miRNAs-27a and -27b were analyzed by qRT-PCR and ACE activity by coomassie blue staining and western blotting, respectively. Soleus angiotensin II (ANG II) and VEGF concentration were evaluated by ELISA. Angiotensinogen (AGT) and ANG II type 1 (AT1) receptor mRNA expression were measured. Changes in miRNA expression compared to T2 were measured using 7900HT Fast Real-Time PCR system.

Results: Rats in T2 showed peak oxygen uptake and soleus citrate synthase activity in T1 and BP. UPD was unchanged while resting HR increased in all trained groups. Skeletal muscle angiogenesis obtained by T1 and T2 was 87% (p=0.01) and 137% (p=0.001), respectively. In contrast, Losartan prevented the increase in angiogenesis in both trained groups. Soleus miRNA-27a levels decreased in both trained groups (23% in T1 and T2, p=0.05) compared with S group. Similar, miRNA-27b reduced 21% in T1 (p=0.01) and 32% in T2 (p=0.01) paralleled with an increase in ACE protein levels (200% in T1 and 251% in T2, p<0.001). Soleus AGT levels (52% in T1 and 96% in T2, p=0.05), ANG II levels (26% in T1 and 46% in T2, p=0.05) and VEGF levels (30% in T1 and 60% in T2, p=0.05) also were higher in all trained groups. In addition, AT1 receptor protein levels increased after training (39% in T1 and 48% in T2, p=0.05).

Conclusions: Our data show that SRA participates ET-induced skeletal muscle angiogenesis, which could be associated with regulation of select miRNAs providing a new target for modulating vascular formation and suggest that miRNA-27a and 27b can be potential therapeutic targets for pathological conditions involving capillary rarefaction.

Estrogen improves vascular function and morphology via peroxisome-proliferator-activated-receptor gamma

V. Tiyeler1, C.M. Mueller, G. Nickenig, U.M. Becker. University of Bonn, Department of Cardiology, Bonn, Germany

Purpose: The exact mechanism of estrogen related atheroprotection is not fully understood. As estrogen receptors (ERs) the peroxisome-proliferator-activated-receptor gamma (PPARγ) belongs to the family of ligand activated nuclear receptors regulating the transcription of atheroprotective genes. Aim of this project was to investigate whether atheroprotection of estrogen is mediated via PPARγ-regulation in the vascular compartment.

Methods and Results: We studied the effect of estrogen deficiency, endogenous and exogenous 17β-estradiol on vascular PPARγ-expression and function in female WT- and ApoE−/−mice. Estrogen deficient ovarioctomized animals (OVX, 21 days) displayed significant reduction of PPARγ-expression in aortic tissue compared to female mice with intact ovarian function (Sham). Hormone replacement with subdermal 17β-estradiol pellets significantly increased vascular PPARγ-expression in ovarioctomized female mice (OVX/E2), ROS generation, endothelial dysfunction and atherogenesis were increased in estrogen-deficient OVX ApoE−/−mice with low vascular PPARγ-expression. Estrogen replacement (OVX/E2) rescued vascular PPARγ-expression, reduced ROS generation, monocyt recruitment, atherosclerotic lesion formation and improved endothelial function. Inhibition of PPARγ by GW9662, a specific PPARγ-antagonist reduced 17β-estradiol mediated vasculoprotection although estrogen replacement therapy was applied to these mice. GW9662, emulates the relevance of PPARγ in mediating 17β-estradiol vasculoprotection. Finally, treatment of OVX ApoE−/−mice with pioglitazone (OVX/pioglitazone), a selective PPARγ-agonist, compensates vascular defects induced by estrogen deficiency by increasing vascular PPARγ-expression and providing subsequent anti-inflammatory and vasculoprotective effects.

Conclusions: In summary, 17β-estradiol regulates vascular PPARγ-expression in WT- and ApoE−/−mice. The presented data demonstrate the fundamental relevance of PPARγ as downstream target of 17β-estradiol-related anti-inflammatory and atheroprotective effects within the vascular wall independent of its cardiovascular risk factor modifications.

MMP-9 released angiogenesis inhibitors prevent adaptive capillary growth in hypertrophy and contribute to progression to heart failure

K. Ablasser1, A. Nikolova1, P. Del Nido2, F. Fuhrwald2, R. Gasser1, B. Pieske1, I. Friehs4, Medical University of Graz, Department of Cardiology, Graz, Austria; Children’s Hospital, Boston, United States of America

Purpose: In left ventricular pressure-overload hypertrophy, lack of adaptive capillary growth contributes to progression to heart failure. Remodeling of the hypertrophied myocardium requires protection of extracellular matrix (ECM) carried by matrix metalloproteinases (MMPs). Specifically, MMP-9, is known to cleave ECM components which generate angiogenesis inhibitors (angiotatin, endostatin, tumstatin). We hypothesized that MMP-9 released anti-angiogenic factors during compensated hypertrophy, which resulted in lack of adaptive capillary growth and progression to heart failure.

Methods: Newborn rabbits underwent aortic banding. At compensated hypertrophy (4 weeks) and systolic heart failure (7 weeks) myocardial tissue from banded and sham-operated control animals was analyzed by immunoblotting for angiostatin, endostatin and tumstatin. MMP-9 activity was determined by zymography. A MMP-9 specific inhibitor [N-(1,1-biphenyl-4-yl)4-yl]phenylalanine (D-Phe-Ala) was administered peripherally via coronary artery and tissue was analyzed as stated above. Weekly echocardiography to determine mass/volume ratio and fractional shortening was performed.

Results: PPARγ was activated in hypertrophied myocardium versus controls (23±1 versus 17±1, p=0.04), which resulted in significantly increased levels of angiotatin (86±7 versus 115±10, p=0.003), endostatin (28±1 versus 33±1, p=0.02) and tumstatin (17±4 versus 35±6, p=0.003). Zymography confirmed inhibition of MMP-9 (hypertrophy: 17±1 versus hypertrophy-MMP-9 inhibitor: 14±6; p=0.01) and angiotatin, endostatin and tumstatin were down-regulated, accompanied by up-regulation of MMP-9 density (hypertrophy: 99±0.7 versus 0.05). Zymography confirmed inhibition of MMP-9 (hypertrophy: 17±1 versus hypertrophy-MMP-9 inhibitor: 2±0.05; p=0.002). Mass/volume ratio by echocardiography, as a measure of hypertrophy, showed a significant increase in the banded group versus the sham group at week 4 (0.84±0.08 versus 1.02±0.06, p=0.05) but declined significantly when the hearts dilated (0.88±0.04 versus 0.77±0.05, p=0.05). Inhibition of MMP-9 prevented the dilation of the left ventricle and, as confirmed by echocardiographic measurements of fractional shortening, prevented systolic heart failure after 7 weeks.
Conclusions: Remodeling resulted in activation of MMP-9 which enhanced the release of angiogenesis inhibitors, angiotatin, endostatin and tumstatin, which prevented adaptive capillary growth in hyperperfused myocardium. Therapeutic intervention aimed at inhibition of MMP-9 was successful in maintaining capillary density and thereby preventing heart failure.

LIPIDS

Identification of a novel soluble APOA-I truncated form increased in diabetic patients

J. Cubedo¹, T. Padro², M. Garcia-Arguinzonis¹, L. Badimon¹

¹Barcelona Cardiovascular Research Center (CSIC-ICCC), CiberOBN, IIB-Sant Pau, Hosp Sant Pau, UAB, Barcelona, Spain; ²Barcelona Cardiovascular Research Center (CSIC-ICCC), IIB-Sant Pau, Hosp Sant Pau, UAB, Barcelona, Spain

Apolipoprotein A-I (APOA-I) is the main protein of HDLs. In addition to its structural role, APOA-I has a functional role in reverse cholesterol transport by promoting the efflux of cholesterol from peripheral cells into HDL and activating lecithin-cholesterol acyltransferase. In fact, APOA-I modifications have an important impact on the cholesterol transport ability and in the regulation of the HDL particle size. By applying proteomic approaches we have investigated APOA-I profile in serum and HDL samples and analyzed its changes in diabetic patients, that often have pro-atherothrombotic phenotype.

Methods: Characterization of serum and HDL APOA-I was performed by 2D-electrore- electrophoresis (2DE) followed by mass-spectrometry (MALDI-TOP/TOF). Serum protein profile of diabetic patients was compared to non-diabetic individuals.

Results: APOA-I characterization depicted a cluster of 5 spots (Mw: 28kDa; pI: 5.75). In addition, serum showed 1 spot of 26kDa and a pI of 5.75 that was not present in HDL. MALDI-TOP/TOF analysis revealed that the 28kDa spot is a truncated form of APOA-I lacking a 1-38 (APOA-I-Barcelona = aa 39-267). Diabetic patients showed decreased levels of total APO A-I (p < 0.05) when compared to the non-diabetic group. A 2-fold increase intensity of the APOA-I-BCN form was detected (p < 0.05).

Conclusions: Our results demonstrate for the first time the presence of a soluble truncated APOA-I form (APOA-I-BCN) that is not found in HDL particles. The increase of this truncated APOA-I form in the diabetic patients may contribute to their higher cardiovascular risk and may have effects in particle turnover.

Carbamylated low density lipoprotein (LDL) induces endothelial dysfunction by uncoupling of endothelial nitric oxide synthase (eNOS)

T. Speer, F. Owalo, E.W. Hoy, B.M. Razavi, A. Akhmedov, T.F. Luescher, F.C. Tanner. Cardiovascular Research, Physiology Institute, University of Zurich, Zurich, Switzerland

Introduction: Cardiovascular events are the main cause of death in Western civil- ization. Lipoproteins play an important role in the regulation of vascular integrity. Recent evidence suggests that urea-driven carbamylation of lysine residues may affect the functional properties of lipoproteins; however, its effect on endothelium- dependent relaxation is unknown. We therefore examined the effect of carbamy- lated low density lipoproteins (cLDL) on endothelial function.

Methods: cLDL from healthy donors was isolated by sequential ultrafiltration and carbamyalted ex vivo using potassium cyanate. The degree of carbamyla- tion and oxidation was assessed by HPLC/ESI-MS/MS and TBARS assay, re- spectively. Vascular reactivity after treatment with native (nLDL) or carbamyalted (cLDL) LDL was examined in organ chamber experiments using aortic rings of wildtype or lectin-like oxidized LDL receptor-1 (LOX-1) transgenic mice. Superox- ide and nitric oxide production in aortic rings and human aortic endothelial cells (HAEC) was determined using electron spin resonance (ESR) spectroscopy. Activ- ation and uncoupling of endothelial NO synthase (eNOS) was assessed by West- ern blot techniques. In HAEC, silencing of LOX-1 was performed using LOX-1 specific siRNA.

Results: Carbamylation of LDL resulted in carbamyl-lysine levels comparable to those in patients with chronic kidney disease; no oxidative changes were ob- served. cLDL impaired endothelium-dependent relaxation of aortic rings, whereas nLDL had no effect. Addition of superoxide dismutase catalase restored vascular relaxation after cLDL treatment, indicating an important role of superoxide pro- duction in cLDL mediated endothelial dysfunction. cLDL directly induced super- oxide production in aortic rings as well as in HAEC via eNOS uncoupling. cLDL induced endothelial dysfunction was enhanced in LOX-1 transgenic mice, reveal- ing LOX-1 as the receptor mediating the actions of cLDL. Accordingly, knockdown of LOX-1 by siRNA improved NO production and attenuated superoxide release in HAEC.

Conclusions: These data newly demonstrate that cLDL induces endothelial dys- function by causing eNOS uncoupling and increasing endothelial superoxide pro- duction via LOX-1. This indicates a new important mechanism in the pathogene- sis of atherosclerotic diseases.

Effects of AMR101 on lipid and inflammatory parameters in patients with diabetes mellitus-2 and residual elevated triglycerides (200-500 mg/dL) on statin therapy at LDL-C goal: the ANCHOR study

E. Brinthon¹, C. Ballantyne², H. Bays³, J. Kastelein⁴, R. Breachman⁵, P. Sori⁶

¹University of Utah School of Medicine, Salt Lake City, United States of America; ²The Methodist Hospital Debakey Heart & Vascular Center, Houston, United States of America; ³Louisville Metabolic and Atherosclerosis Research Center, Louisville, United States of America; ⁴Academic Medical Center, University of Amsterdam, Department of Cardiology, Amsterdam, Netherlands; ⁵Amarin Pharma Inc., Mystic, United States of America

Purpose: To determine the effects of AMR101 (a novel omega-3 fatty acid agent containing ≥96% pure isosapentaenyl ethyl, the ethyl ester of eicosapentaenoic acid) on lipid and inflammatory parameters in patients with diabetes in the phase 3 12- week ANCHOR study (residual high fasting TG levels [200-500 mg/dL] despite optimized LDL-C [≤100 mg/dL]).

Methods: Intent-to-treat analysis of AMR101’s effects on median placebo- adjusted percent change from baseline in endpoint parameters was performed in 3 subgroups: total (all subjects with diabetes), well-controlled diabetes, and less-controlled diabetes (less than > than median baseline HbA1c).

Results: Of 702 patients randomized to AMR101 4 g/d, 2 g/d, or placebo, 514 (73%) had diabetes mellitus-2. Between the two groups except for lower hsCRP in the well-controlled diabetes group. AMR101 signifi- cantly reduced TG, non-HDL-C, apo B, and RLP-C in all groups. LDL-C in the known to have high TG group, and hsCRP in the total of randomized diabetes groups. Interestingly, decreases in hsCRP and apo B were far greater in patients with less-controlled diabetes. Importantly, FPG, HbA1c, insulin, and HOMA-IR were not significantly changed in any group.

Effects of AMR101 4 g/d

<table>
<thead>
<tr>
<th>Change in</th>
<th>Baseline</th>
<th>Baseline Total Diabetes, P</th>
</tr>
</thead>
<tbody>
<tr>
<td>TG (n=78, 87, 165)</td>
<td>-21.6, 0.0001</td>
<td>-24.8, 0.0001</td>
</tr>
<tr>
<td>LDL-C (n=78, 87, 165)</td>
<td>-6.6, 0.0031</td>
<td>-5.7, 0.0304</td>
</tr>
<tr>
<td>Non-HDL-C (n=78, 87, 165)</td>
<td>-11.3, 0.0019</td>
<td>-18.0, 0.0001</td>
</tr>
<tr>
<td>hsCRP (n=78, 87, 165)</td>
<td>-4.0, 0.7372</td>
<td>-34.6, 0.0002</td>
</tr>
<tr>
<td>HDL-C (n=79, 43, 32)</td>
<td>26.7, 0.0002</td>
<td>26.3, 0.0004</td>
</tr>
<tr>
<td>Apo B (n=75, 85, 160)</td>
<td>-6.1, 0.0170</td>
<td>-12.8, 0.0001</td>
</tr>
</tbody>
</table>

Values are from Wilcoxon rank-sum test. Abstract abbreviations: Apo B = apolipoprotein B; FPG = fasting plasma glucose; HbA1c = hemoglobin A1c; non-HDL-C = non-high-density lipoprotein cholesterol; HOMA-IR = homeostasis model index insulin resistance; hsCRP = high-sensitivity C-reactive protein; LDL-C = low-density lipoprotein cholesterol; RLP-C = remnant-like particle cholesterol; TG = triglyceride.

Conclusions: In patients with diabetes and mixed dyslipidemia, AMR101 4g/d significantly improved lipid and lipid-related parameters without worsening glycemic control, with possibly greater effects among those with less-controlled diabetes.

Palmioleotide is increased in epicardial adipose tissue in heart failure and correlates with parameters of progressing failure

L.E. Fosshaug¹, G.P. Dahl¹, I. Risnes¹, O.K. Olsdåd², R.K. Berge¹, S. Nymo¹, L. Gullesdal², P. Aukrust², L.E. Vinge², E. Oie²

¹Diakonhjemmet hospital, Department of Internal Medicine, Oslo, Norway; ²University of Oslo, Rikshospitalet University Hospital, Research Institute for Internal Medicine, Oslo, Norway; ³University of Oslo, Rikshospitalet University Hospital, Dept. of Thoracic & Cardiovascular Surgery, Oslo, Norway; ⁴Ost university Hospital, Department of Medical Biochemistry, Oslo, Norway; ⁵University of Bergen, Institute of Medicine, Section of Medical Biochemistry, Bergen, Norway; ⁶Oslo University Hospital, Department of Cardiology, Oslo, Norway

Purpose: Epicardial adipose tissue (EAT) is a visceral fat depot which location and function are of growing scientific interest in regards to heart disease. The anatomical settings in the junctional area between EAT and the myocardium al- ways provides widespread communication between surrounding tissues which exists and they share the same microcirculation. EAT has been shown to function as an endocrine organ by secreting a wide range of mediators, including factors known to be involved in development of cardiovascular disease in patients with coronary artery disease. However, little is known about a potential role of EAT in development of heart failure (HF). The aim of this study was to characterise EAT as compared to subcutaneous adipose tissue (SAT) in patients with HF.

Methods: Thirty HF patients with ejection fraction <35% and 30 patients without HF undergoing thoracic surgery were included in the study. EAT and SAT were collected during thoracotomy and assessed with microarray analysis, RTPCR of known mediators in HF; and fatty acid (FA) profile.

Results: Unsupervised hierarchical clustering analysis of the microarray analysis in EAT and SAT identified depot-specific transcription patterns, including groups of mediators involved in myocardial inflammation, hypertrophy and apoptosis. Further their clustering analyses of EAT in HF and control patients also identified disease specific transcription patterns. Alterations in miRNA expression of genes involved in cardiac remodelling were observed using RTP-PCR in both SAT and EAT and...
The effects of tocilizumab treatment on lipids and inflammatory/prothrombotic biomarkers in patients (pts) with rheumatoid arthritis (RA): Data from the randomized, controlled, Measure study

I. McInnes 1, J.S. Lee 2, L. Thompson 3, J.T. Giles 1, J.M. Bathon 1, J.E. Salmon 4, A.D. Beaulieu 5, C.E. Codding 6, C. Deleuze 1, N. Sattar 7, 8. 1University of Oklahoma, Oklahoma City, United States of America; 2British Heart Foundation, Glasgow, United Kingdom

Purpose: Tocilizumab (TCZ), an anti-IL-6 receptor signaling inhibitor, has demonstrated efficacy in the treatment of RA. We investigated the net vascular effect of TCZ on lipids and inflammatory/prothrombotic biomarkers in RA patients.

Methods: In the double-blind 24-wk phase, RA pts with inadequate response to methotrexate (MTX) were randomized to receive MTX qw plus either TCZ 8 mg/kg IV or placebo (PBO) qw. Serum lipids were analyzed by NMR spectroscopy and biomarkers by ELISA. Data were analyzed using nonparametric analysis of variance, not corrected for multiplicity.

Results: Demographics were similar between groups. TCZ was superior to PBO in reducing RA disease activity, though 35% (12.9%) PBO and 17% (14.7%) TCZ pts entered open-label TCZ escape therapy at wk 12. The Table shows changes for TCZ vs PBO. Lipid changes occurred primarily in large VLDL/cholesterol and VLDL triglycerides. Though not significant (P>0.05), LDL increases occurred primarily in small particles. TCZ induced an increase in paraoxonase and reductions in HDL-associated SAA and sPLA2-IIA, hs-CRP, and prothrombotic biomarkers D-tirosine, fibrinogen, and Lp(a).

Selected outcomes at wk 12 and 24

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Wk 12</th>
<th>Wk 24</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCZ vs PBO, Kruskal-Wallis test:</td>
<td>*&lt;p&gt;0.001</td>
<td>*&lt;p&gt;0.005</td>
</tr>
</tbody>
</table>

Conclusions: TCZ induces quantitative and qualitative changes in lipids, as well as suppressing inflammation and lowering thrombotic potential in RA patients. The net vascular effect requires further study.

P1741

Concentration-dependent biphasic effects of high density lipoprotein on endothelial progenitor cells in vitro and related vasculogenesis in vivo

C.Y. Huang 1, Ph.D. Peng-Yen Lin 1, Ph.D. Chun-Ming Shih 2, Ph.D. Nor-Chung Chang 1, Ph.D. Jaw-Wen Chen 3, Ph.D. Kou-Gi Shyu 4, 1Taipei Medical University Hospital, Taipei, Taiwan; 2Taiwan Veterans General Hospital, Department of Internal Medicine, Taipei, Taiwan; 3Shih Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan

High-density lipoprotein (HDL) has the potential to prevent atherosclerosis. However, the mechanism by which native HDL may affect endothelial progenitor cells (EPCs), which are pivotal for the renewal of denuded or aging endothelium and neo-vasculogenesis, remains mostly unknown. Here, we studied the effects of native HDL (5-800 μg/mL) on late-outgrowth human EPCs.

Methods and Results: We explored that intracellular signaling, including the PI3K/Akt, NO, p38 MAPK, and JNK/SAPK-related pathways, are involving in the endogenous capacity of EPC tube formation. HDL at low concentrations (5-50 μg/mL) further enhanced EPC tube formation via the PI3K/Akt/eNOS pathway. However, moderate to high concentrations of HDL (400-800 μg/mL) may enhance EPC senescence and impair EPC tube formation, which was found to be mediated by Rho-associated kinase (ROCK) activation, and promote the inhibition of PI3K/Akt phosphorylation as well as the inhibition of the p38 MAPK pathway. Treatment with ROCK inhibitors, either Y27632 or statins (atorvastatin and rosvastatin), may reverse high HDL-induced EPC senescence and impairment of EPC tube formation both in vitro and in vivo.

Conclusions: We present the novel finding that HDL may have biphasic effects on EPC functions and related vasculogenesis; and our current results could possibly provide some preliminary explanations on the “paradoxical” effects of high HDL.

P1742

Effects of Pitavastatin on increasing of high-density lipoprotein cholesterol and regression of carotid artery plaque


Background and Objective: A low level of high-density lipoprotein cholesterol (HDL-C) and the increase of carotid intima-media-thickness (IMT) are important risk factors for cardiovascular diseases. The aim of this study is to evaluate the efficacy of pitavastatin (2mg/day) for 12 months. Bilateral carotid IMTs were measured by ultrasonography at baseline and 12 months later. Pitavastatin significantly decreased total cholesterol, triglyceride, low-density lipoprotein cholesterol, apolipoprotein B and apolipoprotein E, and significantly increased HDL-C and apolipoprotein A1 (ApoA1). Max IMT (-0.0829 ± 0.1864 mm, p = 0.0001) was significantly decreased by -0.138 ± 0.06 (p=0.0001). Lp(a) significantly decreased by -0.1864 (p=0.0001). Plaque Score (%) significantly decreased in patients with increasing ApoA1, but not in patients without increasing ApoA1 (-0.138 vs. 0.41, p=0.02). There is no correlation between the change of HDL-C and IMT reduction. There is significant correlation between the %change of ApoA1 and PS. (P = 0.039)

Conclusion: Pitavastatin significantly improved lipid profile and induced the regression of carotid plaque, which favorable effects may be contributed through the increase of HDL-C and ApoA1.

P1743

Effects of ezetimibe, simvastatin and ezetimibe/simvastatin on correlations between apolipoprotein B, LDL cholesterol and non-HDL cholesterol in patients with primary hypercholesterolemia

M. Farrier 1, J.R. Guyton 2, E. Jensen 3, A. Polis 4, A.O. Johnson-Levonas 2, P. Brud 5, 1Point Medical, Dien, France; 2Duke University Medical Center, Durham, United States of America; 3Merck Sharp & Dohme Corp, Whitehouse Station, NJ, United States of America

Purpose: LDL-C is the primary target and non-HDL-C and apoB are secondary targets of therapy. Statin monotherapy lowers LDL-C and non-HDL-C more than apoB, thus statin-treated patients (pts) may be at increased coronary risk due to elevated levels of apoB-containing particles.

Abstract P1743 – Table 1

<table>
<thead>
<tr>
<th>N</th>
<th>apo B/LDL-C Pearson Correlation Coefficient (95% CI) (R²)</th>
<th>Predicted LDL-C (mg/dL) at apo B=0 (mg/dL)</th>
<th>apo B/non-LDL-C Pearson Correlation Coefficient (95% CI) (R²)</th>
<th>Predicted non-LDL-C (mg/dL) at apo B=90 (mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo (untreated patients)</td>
<td>302</td>
<td>0.30 [0.72, 0.72]</td>
<td>0.81 (0.60, 1.00)</td>
<td>302</td>
</tr>
<tr>
<td>EZI 10 mg</td>
<td>291</td>
<td>0.77 [0.72, 0.82]</td>
<td>0.60 (0.50, 1.00)</td>
<td>291</td>
</tr>
<tr>
<td>Pitted SMIWA</td>
<td>119</td>
<td>0.76 [0.73, 0.79]</td>
<td>0.57 (0.50, 1.00)</td>
<td>119</td>
</tr>
<tr>
<td>Pitted EZI/SMIWA</td>
<td>120</td>
<td>0.76 [0.73, 0.79]</td>
<td>0.57 (0.50, 1.00)</td>
<td>120</td>
</tr>
<tr>
<td>Week 12 (following randomized treatment)</td>
<td>302</td>
<td>0.30 [0.72, 0.72]</td>
<td>0.81 (0.60, 1.00)</td>
<td>302</td>
</tr>
<tr>
<td>EZI 10 mg</td>
<td>291</td>
<td>0.82 [0.76, 0.85]</td>
<td>0.67 (0.50, 1.00)</td>
<td>291</td>
</tr>
<tr>
<td>Pitted SMIWA</td>
<td>119</td>
<td>0.82 [0.76, 0.85]</td>
<td>0.67 (0.50, 1.00)</td>
<td>119</td>
</tr>
<tr>
<td>Pitted EZI/SMIWA</td>
<td>120</td>
<td>0.82 [0.76, 0.85]</td>
<td>0.67 (0.50, 1.00)</td>
<td>120</td>
</tr>
</tbody>
</table>
Earlier senescent phenotype in Tangier disease skin fibroblasts

M. Puntero, F. Bigagzi, A. Ragusa, S. Vicari, E. Grisanti, F. Strana, T. Sampietro, Gabriele Monastero Foundation-CNR Region Toscana, Institute of Clinical Physiology, Pisa, Italy

Purpose: Tangier disease (TD) is characterized by virtual absence of high density lipoprotein (HDL) in plasma; TD patients are at increased risk for coronary artery disease (CAD). A relationship between cellular senescence and development of atherosclerotic CAD has been proposed and increased senescence in TD fibroblasts has been reported.

We investigated replicative senescence of skin fibroblasts in vitro in an Italian homozygous case of ABCA1 mutation (TDho) and his heterozygous father (TDhe).

Methods: Primary TDho and TDhe fibroblast cell lines, established from skin biopsies, were cultured according to the standard conditions. The cells were passaged by split to increase cumulative population doubling level. At the same passages of culture (early, intermediate and late) in TDho and TDhe fibroblasts, we analysed the expression of the particular isoform senescent-associated β-galactosidase (SA-β-gal). Furthermore, gene expression of ABCG1 and its involvment in the cholesterol efflux and influx were analysed at the same passages.

Results: TDho fibroblasts expressed the phenotype associated to senescence such as slow cell proliferation and increased staining for SA-β-gal compared to TDhe fibroblasts. TDho and TDhe cells were mildly stained with SA-β-gal at passage 8 (22.84% vs 20.35% respectively) and passage 17 (36% vs 29.62% respectively). The percentage of SA-β-gal positive cells was highly increased in TDho at passage 22 compared to TDhe cells (66.15% vs 41.35% respectively). TDho fibroblasts expressed ABCG1 gene significantly more than TDhe cells, especially in first replication cycles (0.44 vs 0.14 arbitrary unit respectively) with a down-regulation at higher cycles (0.14 vs 0.08 arbitrary unit respectively). LDLr down-regulation at higher cycles (0.14 vs 0.08 arbitrary unit respectively). LDLr was markedly reduced in ApoE-/- mice compared to untreated ApoE-/- mice controls (33.5±3% vs 19.5±1%, p<0.01). Treatment with ivabradine increased circumferential strain by approximately 40% compared to untreated ApoE-/- mice controls (33.5±3% vs 19.5±1%, p<0.01). The renal mass reduction results in important cholesteryl esters stored in the renal cortex. Therefore we characterized effects of heart rate reduction (HRR) by I(f) current inhibition on aortic endothelial cell senescence (Apoe-/- mice). Our kinetic model considered that CE were removed from plasma via LDLr and ABCA1 pathway.

Conclusions: Earlier senescent phenotype in TDhe fibroblasts was significantly associated with decreased expression of ABCG1 gene and reduced LDLr expression. However, the percentage of SA-β-gal positive cells did not show any association with LDLC-lowering in EZ group. The percentage of SA-β-gal positive cells showed significant and positive association with CE-LDLr and CE-ABC transporter. However, the percentage of SA-β-gal positive cells did not show any association with LDLC-lowering in EZ group.

Circulating PCSK9 levels and additional LDL cholesterol-lowering after standard dose atorvastatin therapy: comparison with doubling dose and ezetimibe combination


Background: PCSK9 plays a pivotal role in LDL-receptor mediated cholesterol metabolism. However, little is known about the clinical significance of its circulating levels during cholesterol-lowering therapy. To clarify this, relations between circulating PCSK9 levels and additional cholesterol-lowering and vascular inflammation induced Rac1 activity and p47 phox membrane translocation. The results underline the importance of heart rate as a vascular risk factor.

Methods: This post-hoc analysis evaluated relationships between apoB:LDL-C and apoB:non-HDL-C using data from 3 similarly designed, randomized, double-blind studies in 3083 pts with primary hypercholesterolemia (LDL-C 145–250mg/dL). Participants received simvastatin (SIMVA) 10, 20, 40 or 80mg, or EZE 10mg/SIMVA 10, 20, 40 or 80mg for 12 wk. Simple linear regression analyses calculated LDL-C and non-HDL-C lev

Results: LDL-C and non-HDL-C were well correlated with apoB at baseline. Treatment with lipid-lowering therapy generally improved these correlations, especially for SIMVA and EZE/SIMVA. At baseline, predictors LDL-C and non-HDL-C values corresponding to apoB-90mg/dl were similar across all groups. At Wk12, LDL-C and non-HDL-C values were closer to the more aggressive LDL-C and non-HDL-C goals (70 and 100mg/dl, respectively). In general, predicted LDL-C and non-HDL-C values decreased with increasing dose of SIMVA or EZE/SIMVA.

Conclusions: Heart rate reduction induced by I(f) current inhibition reduces aortic compliance in ApoE-/- mice. The underlying mechanisms include reduced AT1 receptor expression, vascular inflammation and reduced Rac1 activity and p47 phox membrane translocation. The results underline the importance of heart rate as a vascular risk factor.
accumulation in the HDL particles. The kinetic basis of such accumulation was an increased exchange of cholesterol esters from apoB-containing lipoproteins towards HDL. These results strongly suggests an important role of the kidneys to HDL-cholesterol metabolism

**P1748**

The release of sphingosine-1-phosphate from human platelets during acute coronary syndrome is attenuated by aspirin

A. Polzin1, A. Boehm2, A. Lueth2, B. Kleusser3, T. Zeus4, Rassaf6, M. Kelm5, H.K. Kroenen6, K. Schrauf6, B.H. Rauch2.

1 Heinrich-Heine University of Dusseldorf, Department of Cardiology, Dusseldorf, Germany; 2 Ernst Moritz Arndt University of Greifswald, Institute of Pharmacology, Greifswald, Germany; 3 Heart Centre & Department of Public Health & Clinical Medicine, University of Greifswald, Germany; 4 Heinrich-Heine University of Dusseldorf, Institute of Pharmacology and Clinical Pharmacology, Dusseldorf, Germany

**Purpose:** The sphingosine-derived lipid signaling molecule sphingosine-1-phosphate (S1P) is an important mediator of vascular homeostasis. It is stored in large quantities in platelets. Recently, we have shown that its release from platelets after activation of the protease-activated receptor-1 (PAR-1) by thrombin is dependent on thromboxane (TX) formation. In the present study, we aimed to treat our in vitro findings with clinical data, by directly using, without data interpretation, the cyclooxygenase inhibitor aspirin (acetylsalicylic acid) affects the release of S1P in patients with an acute coronary syndrome (ACS). Secondly, by applying an anti-thrombin anticoagulation (TAT)-complex, we examined if an ACS leads to an enhanced intrathrombin formation. We hypothesized that administration of 500 mg aspirin during acute coronary syndrome inhibits the release of S1P from human platelets.

**Methods:** Blood samples were taken from patients with ACS before and after intravenous treatment with 500 mg aspirin. S1P was quantified in platelet-rich plasma (PPP), platelet-poor plasma (PPP) and washed platelets (WP) by mass spectrometry; TAT-complexes by ELISA.

Patients characteristics were as follows (n=22), age 60±10 years, 60% male, 3±2 cardiac risk factors. 40% were on a 100 mg aspirin pretreatment, 9% on a dual antiplatelet therapy with 100 mg ASA and 75 mg Clopidogrel and 61% were on aspirin naive. Age matched patients (n=10) with stable coronary syndrome (all on 100 mg aspirin) were used as control group.

**Results:** The concentration of S1P before and after acute aspirin treatment did not differ in PPP (866±70 pmol/mL vs 927±82 pmol/mL). However, aspirin treatment significantly decreased S1P levels in PPP (621±51 pmol/mL vs 548±46 pmol/mL) and increased S1P in WP (5126±245 pmol/mL vs 382±45 pmol/mL). The levels of S1P in PRP, PPP and WP from patients were significantly lower than in patients with a stable CAD (PRP: 866±70 pmol/mL vs 176±84 pmol/mL, PPP: 621±51 pmol/mL vs 128±54 pmol/mL, WP: 199±25 pmol/mL vs 634±39 pmol/mL). Enhanced formation of thrombin in platelets with ACS was evidenced by detection of increased plasma TAT-complexes (11.6±4.9 μg/L) versus control patients (3.3±0.2 μg/L).

**Conclusions:** Acute coronary syndrome leads to S1P release from human platelets. This can be attenuated by intravenous treatment with 500 mg aspirin. S1P was quantified in platelet-rich plasma (PRP), platelet-poor plasma (PPP) and washed platelets (WP) by mass spectrometry; TAT-complexes by ELISA.

**P1750**

Protective effects and mechanisms of baicalein on lysophosphatidylcholine-induced injury in cardiomyocytes

J.H. Hsu1, J.R. Wu1, J.L. Yeh2, 1 Kaohsiung Medical University, College of Medicine, Department of Pediatrics, Kaohsiung, Taiwan; 2 Kaohsiung Medical University, College of Medicine, Department of Pediatrics, Kaohsiung, Taiwan

**Background:** Lysophosphatidylcholine (LysoPC), a metabolite from membrane phospholipids, accumulates in the ischemic myocardium and plays important role in the development of myocardial dysfunction and ventricular arrhythmia. Baicalein is a flavonoid extracted from the root of Scutellaria baicalensis Georgi, a medicinal plant traditionally used in oriental medicine. The aim of this study was to determine the protective effects and mechanisms of baicalein on LysoPC-induced injury in rat H9c2 embryonic cardiomyocytes.

**Methods:** We first examined the cellular survival rate by MTT assay. The protective effect of baicalein on LysoPC-induced apoptosis of H9c2 cells was investigated by evaluating caspase activities. The protective effects of baicalein against LysoPC-induced apoptosis of H9c2 cells by evaluating caspase activities were assessed using a caspase activity assay kit. The protective effect of baicalein on LysoPC-induced apoptosis of H9c2 cells was investigated by measuring caspase activities and inactivation of the caspase-Bax pathway.

**Results:** Results of the MTT assay and morphological observation showed that baicalein increased cell viability and reduced the viability of H9c2 cells, and these were attenuated by aspirin. Baicalein treatment with baicalein significantly inhibited LysoPC-induced Ca2+ influx and phosphorylation of mitogen-activated protein kinase in H9c2 cells. Furthermore, incubation of H9c2 cells with baicalein significantly decreased the intracellular Ca2+ concentration levels induced by LysoPC. In addition, baicalein increased expression of anti-apoptotic Bcl-2 protein, inhibited expression of pro-apoptotic Bax protein and attenuated expression of caspase-3/9 induced by LysoPC.

**Conclusion:** These results indicate that baicalein possesses abilities to suppress apoptosis and protect against LysoPC-induced cell death through inhibition of Ca2+ influx and ROS generation and inactivation of the caspase-Bax/Bcl-2 pathway. These findings suggest that baicalein may be valuable in the prevention of lipid-induced cardiac damage.

**P1775**

Association of apolipoprotein A-IV A347T gene polymorphism and high density lipoprotein cholesterol among north Indians

H. Rai1, S. Kumar1, A.K. Sharma2, C.M. Pandey3, S. Mastaana3, S. Agrawal1, N. Sinha1, 1 Sanjay Gandhi Post Graduate Institute of Medical Sciences (SGPGIMS), Lucknow, India; 2 Department of Zoology, University of Lucknow, Lucknow, India; 3 School of Sport Exercise and Health Sciences, Loughborough University, Leicestershire, United Kingdom; 4 Sahara Hospital Lucknow, Lucknow, India

**Background:** In studies conducted among various ethnic populations, an inverse relationship has been seen between serum levels of high density lipoprotein cholesterol (HDL-c) and the risk for cardiovascular events including myocardial infarction, stroke and mortality. It is also noteworthy that lower levels of HDL-c are prevalent among Indians, who also demonstrate highest incidences of coronary artery disease (CAD) among various populations around the world. These lower levels of HDL-c among Indians may be attributed to several genetic polymorphisms especially those in the apolipoprotein(Apo) AI-CIII-AIV gene cluster. Some workers have demonstrated the association of Apo AIV A347T gene polymorphism with lower levels of high density lipoprotein cholesterol(HDL-c), however, earlier studies among subjects of Indian ethnicity are lacking.

**Objective:** The current study was aimed to examine and replicate the association of Apo AIV A347T gene polymorphism and the levels of HDL-c among healthy individuals of north Indian ethnicity.

**Methods:** We prospectively enrolled 200 healthy individuals of north Indian ethnicity consented and sampled them for serum lipid and subsequent genotyping. Genotyping technique used was standard polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP).

**Results:** A total of 163 (81.5%) of the subjects were males, mean age 44.5±33.13 years. Among CAD risk factors, a total of 44 (22%) were smokers, 35 (18%) hypertensives, 13 (6.5%) diabetics and 13 (6.5%) had familial history of CAD. We found 19 (9.5%) homozygous mutants(TT), 75 (37.5%) heterozygous (AT) and 106 (53%) of wild type (AA) genotypes in our sample. The results were found consistent with Hardy-Weinberg proportions. We found no significant difference in mean total cholesterol between the TT group and the AT group. In addition, the TT or AT genotypes did not influence the lean mass, weight and BMI. The HDL levels were compared among the three genotypes, TT, AT and AA, using ANOVA. The results showed no significant difference in mean levels of HDL-c.

**Conclusions:** This study demonstrated that Apo AIV A347T gene polymorphism and high density lipoprotein cholesterol(HDL-c) and the risk for cardiovascular events including myocardial infarction, stroke and mortality. It is also noteworthy that lower levels of HDL-c are prevalent among Indians, who also demonstrate highest incidences of coronary artery disease (CAD) among various populations around the world. These lower levels of HDL-c among Indians may be attributed to several genetic polymorphisms especially those in the apolipoprotein(Apo) AI-CIII-AIV gene cluster. We found no significant differences in mean total cholesterol between the TT group and the AT group. In addition, the TT or AT genotypes did not influence the lean mass, weight and BMI. The HDL levels were compared among the three genotypes, TT, AT and AA, using ANOVA. The results showed no significant difference in mean levels of HDL-c.
type [26.18±0.97(SE=0.95) versus 29.10±10.27(SE=0.99);95%CI=5.66 to 0.18, p=0.04 mg/dL respectively]. As a result TC/HDLC ratio was also found to be significantly lower in mutants as opposed to wild genotypes[5.53±1.41 versus 5.03±1.42; 95%CI=0.09 to 0.89, p=0.01 respectively].

Conclusion: We conclude a positive association between lower levels of serum HDLC and ApoAVI437T gene polymorphism among North Indians. This may prove to be one of the causes of lower levels of HDLC among Indians which significantly contributes to the cumulative risk of an individual in a multifactorial disease such as CAD.

P1752

ApoB/ApoA-I ratio and atherogenic index of plasma (AIP) in young health subjects

S.H.V. Oliveira1, G.A. Oliveira1, C.A.S. Morais2, L.M. Lima1
1Federal University of Viçosa, Department of Medicine and Nursing, Viçosa, Minas Gerais, Brazil; 2Federal University of Viçosa, Department of Biochemistry and Molecular Biology, Viçosa, Minas Gerais, Brazil

Purpose: Lipoprotein ratios can provide better information about metabolic and clinical interactions between lipid fractions than isolated LDL cholesterol levels. Apolipoprotein B (apoB)/apolipoprotein A-I (apoA-I) ratio and Atherogenic Index of Plasma (AIP) reflects the balance between atherogenic and protective particle. AIP is the result of logarithmic transformation of the triglyceride/HDL and LDL/HDL cholesterol concentration ratio. The reference values of these indices are not yet fully understood in all populations. The present study determined ApoB/ApoA-I and AIP using a study setup new and complex methods, such as 4D echo and 2D speckle tracking imaging (STI) to evaluate deformation and rotation of the LV, in order to test ventriculo-arterial coupling and its benefits on cardiac function.

Methods: We included 110 students, with 44% male and 56% female, mean age of 20.9±1.7 years. Their blood pressure was measured in recline state. Anthropometric measurements such weight, height and abdominal circumference were taken and Body Mass Index (BMI) calculation was performed. Blood samples were obtained from the student in 12-hour fast, using vacuum tubes without anti-coagulant. ApoB, apoA-I, HDL cholesterol, LDL cholesterol and triglyceride were analyzed using specific methods. Statistical analysis was performed by t-Student test after logarithmic transformation of data. The Pearson correlation test was used to verify the correlation between continuous variables.

Results: Cholesterol total, HDL and apoA-I were significantly higher in women than in men (p<0.001). No significant differences were observed between men and women for ApoB/ApoA-I ratio, LDL, triglyceride or apoB levels. The means obtained for ApoB/ApoA-I index and AIP were 0.62±0.35 and 0.035±0.010, respectively. AIP values were significantly lower (p=0.002) in women (0.033±0.009) when compared with men (0.039±0.010). Positive and significant correlations were observed between ApoB/ApoA-I ratio and BMI (r=0.25; p=0.04), abdominal circumference (r=0.25; p=0.04) and LDL (r=0.67; p<0.001). And also observed significant positive correlations between AIP and triglycerides (r=0.46; p<0.001) and between AIP and LDL (r=0.33; p=0.036). Negative and significant correlations were obtained between ApoB/ApoA-I ratio and HDL (r=-0.57; p<0.001), and between AIP and HDL (r=-0.86; p=0.001).

Conclusions: These findings indicate that ApoB/ApoA-I ratio showed a higher correlation with LDL than the AIP in studied subjects. Becomes necessary to consider that LDL, a parameter not used to calculate the lipid indices studied is widely used in clinical practice for cardiovascular risk assessment. Additional studies may contribute for a more precise standardization of these indexes in different population.

CARDIAC ADAPTATIONS IN ATHLETES

P1753

Optimized ventriculo-arterial coupling in endurance-athletes, determining better left ventricular deformation and rotation

M. Fiorescu1, O.A. Enescu1, D. Mihalces2, R. Minuc1, R.C. Rimbas1, L.S. Magda1, M. Cintzea1, D. Vinereanu2
1University Emergency Hospital, Bucharest, Romania; 2University of Medicine and Pharmacy Carol Davila, Bucharest, Romania

Endurance exercise training is associated with left ventricular hypertrophy (LVH) and spreading of "supranormal" cardiac function, suggesting that this is a physiological phenomenon. Hypertrophy alone cannot explain increase in cardiac function, therefore, other mechanisms, such as better arterial function, might be involved. Our study uses new and complex methods, such as 4D echo and 2D speckle tracking imaging (STI) to evaluate deformation and rotation of the LV, in order to test ventriculo-arterial coupling and its benefits on cardiac function.

Methods: 64 subjects (21±4 years, 44 male) were enrolled: 40 endurance athletes and 24 control. Subjects were stratified according to former marathon participation. Controls (n=24), endurance-athletes (n=40). The LV was imaged using conventional and 4D auto LV quantification echo was used to assess LV geometrical measurements such weight, height and abdominal circumference (r=0.25; p=0.04) and LDL were observed between ApoB/ApoA-I ratio and BMI (r=0.25; p=0.04), abdominal circumference (r=0.25; p=0.04) and LDL (r=0.67; p<0.001). And also observed significant positive correlations between AIP and triglycerides (r=0.46; p<0.001) and between AIP and LDL (r=0.33; p=0.036). Negative and significant correlations were obtained between ApoB/ApoA-I ratio and HDL (r=-0.57; p<0.001), and between AIP and HDL (r=-0.86; p=0.001).

Conclusions: These findings indicate that ApoB/ApoA-I ratio showed a higher correlation with LDL than the AIP in studied subjects. Becomes necessary to consider that LDL, a parameter not used to calculate the lipid indices studied is widely used in clinical practice for cardiovascular risk assessment. Additional studies may contribute for a more precise standardization of these indexes in different population.

P1754

Long-term cardiac remodeling and arrhythmias in nonelite marathon runners: focus on the right heart

M. Wilhelm1, L. Roten2, H. Tanner3, J.P. Schmid1, H. Saner4
1University Hospital of Bern, Department of Cardiology, Bern, Switzerland

Background: Long-term endurance sport is associated with atrial remodeling and atrial arrhythmias. More importantly, high-level endurance training may promote complex ventricular arrhythmias originating from a dysfunctional right ventricle (RV). We investigated the long-term consequences of marathon running on cardiac remodeling as potential substrate for arrhythmias with a focus on the right heart.

Methods and Results: We invited runners of the 2010 Grand Prix of Bern, a 10 mile race. 673 marathon and non-marathon runners applied, 122 (61 women) entered the final analysis. Subjects were stratified according to former marathon participations: control group (non-marathon runners, n=34), group 1 (1 to 5 marathons, mean 2.7, n=46), and group 2 (<6 marathons, mean 12.8, n=42). Mean age was 42±7 years. Echocardiography and Holter monitoring was performed. Results were adjusted for gender, age, and lifetime training hours. Right and left atrial size increased with marathon participations. In contrast, RV and left ventricle (LV) dimensions showed no differences between the groups (Figure 1). In Group 2, right and left atrial enlargement was present in 60% and 74% of athletes, respectively. RV and LV enlargement was present in only 2.4%/4.3% of marathon runners, respectively. In a multiple linear regression analysis, marathon participation was an independent predictor of right and left atrial size, but had no impact on RV and LV dimensions, and systolic and diastolic function. Atrial and ventricular ectopy was low and equally distributed between the groups.

P1755

Early repolarisation in young athletes: electrocardiographic characteristics and prevalence of risky phenotype

M. Di Valentino1, S. Siragusa1, M. Maggi2, G.A. Romano3, P. Pezzoli4, G. Moschovitis5, A. Gallino1, A. Menadlogl6
1Hospital of San Giovanni, Department of Cardiology, Bellinzona, Switzerland; 2Locarno Regional Hospital, Locarno, Switzerland; 3Lugano Regional Hospital, Lugano, Switzerland

Purpose: Early repolarisation in infero-lateral leads (ER) was traditionally con-
sidered a normal ECG variant more prevalent in young, males, black and athletes. However, recent reports have linked ER with an increased risk of sudden cardiac death. Some phenotypes of ER seems to be more ‘risky’: magnitude of J wave, inferior leads, ST segment elevation. The aim of this study was to analyse the phenotypic characteristics and the prevalence of “risky” ER in a cohort of young athletes. Methods: ECG was analysed as part of a prospective ongoing study about the impact of cardiovascular screening with ECG in young (14-35 years) competitive athletes. ER was defined as J point elevation ≥ 1 mm in 2 or more contiguous leads (except V1-V3). Following features were noted: localisation of ER (inferior, lateral or infero-lateral), amplitude of J point, morphology of J wave (notch, slurred or indeterminate), ST segment pattern (ascending, horizontal or descending). “Risky” ER was defined as follows: amplitude of J point ≥ 2 mm, inferior leads, ST segment elevation. Results: ECG of 920 athletes (75% males, age 19.9±6.5 years) was analysed. An ER pattern was present in 318 athletes (35%). In 14% of athletes it was localised in infero-lateral leads, in 11% in lateral leads and in 10% in inferior leads. Maximal amplitude of J point was ≥ 2 mm in 35% of ER pattern. The morphology of J wave was notch in 54%, slurred in 26% and indeterminate in 20%. The ST segment was ascending in 52%, horizontal in 28% and descending in 20%. ER with a descending ST segment in inferior leads was present in 7% of athletes, with J point amplitude ≥ 2 mm (“risky” ER) in 3% of athletes. No athlete with ER suffered from syncope of undefined origin or had family history of premature sudden death. Conclusions: ER is a common ECG pattern in young athletes. The most frequent phenotype is a notch J wave in lateral leads with ascending ST pattern. The phenotype that seems to be more “risky” (inferior leads, ST segmenting, J point ≥ 2 mm) is relatively frequent. This should be taken into account before drawing premature conclusion about risk stratification in this young healthy population.

**P1756**

The “early repolarisation” phenomenon: association with other cardiovascular findings in middle-aged long distance runners

P. Aagaard1, L. Wecke1, A. Sahlen1, L. Bergfeldt2, F. Braunschweig1, 1Karolinska Institutet, Department of Cardiology, Karolinska University Hospital, Stockholm, Sweden; 2Sahlgrenska Academy, University of Gothenburg, Dept. of Molecular & Clinical Medicine/Cardiology, Gothenburg, Sweden

**Purpose:** Early ST elevation (early repolarisation phenomenon, ER) is a common ECG feature in athletes. The prognostic implication of this finding is under debate. We performed a detailed assessment of cardiovascular function in long distance runners with and without ER. Methods: 153 male runners ≥45 years (50.5±8 years), participating for their first time in the worlds largest cross-country race (Lidingöloppet), were assessed 10±4 days before the race by medical history and physical exam, 12-lead ECG, vector-cardiography (VCG), blood tests, and echocardiography. Subjects were classified according to the presence, localisation and morphology of ER, defined as ST-segment elevation according to AHA/ACC/HRS recommendations 2009 (≥5mm in leads V2 or V3, or ≥1mm in any other lead). Results: ER was present in 43% (286/650; 95% CI: 21-35%), compared with 5-10% reported for the general population. The predominant localisation of ER was anterior in 32, inferior in 5 and lateral in 6 subjects. All had a rapidly ascending ST-segment morphology. Subjects with ER, regardless of localisation, were characterized by lower resting heart rate (50.9±9 vs. 59±8 bpm, p=0.005), lower body mass index (24.0±2.2 vs. 25.7±2.8 kg/m², p<0.001), and direct-3D (0.3±0.8 vs. 3.4±0.9 mm/mL, p=0.03). They also had a higher weekly training load (3.2±2.6 vs. 2.2±2.9 hours/week, p=0.04) and faster runtimes over 30 km (189±21 vs. 207±31 min, p=0.004; n=93). On ECG, subjects with ER had a larger vector gradient (QRS Tarea) (13±25 vs. 93±29 mV, p<0.001), larger QRS amplitude (1.9±0.5 vs. 1.6±0.4 mV, p<0.001), and T amplitude (0.7±1.3 vs. 0.5±0.16 mV, p<0.001), differences that could partly be attributed to between-group differences in HR. Following the race (1.05±0.80 hours; n=94) VCG differences between runners with and without ER remained unaltered. Conclusion: ER was more common in middle-aged male long-distance runners than reported in the general population. Such ECG-patterns, regardless of localisation, were associated with benign cardiac exams, including VCG, and with features of good physical fitness (“athlete’s heart”). These findings further support the view that, currently, all asymptomatic individuals with ER should be reassured.

**P1757**

Characterization of right atrial function and dimension in top-level athletes: a speckle tracking study

F. D’Ascenzo1, M. Camelli1, M. Pedeleli1, M. Lisi1, B. Natali1, A. Malandrino1, F. Alivio1, V. Zaca1, A. Causarano2, S. Mondolfo1

1University of Siena, Department of Cardiovascular Diseases, Siena, Italy; 2Santa Maria alle Scille Polytechnic, Department of Cardiovascular and Thoracic Cardiology Division, Siena, Italy; 3Staff Siena Football Club, Siena, Italy

**Background:** Although many echocardiographic studies are available about the adaptation of left ventricle to intensive training, right heart function has been poorly investigated in top-level athletes and no data are available about the functional role of right atrium (RA). The aim of this study is to investigate RA function and dimension by standard echocardiography and by 2D speckle tracking echo-cardiography (STE).

**Methods:** From professional sports team 100 top-level athletes were recruited and compared with 78 controls. Athletes in an off-training period or during prolonged forced rest resulting from injuries were excluded from the study. Results: Top-level athletes showed higher BSA as compared with controls and a lower resting heart rate (p<0.001). RA area and volume were significantly greater in athletes than in controls (p<0.001) and a significant difference was observed also when RA volume was indexed to BSA (20.96±7.28 vs. 19.89±4.99, p<0.001). Athletes exhibited greater right ventricular and inferior vena cava diameters (p<0.001). A typical pattern of myocardial deformation dynamics was observed in athletes, with a lower peak atrial longitudinal strain (40.9±8.86 vs 48.00±12.68, p<0.001) and a lower peak atrial contraction strain (13.05±4.84 vs 15.9±5.74, p<0.001) in comparison with controls. Interestingly, while athletes presented a higher E/A ratio (p<0.001), the E/e′ ratio did not differ between the two groups.

**Figure 1.** Typical pattern of RA strain by 2D STE

**Conclusions:** Top-level athletes present a physiological remodeling of the RA associated with intensive training that encompasses not only a morphological but also a functional adaptation. We reported for the first time reference values of RA strain in athletes, demonstrating that 2D STE is a useful tool to investigate RA function in the athlete’s heart.

**P1758**

Different LV systolic function in Norwegian elite football players with large and small left atrial volumes

G.F. Gjerda1, J. Hisdal1, E.E. Solberg2, T.E. Andersen2, Z. Raunovic3, K. Steine4, Ø. Oslo University Hospital, Akers and Bjornes College, Oslo, Norway; 2Diakonhjemmet Hospital, Oslo, Norway; 3Oslo Sports Trauma Research Center, Norwegian Football Association, Oslo, Norway; 4Oslo University Hospital, Akers, Oslo, Norway; 5Akershus University Hospital, Oslo, Norway

**Purpose:** Previously we have shown that a threefold difference in LA volume did not affect LA global systolic function by 2D strain. Since this enlargement also leads to larger LV volume and thus total volume (LVTV) on the left side, we wanted to explore any potential impact on LV systolic function. Methods: From our database of 595 male Norwegian football players, the 30 football players with respectively the largest and smallest left atrial end systolic volumes (LAESV) were defined. LV end diastolic volume (LVEDV) was measured by 2D echo and LVTV was calculated as LAESV + LVEDV. The following measurements of LV systolic function were performed: Biplane LVETV by 2D, maximal fractional shortening of septal and lateral mitral valves attachments by TVI, denoted TVIs, fractional shortening (FS) by M-mode, LV global longitudinal strain (GLS) by automated function imaging. LV myocardial performance index (MPI) was measured as a combined global parameter for LV systolic and diastatic function. All volumes were indexed by body surface area (BSA).

**Results:** All four echo indices for LV systolic and MPI were improved in athletes with large vs. small LAESV (Table). Moreover, EF, FS, TVI, GLS and MPI, correlated significantly to LVTV with r values of 0.3, 0.5, 0.4, 0.3 and 0.3 (all p<0.05), respectively. HR correlated only to FS, r = -0.3, and to MPI, r = -0.4 (both p<0.05).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Large LAESV (n=14)</th>
<th>Small LAESV (n=16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LAESV/BSA (ml/m²)</td>
<td>60.6±5.4</td>
<td>91.4±2.9</td>
</tr>
<tr>
<td>LVEDV/BSA (ml/m²)</td>
<td>85.3±16.6</td>
<td>60.6±7.6</td>
</tr>
<tr>
<td>LVTV/BSA (ml/m²)</td>
<td>145±16.4</td>
<td>80±8</td>
</tr>
<tr>
<td>EF (%)</td>
<td>58.0±3.9</td>
<td>55.3±3.1</td>
</tr>
<tr>
<td>TVI (cm/s)</td>
<td>7.4±1.2</td>
<td>6.7±1.2</td>
</tr>
<tr>
<td>FS (%)</td>
<td>34.2±6.6</td>
<td>27.7±3.9</td>
</tr>
<tr>
<td>GLS (%)</td>
<td>19.5±1.2</td>
<td>18.4±1.7</td>
</tr>
<tr>
<td>MPI</td>
<td>0.36±0.06</td>
<td>0.40±0.06</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>49±7.7</td>
<td>58±8.4</td>
</tr>
</tbody>
</table>

*Significantly different from LAmall (p<0.05).*

**Conclusions:** Athletes with large LA volumes have improved LV systolic function as measured by all four different LV systolic function indices and one global LV function index. These findings may indicate that the Frank Starling mechanism plays a role even in the heart of these young athletes.
Electrocardiograms in young athletes, characteristics and prevalence of abnormalities

M. Di Valentin1, P. Siragusa2, M. Maggi2, G.A. Romano2, R. Pezzoli2, G. Moscovits1, A. Galillo1, A. Menafoglio1, L. Cella2, L. Spano1, A. Azzurra2, S. Mongillo3

1Locarno Regional Hospital, Locarno, Switzerland; 2Lugano Regional Hospital, Lugano, Switzerland

Purpose: Regular physical training is associated with structural and functional changes in the heart which are reflected on the 12-lead electrocardiogram (ECG). Such changes may simulate cardiac diseases rendering ECG interpretation of young athletes sometimes difficult. The aim of this study is to evaluate the ECG characteristics and the prevalence of ECG abnormalities in a cohort of young athletes.

Methods: ECG was analysed as part of an ongoing prospective study on the impact of cardiovascular screening with ECG in young (14-35 years) competitive athletes. ECG was interpreted according to the 2010 recommendations of the European Society of Cardiology (adapted) distinguishing common (physiologic) and uncommon (abnormal) changes.

Results: ECG of 920 athletes was analysed (75% males, age 19.9±6.5 years). The following common ECG changes were present: sinus bradycardia (<50 bpm in 10.2%, ectopic atrial rhythm in 4.2%, prolonged (>200 msec) PR interval in 3.3%, incomplete right bundle branch block in 9.6%, voltage criteria (Sokolofo Lyon) for left ventricular hypertrophy in 16.7%, for right ventricular hypertrophy in 2.5%, J wave in inter-lead leads in 34.6%. There were also 0.4% of Brugada type 1 pattern and 0.1% of a left atrial enlargement.

The following common ECG abnormalities were present: T wave inversion in 2.0% (1.6% were minor inversion, <2 mm), ventricular premature beats (>1 ECG trace) in 0.5%, atrial premature beats (>1 ECG trace) in 0.5%, left axis deviation in 0.4%, Wolff-Parkinson-White pattern in 0.3%, prolonged QT interval (>470 msec in men, >480 msec in women) in 0.2%, abnormal Q-waves in 0.1%, right axis deviation in 0.1%, left anterior hemiblock (LAP) in 0.1%.

Conclusions: As has been reported, common ECG changes of young athletes are frequent. Following the European Society of Cardiology recommendations (adapted), the abnormal ECG are relatively rare rendering ECG a useful tool to detect the dynamic cardiac adaptation occurring within the training season. The aim of this study is to investigate the longitudinal variations of LVM and fat-free mass (FFM) occurring in a selected cohort of top-level soccer players during the entire season.

Methods: Twenty-three male top-level soccer players were recruited. LVM was assessed by echocardiography and body composition by DXA. Serial measurements were performed: at the beginning of the season, after 1, 4, and 8 months.

Results: During the regular season, LVM significantly increased after 4 months and this variation remained significantly different between baseline and 8-month measurement (195.0±25.8 vs 213.5±22.8 g, p<0.05). The change in LVM was confirmed also when LVM was indexed to BSA or to FFM (p<0.05). Heart rate, stroke volume (SV) and cardiac output (CO) significantly increased during the season, reaching the highest values after 4 months. Interestingly, in the cohort of subjects not engaged in a regular training for 2 months after the end of the season, no significant differences were demonstrated between echocardiographic parameters collected at the beginning of the season and values obtained at the end of detraining. FFM and SV were independent predictors of LVM.

Conclusions: The present study reported for the first time the longitudinal variations of LVM and FFM in a selected cohort of top-level athletes engaged in an intensive training program, demonstrating that athletes exhibit a significant remodeling of the left ventricle and of the body mass during the entire regular season.

Three months of detraining at the end of the season were able to determine a decrease of LV parameters to baseline values.

References

P1763 The interplay of exaggerated blood pressure response and delayed blood pressure recovery after graded exercise as predictor of incident arterial hypertension

C. Liakos1, A. Michaelides1, G. Vysousili1, E. Chatzistamatiou2, M. Markou3, V. Tzamou1, C. Stefanadis1. 1st Department of Cardiology, University of Athens Medical School, Hippokration Hospital, 11527, Athens, Greece; 2 Department of Cardiology, Hippokration Hospital, 11527, Athens, Greece; 3st Department of Internal Medicine, 417 VA Hospital (NIMTS), 11521, Athens, Greece

Purpose: Exaggerated blood pressure (BP) response to exercise and delayed BP decline at recovery after exercise have emerged as independent predictors of future arterial hypertension (AH). The aim of this study was to test the hypothesis that the combination of the 2 prognostic measures provides an additive predictive value for AH than its components.

Methods: A total of 374 normotensive individuals undergoing a diagnostic treadmill exercise testing were followed for new-onset AH during a 5-year period. A change in systolic BP from rest to peak exercise >65mmHg and a ratio of systolic BP at 3 min of recovery to peak exercise ≥0.90 (representing the 75th percentiles for the population) were considered as exaggerated BP response and delayed BP recovery, respectively. Cox regression analysis was applied to estimate the relative risk (RR) of AH and the 95% confidence intervals (CI) in patients positive for one or both exercise prognostic markers after adjusting for age, gender, family history, obesity, smoking and resting BP.

Results: New-onset AH was detected in 41 participants (11.0%). The 5-year incidence of AH was 3.6% for subjects with normal BP response and recovery (n=195), 16.7% for individuals with exaggerated BP response and normal BP recovery (n=44), 17.3% for those with normal BP response and delayed BP recovery (n=81) and 42.9% for participants with both abnormal BP response and recovery (n=14). The adjusted RR for AH in the last group was 2.48 (95%CI, 1.14-4.97; p=0.038) compared to individuals with exaggerated BP response and normal BP recovery and 2.18 (95%CI, 1.03-4.72; p=0.047) compared to subjects with normal BP response and delayed BP recovery.

Conclusions: The combination of abnormal BP response and BP recovery after graded exercise is stronger predictor of AH than its components.

P1764 The interplay of delayed blood pressure and heart rate recovery after graded exercise as predictor of incident coronary artery disease

C. Liakos1, A. Michaelides1, G. Vysousili1, E. Chatzistamatiou2, M. Markou3, V. Tzamou1, C. Stefanadis1. 1st Department of Cardiology, University of Athens Medical School, Hippokration Hospital, 11527, Athens, Greece; 2 Department of Cardiology, Hippokration Hospital, 11527, Athens, Greece; 3st Department of Internal Medicine, 417 VA Hospital (NIMTS), 11521, Athens, Greece

Purpose: Delayed blood pressure (BP) and heart rate (HR) recovery after exercise have emerged as independent predictors of incident coronary artery disease (CAD). The aim of this study was to test the hypothesis that the combination of the 2 prognostic measures provides an additive predictive value for CAD than its components.

Methods: A total of 800 non-CAD patients (mean age 54 years, 66% males) were followed for new-onset CAD for 5 years after a diagnostic treadmill exercise test (ET). A 3 min of recovery systolic BP to peak exercise ratio >0.90 (4th quartile) and a difference between peak HR and HR at the 1st min of recovery ≥32bpm (1st quartile) were considered as delayed BP and HR recovery, respectively. At the end of follow-up, patients without overt CAD underwent a 2nd diagnostic ET. Stress imaging modalities and coronary angiography, if necessary, were performed for ruling out CAD. Cox regression analysis was applied to estimate the relative risk (RR) of CAD and the 95% confidence intervals (CI) in patients positive for one or both exercise predictors.

Results: New-onset CAD was detected in 110 patients (13.3%). The 5-year incidence of CAD was 7.5% for subjects with normal BP and HR recovery (n=465), 16.0% for individuals with delayed BP and normal HR recovery (n=156), 18.2% for those with normal BP and delayed HR recovery (n=137) and 34.7% for participants with both abnormal BP and HR recovery (n=72). The adjusted (for potential covariates) RR for CAD in the last group was 1.95 (95%CI, 1.28-2.98; p=0.011) compared to individuals with delayed BP and normal HR recovery and 1.71 (95%CI, 1.08-2.75; p=0.014) compared to subjects with normal BP and delayed HR recovery.
Blood pressure response to exercise predicts successful weaning from LVAD in heart transplantation candidates

M. Fukumitsu1, Y. Sata2, Y. Murata1, O. Seguchi1, M. Yanase1, T. Noguchi1, T. Nakatani1, Y. Goto1, M. Sugimachi1, H. Takakii1, 1National Cerebral and Cardiovascular Center Hospital, Department of Cardiovascular Medicine, Suita, Osaka, Japan; 2National Cerebral and Cardiovascular Center Research Institute, Dept of Cardiovascular Dynamics, Suita, Osaka, Japan

Left ventricular assist device (LVAD) is a clinical routine for patients with severe heart failure (HF) who are awaiting for cardiac transplantation. With significant LV unloading and reverse remodeling, LVAD support has demonstrated the potential to lead cardiac recovery for a certain subset of patients. Nevertheless, the incidence of LV unloading remains relatively low, partly because of lack of the reliable criteria for successful weaning. Cardiopulmonary exercise testing (CPET) provides useful information to predict prognosis of patients with severe HF. Peak VO2, the most reliable established prognostic predictor, may not be useful for patients with LVAD because of long-term deconditioning. We hypothesized that blood pressure response to exercise would be more reliable for selecting candidates who might be weaned from LVAD. We studied 106 consecutive patients with severe HF who received pulsatile LVAD implantation for a bridge to heart transplantation between 1998 and 2011. During mean follow up of 2.0±1.2 years, 38 LVAD patients were considered for weaning and performed CPET; 8 cases were successfully weaned and received LVAD unloading, 21 received heart transplantation, and 9 died before transplantation. Although the patients characteristics were similar, those hemodynamic and exercise variables of CPET were significantly different; peak exercise systolic blood pressure (pSBP) and peak VO2 were higher, and VE/VO2 slope were lower in the patients with successful weaning (Figure).
**P1770**

**Right ventricular systolic dysfunction is an independent predictor of reduced exercise capacity in patients after myocardial infarction**

K. Smarz, B. Zaborska, T. Java-Chamiec, P. Maciejewski, A. Budaj, Department of Cardiology, Postgraduate Medical School, Grochowski Hospital, Warsaw, Poland

**Background:** Right ventricular (RV) systolic dysfunction reduces exercise capacity (EC) in patients with left ventricular (LV) dysfunction in chronic heart failure and causes poor prognosis. Data on the impact of RV dysfunction on EC in patients after inferior myocardial infarction (MI) with preserved LV function are scarce.

**Aim:** To assess influence of RV dysfunction on EC in patients with MI and preserved LV systolic function.

**Methods:** We prospectively enrolled 90 consecutive patients admitted to our department with the first ST-elevation inferior MI and preserved LV systolic function (EF > 45%). All included patients were treated by primary percutaneous coronary angioplasty. Cardiopulmonary exercise test was done on day 14±10. We used a regression model to analyze the following variables for potential influences on EC: gender, age, body mass index, physical activity before MI, diabetes mellitus/impaired glucose tolerance, hypertension, smoking, LV ejection fraction, wall motion score index, maximal troponin concentration, RV Sm, RV Em, LV Sm, LV Em and early transmitral inflow velocity to LV Em ratio. Parameters with no influence on EC were removed from the model (p > 0.1).

**Results:** According to the multivariate regression analysis independent factors that negatively influenced EC were: RV systolic dysfunction, female gender, age, lower body mass index, current smoking and maximal troponin I concentration (Table).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient</th>
<th>95% CI</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right ventricular systolic dysfunction</td>
<td>-0.161</td>
<td>(-0.339; 0.018)</td>
<td>0.11</td>
</tr>
<tr>
<td>Gender female vs male</td>
<td>-0.676</td>
<td>(-0.527; -0.826)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (in decades)</td>
<td>-0.270</td>
<td>(-0.340; -0.201)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>0.003</td>
<td>(0.006; 0.014)</td>
<td>0.11</td>
</tr>
<tr>
<td>Diabetes mellitus/impaired glucose tolerance</td>
<td>0.151</td>
<td>(0.303; 0.001)</td>
<td>0.05</td>
</tr>
<tr>
<td>Current smoker vs never/past smoker</td>
<td>-0.208</td>
<td>(-0.345; 0.072)</td>
<td>0.03</td>
</tr>
<tr>
<td>Troponin I maximal concentration (at every 10 ng/ml)</td>
<td>-0.002</td>
<td>(-0.040; 0.002)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

**Conclusion:** Presence of RV systolic dysfunction in acute MI independently decreases EC in patients without significant LV dysfunction.

**P1771**

**Anti-inflammatory properties of HDL after short-term exercise training in patients with metabolic syndrome**

A. Casella-Fillo, I.C. Trombetta, L.B. Casella, P.M.M. Dourado, A. Sergé, D. Favatato, L. Rower-Borges, C.E. Negrao, R.C. Maranhão, A.C.P. Chagas, Heart Institute (InCor) HC FMUSP, Sao Paulo, Brazil

**Background:** Recent study showed that short-term exercise, associated with diet and weight loss, improves the anti-inflammatory properties of HDL in metabolic syndrome (MS). However, diet and weight loss, per se, can alter the functionality of HDL and, in real life, many patients do not follow the medical counseling of diet and exercise simultaneously.

We showed previously that the antioxidative characteristics and the capacity to accept lipids of HDL are early improved by short-term exercise training (Tr) with no diet associated.

We sought to verify whether the anti-inflammatory properties of HDL are affected by Tr, without any diet associated, in patients with MS.

**Methods:** Forty sedentary persons (30 with MetS,10 controls) were evaluated. Twenty of those with MS were subjected to a 3 times/week training load (45 min/day) for 3 months on a bicycle.

Plasma high-sensitivity C-reactive protein (hs-CRP) was analyzed and HDL subfractions were obtained by plasma ultracentrifugation. Endothelial cells were cultured, stimulated with TNF-α and lipopolysacharide, and coincubated with HDL subfractions obtained before and after Tr. Sequentially, the cultures of endothelial cells were coincubated with THP-1 cells labeled with a fluorescent marker. The labeled THP-1 cells that adhered on endothelial cells were counted under fluorescent microscope.

**Results:** Baseline plasma levels of HDL-C were lower in the MS group compared to controls and Tr did not change neither HDL-C nor mass in MS group. hs-CRP plasma levels from patients with MetS were higher than controls (3.0±1.5 vs 1.5±1.5 mg/L respectively, p < 0.05) and did not change after Tr (3.0±1.5 vs 2.8±1.8 mg/L, before and after Tr respectively, p > 0.05).

The number of adhered labeled THP-1 cells coincubated with endothelial cells did not change significantly when mixed with HDL2a or HDL3b from patients with MS after Tr, compared with HDL2a or HDL3b obtained before Tr.

**Conclusion:** Our results showed that Tr did not change an inflammatory serum marker (hs-CRP) and the adherence of THP-1 cells on endothelial cells, suggesting that the anti-inflammatory properties of HDL are not early improved by short-term exercise, when there is no diet associated.

**P1773**

**Effects of aerobic exercise and resistance exercise training on oxidative stress in patients with lifestyle-related disease**

N. Yoshida1, H. Ikeeda2, Kurume University, Kurume, Japan; 2Kurume University Medical Center, Kurume, Japan

**Purpose:** Oxidative stress plays important roles in pathophysiology of lifestyle-related diseases (LRD). However, little is known about the effects of aerobic exercise and resistance exercise on the oxidant defense and antioxidant defense systems in patients with LRD. The purpose of the present study was to examine the effects of aerobic exercise and resistance exercise training on oxidative stress in patients with LRD.

**Methods:** The study subjects were consisted of 31 sedentary patients with LRD (mean age, 50.1 years), and divided into three groups including aerobic exercise training (AT; n=18), aerobic exercise training and resistance training (ART; n=6), and non-training (NET; n=7) group. Patients underwent bicycle ergometer exercise test to measure the estimated maximum oxygen consumption (eVO2max). Aerobic training (50% eVO2max) consisted of 30-60 minutes of exercise, 3-5 days/week during 12-week training period. ART group underwent 3 resistance training (20-30% of 1-repetition maximum) per week before aerobic training sessions. Reactive oxygen metabolites (d-ROMs) and biological antioxidant potential (BAP) were measured using the FRAS4 (Diacon International, Italy). For evaluation of effects of exercise training, all measurements including d-ROMs, BAP, eVO2max were carried out before and after 12 weeks training.

**Results:** In the ET and ART group, eVO2max significantly increased after exercise training. In the ET group, although d-ROMs did not change, BAPs significantly increased after exercise training (1970±434 to 2301±288 M/L, p < 0.05). As a result, BAP/d-ROMs ratio significantly increased (6.3±1.72 to 7.28±1.03, p < 0.05). In the ART group, d-ROMs decreased and BAP increased after exercise training. Consequently, BAP/d-ROMs ratio increased (7.9±0.53 to 9.38±1.62, p < 0.1) after training. In the NET group, no significant changes in eVO2max and oxidative stress parameters were observed. No significant differences in baseline values of d-ROMs were observed between ET and NET groups. However, after 12-week observation period, the mean value of d-ROMs in the ET group was significantly lower than those in the NET group (p = 0.05). A significant correlation was noted between BAP/d-ROMs ratio and eVO2max (r=0.45, p < 0.001).

**Conclusions:** These findings suggest that aerobic exercise and resistance exercise training may decrease oxidative stress by augmentation of the biological antioxidant potential in patients with LRD. Furthermore, the higher levels of exercise tolerance may be indicative of the higher levels of antioxidant defense against oxidative stress.

**P1774**

**Impact of short-term exercise training and residual ischemia on QT dispersion and double product in patients after myocardial infarction**

V. Stoicov1, S. Ilc1, M. Dejanin Ilic1, M. Stoicov2, M. Golubovic3, P. Babovic4, 1University of Niš, Medical Faculty, Institute of Cardiology Niska Banja, Niš, 2Institute of Cardiology, Niska Banja, 3Clinical Center, Niš, 4University of Niš, Medical Faculty, Niš, Serbia

Patients after myocardial infarction (MI) are at high risk of new cardiovascular and arrhythmic events. QT dispersion (QTd) is a measure of inhomogeneous repolarization of myocardium and is used as an indicator of arrhythmogenicity.

**Purpose:** The aim of this study was to establish the influence of short-term exercise training and residual ischemia (RI) on QT dispersion and double product (DP) as well, in patients after MI.
Methods: The study involved 317 patients after MI in the sinus rhythm without AV blocks or branch blocks. Average age of patients was 57.2 years. Patients were randomly divided into the physical training group (TG: 275 patients) and non-training group (42 patients). Patients were of similar age, site of infarction and baseline stress test duration. In all subjects clinical examination, standard ECG and exercise test on treadmill according to Bruce protocol, were performed and after the TG patients were included in rehabilitation treatment for three weeks. TG of patients were instructed to follow a training program using the bicycle ergometer (10 min, 2 times a day). The patients continued to take the same medications in the same doses. From standard ECG corrected QT dispersion (QTc) was calculated.

Results: RI was present in 153 (55.6%) patients in the TG and in 24 (57.1%) patients in the control group. In the TG, before starting with the program of physical training, patients with RI had significantly higher values of QTd (83.6 ± 29.6 ms; p < 0.001), while the values of DP did not significantly vary (12360.7 ± 2120.8 vs 11943.5 ± 1722.6 beat/min x mmHg; p NS) in comparison to those without RI. After three weeks, in the TG, significant reduction of QTd was found (from 83.6 ± 29.6 to 75.8 ± 27.4 ms; p < 0.02 in patients with RI and from 66.7 ± 21.4 to 56.7 ± 20.6 ms; p < 0.01 in patients without RI). In the TG, significant reduction of DP was found (from 12360.7 ± 2120.8 to 11763.8 ±1639.4 beat/min x mmHg; p < 0.01 in patients with RI and from 11943.5 ± 1722.6 to 10823.7 ± 1424.8 beat/min x mmHg; p < 0.001 in patients without RI). In contrast, the non-training group showed no significant changes.

Conclusions: The study showed that short-term exercise training has favourable effects on QT dispersion and double product in patients after MI. In patients without RI physical training had more favourable effects on the followed parameters. Physical training led to the significant decrease of myocardial oxygen uptake at rest and probably decreased the possibility of arrhythmia events, especially in patients without RI.

**P1775 Impairment of heart rate recovery index in autosomal-dominant polycystic kidney disease patients without hypertension**

M.G. Kaya1, O. Orscevik1, O. Baran1, O. Dogdu1, S. Karadavut1, M. Duran1, B. Çakapakur1, I. Köçyiğit1, E. Erciyes University School of Medicine, Department of Cardiology, Kayseri, Turkey; 2 Erciyes University School of Medicine, Department of Nephrology, Kayseri, Turkey

**Background:** We aimed to determine the status of the autonomic nervous system in patients with autosomal dominant polycystic kidney disease (ADPKD) who were normotensive and had normal renal function.

**Methods:** A total of 28 normotensive ADPKD patients with normal renal function and 30 healthy control subjects consented to participate in the study. Heart rate recovery (HRR) indices were defined as the reduction in heart rate from the rate at peak exercise to the rate at the 1st, 2nd, 3rd and 5th minutes after the cessation of the exercise stress test; these results were indicated HRR1, HRR2, HRR3 and HRR5 respectively.

**Results:** The 1st- and 2nd-minute HRR indices of patients with ADPKD were significantly lower than those of the healthy control group (27.1 ± 7.9 vs 32.0 ± 7.9; p = 0.023 and 46.9 ± 11.5 vs 53.0 ± 9.0; p = 0.025, respectively). Similarly, HRR indices after the 3rd- and 5th-minutes of the recovery period were significantly lower in patients with ADPKD when compared with indices in the control group (56.7 ± 12.3 vs 65.1 ± 11.2; p = 0.008 and 62.5 ± 13.8 vs 76.6 ± 15.5; p = 0.001, respectively).

**Conclusion:** Improved heart rate recovery index is associated with normotensive early stage ADPKD patients. Increased renal ischemia and activation of the renin-angiotensin-aldosterone system (RAAS) may contribute to impairment in the autonomic nervous system in these patients before the development of hypertension. Even if ADPKD patients are normotensive, there appears to be an association with autonomic dysfunction and polycystic kidney disease.

**P1776 Parasympathetic activity as a predictor of performance in elite swimmers**

S. Chalencou1, T. Bussu2, M. Garet1, V. Pichot1, P. Connes3, J.R. Lacour1, F. Rochel1, J.C. Barthelemy1, 1 University of Lyon, Laboratory SNA-EPIS EA 4607, Jean Monnet University, Saint Etienne, France; 2 University of Lyon, Laboratory of Exercise Physiology EA 4338, Jean Monnet University, Saint Etienne, France; 3 University of the French West Indies and Guiana, Laboratory ACETS, Department of Physiology, Pointe à Pitre, Guadeloupe

**Purpose:** The modelling adequacy of the effects of training on both performance and High-frequency spectral component of Heart Rate Variability (HRV) was evaluated through a two-components mathematical model in elite swimmers.

**Methods:** Training load, performance and wavelet indices of nocturnal Autonomic Nervous System (ANS) activity were assessed every week during thirty consecutive weeks, including two intensive periods, of a competitive season in ten swimmers. The indexes of adaptation and fatigue from the model were computed in swimmers to analyse autonomic nervous activity and performance alterations with training.

**Results:** The fit between the estimated and measured performances (R2=0.84±0.14, p<0.01) and between the calculated and actual High Frequency (HF) powers (R2=0.79±0.07, p<0.01) demonstrated the statistical adequacy of the two-component system model to describe the effects of training on performance and on ANS activity. The time to recover from fatigue and return to the initial level of performance (t0, P) was significantly correlated with the time needed to return to the initial level of HF power (t0, HF) (r=0.76 p<0.01). The time to peak performance (tP, P) was correlated with the time to reach maximal level of HF power (tP, HF) (r=0.71, p<0.02). During the two taper periods, improvements in both performance and HF power were mainly related with a significant reduction in the level of Negative Influences (NI), rather than to an increase in Positive Influences (PI) of the training load.

Figure 1. Application of the two-component model

**P1777 Blatrical adaptation to training in elite female volleyball players: a longitudinal speckle-tracking study**

F. D’Ascanio1, V. Zaza2, B. Nataf1, M. Cameli1, M. Lis1, A. Malandrino1, F. Alvino1, M. Losito1, M. Bonifazi1, S. Mondolfo1, University of Siena, Department of Cardiovascular Diseases, Siena, Italy; 2 Santa Maria alle Scotte Polyclinic, Department of Cardiovascular and Thoracic, Cardiology Division, Siena, Italy; 3 Department of Neurosciences, University of Siena, Siena, Italy

**Purpose:** Athletic training is associated with heart remodeling in athletes. Although several echocardiographic studies have investigated the role of training in male athletes, few data are available about female athlete’s heart and exercise conditioning, and most are limited to cross-sectional study. The aim of this study is to determine by standard and 2D speckle tracking echocardiography (STE) the adaptations of left and right atria (LA, RA) in a longitudinal study in female volleyball players. The diastolic properties of right and left heart were also evaluated through pulsed-wave and tissue Doppler imaging (TDI).

**Methods:** Twenty-three elite female volleyball players, engaged in a 4-month training program, participated in the study. Echocardiographic analysis was performed at baseline (after 3 months of detraining) and after 4 months of regular intensive training. LA and RA size was assessed by area, volume and volume index (volume/body surface area). We analyzed by 2D STE RA and LA longitudinal myocardial deformation dynamics, obtaining values of global peak atrial longitudinal strain (PALS) and global peak atrial contraction strain (PACS).

**Results:** As expected, heart rate significantly decreased after 4 months (p<0.01). LA mean volume index increased after 4 months of training (24.0±3.6 ml/m² vs 26.7±6.9 ml/m²; p<0.001). The same trend was demonstrated for RA volume index (15.6±3.0 ml/m² vs 20.4±3.8 ml/m²; p<0.001). Although PALS and PACS values for both RA and LA showed a trend toward lower values after 4 months of training, no significant differences were observed. Pulsed-wave Doppler of left ventricle did not show significant variations, while TDI demonstrated...
Cardiopulmonary exercise test in patients with congestive heart failure and sleep disorder breathing

University of Foggia, Foggia, Italy

Introduction: In patients with congestive heart failure (CHF) the presence of obstructive Sleep Apnea Syndrome (OSAS) is very common, however few studies have investigated which is the relationship between the presence of OSAS and Cardiopulmonary performance, moreover even if it’s well known that patients with CHF have higher probability to develop Central Sleep Apnea and Cheyne-Stokes Respiration (CSA-CSR) during the night, the mechanisms which link CSA and CHF are still unclear. The aim of the study was to improve the understanding about the relationship between CHF and Sleep Disorder Breathing (SDB) and better understand the pathophysiology of CSA-CSR.

Methods: 43 female athletes with congestive heart failure underwent to cardiopulmonary test, transthoracic echocardiography, global spirometry, and EGA parameters. The percentage of CSA and noSDB according to nocturnal test. Statistical analysis was by ANOVA applied to evaluate the differences among three groups. Spearman’s correlation test was used to analyze the correlation between each variable.

Results: 35 patients with congestive heart failure (FE% 36,4±11,4) were enrolled; 13 (37%) had OSAS, 15 (42%) had CSA-CSR while only 7 (20%) haven’t any SDB. The patients were matched for BMI and FE% but not for age because the OSAS were older than others groups: 69,3±7,2 vs 56,7±11,4 (noSDB) and 60,2±5,1 (CSA-CSR). Any differences were found among the groups about CPT, echocardiographic signs, spirometry and EGA parameters. The percentage of CSR was correlated with VO2max (r=-0,47, p<0,05), AT (r=0,40, p<0,05) VE/VCO2 slope (r=-0,47, p<0,05), any other correlation was found between index of SDR like AH, ODI or TST90% and CPT performance.

Conclusion: Our results confirm that in patients with CHF sleep disorder breathing are very common. The severity of heart failure evaluated by CPT is correlated with tendency of patient to develop CSR during sleep independently of the FE% or other echocardiographic parameters. On the contrary the presence of SDB hasn’t any influence on performance at CPT.

Copeptin and high-sensitivity cardiac troponin T measurements for improving exercise stress test in patients with suspected coronary artery disease

C. Liebreu1, O. Doen2, S. Szard0en, C. Troid0, M. Willmer1, J. Rixe2, A. Rollf, H. Moellmann1, C. Hamm1, H. Neh1, 1Kerckhoff Heart and Thorax Center, Bad Nauheim, Germany; 2Justus-Liebig University Giessen, Medical Clinic I, Cardiology, Giessen, Germany; 2Franz-Groedel Institute of the Kerckhoff Clinic Heart & Thorax Center, Bad Nauheim, Germany

Purpose: Copeptin is co-secreted with arginine vasopressin (AVP) prohormone from the neurohypophysis. As recently shown, in patients with acute myocardial infarction or acute decompensated heart failure copeptin plasma concentrations are elevated. High-sensitivity cardiac troponin T (hs-cTnT) assays are able to detect small amounts of myocardial necrosis. The aim of the present study was to examine whether changes of copeptin or hs-cTnT levels during exercise stress testing (EST) improve its diagnostic sensitivity.

Methods: Measurement of copeptin and hs-cTnT was performed during the semi-supine bicycle test; further analysis of the results will help explaining the pathophysiology of CSA-CSR.

Results: After adjusting by potential confounders, multiple regression analysis showed that copeptin levels were significantly higher during the semi-supine bicycle test; further analysis of the results will help explaining the pathophysiology of CSA-CSR.

Conclusion: Cardiopulmonary exercise testing: role of VE/VCO2 slope in patients with chest pain suspected of coronary artery disease

A. Dominguez Rodriguez1, E. Arroyo-Ucà2, C. Hernandez-Garcia1, M. Carrillo-Perez Tome1, G. Blanco-Palacios1, B. Man-Lopez1, J. Gonzalez-Gonzalez1, M.A. Gomez1, 1Perez-Anguez2, P. Avanzas3. 1University Hospital of Canarias, Tenerife, Spain; 2University of La Laguna, Tenerife, Spain; 3Hospital Central de Asturias, Oviedo, Spain

Purpose: Cardiopulmonary exercise testing (CPET) might aid in the diagnosis of coronary artery disease (CAD). The ventilatory response evaluation by blood lactate and carbon dioxide production during the VO2 max test is of great importance in heart failure. In the present study we assessed the relationship among VE/VCO2 slope and the myoccardial perfusion defects quantified by single photon emission computed tomographic myocardial perfusion study (MPS) in subjects with symptoms suggestive of CAD.

Methods: We prospectively enrolled 55 subjects (age 57±8 years, 30 men) with symptoms of chest pain suggestive of CAD. All subjects underwent at rest and a stress MPS, in conjunction with the standard exercise test with ventilatory expired gas analysis. Coronary angiography was performed by conventional technique in those subjects who showed perfusion abnormalities in MPS.

Results: Of the 55 subjects, 25 (45.4%) had positive MPS findings. Of these subjects with positive MPS findings, 1 vessel disease was present 12 subjects, 2 vessel disease in 9 and triple vessel disease in 4. There were differences in peak oxygen uptake (VO2) and VE/VCO2 slope, between patients with and without myocardial perfusion defects (Table). After adjusting by potential confounders, multiple regression analysis showed that VE/VCO2 slope was a significant predictor of myocardial perfusion defects (OR ranging from [1.840, CI 95%: 1.335-2.537, p < 0.001] to [1.905, CI 95%: 1.366-2.606, p < 0.001]). VE/VCO2 slope was a good predictor of CAD.
predictor of myocardial perfusion defects with an area under the ROC curve of 0.89 (CI 95% 0.80-0.97, p < 0.0001).

Exercise variables stratified by myocardial perfusion study (MPS)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Positive MPS (n=25)</th>
<th>Negative MPS (n=30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Predicted peak VO2</td>
<td>27.99±7.28</td>
<td>27.06±6.21</td>
<td>0.62</td>
</tr>
<tr>
<td>Predicted VO2 at target</td>
<td>22.62±7.25</td>
<td>26.25±7.07</td>
<td>0.03</td>
</tr>
<tr>
<td>VO2 at anaerobic threshold</td>
<td>16.38±6.62</td>
<td>17.39±6.92</td>
<td>0.39</td>
</tr>
<tr>
<td>VE/VO2 slope</td>
<td>34.73±5.55</td>
<td>30.58±8.34</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusions: This is the first study to demonstrate that VE/VO2 slope could be valuable as a robust and independent predictor of myocardial perfusion defects. The original finding of our study is that this parameter of CFRF might predict CAD in patients with symptoms of anginal chest pain.

P1784 The training with blood flow reduction improves the peripheral blood circulation in the elderly

R. Shimizu1, K. Hitoda1, D. Kametaka1, A. Akiyama1, Y. Yokoyama2, M. Tabata2, K. Kamiya2, N.M. Ogas2, A. Matsunaga3, T. Masuda1

1Kitsato University, Graduate School of Medical Sciences, Sagamihara, Japan; 2Kitsato University, School of Allied Health Sciences, Department of Rehabilitation, Sagamihara, Japan

Recently, it was reported that the training with blood flow reduction (BFR) performed with compressing the stem of upper or lower extremities increased muscle strength of extremities even at shorter training period. Although the hypertonic stress is known to induce angiogenesis and increase the blood flow in tissues, it is unclear whether or not the training with BFR improves the peripheral blood circulation.

Purpose: The purpose of the present study was to investigate whether the intervention of the training with BFR improves the peripheral blood circulation in the elderly.

Methods: Twenty-four healthy old volunteers with a mean age of 72±3 years, 20 males and 4 females, were enrolled in the present study. They were divided into two training groups: 12 subjects performing the resistance training of the extremities with BFR compression in BFR group, and 12 doing without BFR in control group. Subjects performed 3 sets of the resistance training composed of 4 movements. Each movement was repeated 20 times by the 20% of 1 repetition maximum. All subjects performed a series of resistance training 3 times a week for 4 weeks. We measured serum growth hormone (GH) and plasma vascular endothelial growth factor (VEGF) before and after the initial resistance training. We also assessed the peripheral blood circulation and muscle strength before and after a week of the intervention of the resistance training. Transcutaneous oxygen pressure (tcPO2) on the dorsum of the right foot was evaluated using transcutaneous O2/CO2 gas device as an index of the peripheral blood circulation. Subjects performed isokinetic leg extension with the maximal strength 3 times in each leg using isokinetic dynamometer as an index of muscle strength.

Results: The GH and VEGF increased significantly from 0.9±1.1ng/mL and 32.9±12.7ng/mL before the training to 3.0±1.5ng/mL and 49.0±13.3ng/mL after the training, respectively, in the BFR group (P < 0.001 and P < 0.05, respectively). The Lac and muscle strength increased significantly from 60.1±12.9mmHg and 96.7±21.8mmH4 before the 4-week training to 69.3±17.0mmHg and 110.5±22.6mmH after the 4-week training, respectively in the BFR group (P < 0.01 and P < 0.01, respectively).

Conclusion: The resistance training with BFR improved the peripheral blood circulation in addition to the increase of muscle strength.
Acute coronary syndrome related to sport: profile and patient preferences for chronic treatment for stroke

Acute coronary syndrome (ACS) related to sport is a rare condition that occurs during or immediately after physical activity. The acute event is often followed by a period of recovery, and patients may return to their professional activity or resume sport after a mean delay of 8.6 months. However, only 32% of patients were able to resume their professional activity, and 21 patients took up sport again. Younger patients (<35 years) had a better outcome than conventional coronary patients, partly due to their favorable lipid profile (LDLc 59 ± 8% vs. control group: 59 ± 8%; p = 0.01). The evolution of quality of life (QOL) was not related to age or original level. QOL was worse than before ACS, but was better in those who resumed sport (mean delay: 8.6 months) but only 32% amongst them rediscovered their professional activity (mean delay: 2.6 months); 21 patients took up sport again (4.8%) and cycling (24%) were the most represented sports; 16 patients were registered in CR (pre exercise: 30 ± 8% vs. post exercise: 45 ± 7%; p = 0.04) whereas they were reduced in CR group (pre exercise: 59 ± 5% vs. post exercise 51 ± 6%; p = 0.03). Thus, the exercise response was different between the groups (ΔCT group: +15 ± 7% vs. ΔCR group: -8 ± 3%; p = 0.01). There were no differences between the groups in the control session (p = 0.05).

Conclusions: Aberrant coronary syndromes related to sport is a rare and dramatic event. The aim of this study is to define the profile of these patients and to increase awareness of this diagnosis and etiology.

Methods: Prospective study of patients who presented with ACS during or immediately subsequent (2 hours) to a sporting activity. Cardiovascular risk factors (CVRF), clinical and angiographic presentation were analyzed. The response of the sport level and opioid level were noted. A questionnaire was sent to the patients for follow-up (FU) evaluation: CVRF control, compliance, occurrence of new cardiac events, resumption of sport, professional activity and quality of life (QOL) were studied.

Results: We included 25 patients (24 men), mean age 47 (±14) years, who experienced ACS during or after sport. CVRF were: smoking (9 patients), overweight (9, heredity (7), hypercholesterolemia (6), hypertension (2), diabetes (5). Twenty patients (80%) were doing a sport with high dynamic component; running (28%) and cycling (24%) were the most represented sports; 16 patients were regular exercisers (3 h per week). Particular circumstances included competition (6 cases), meteorological particularities (7) and altitude (1). We observed 17 ACS with ST-segment elevation, 2 patients presented with aborted sudden death (17 (6%) had single-vessel coronary disease, preferentially active exercisers (p = 0.03); minimal atherosclerotic plaques were identified with IVUS in 4 patients with normal arteries by angiography; 3 patients had a myocardial bridge without any athrotherosclerotic lesion. LVEF was decreased in 6 patients. Mean FU was 3 years and no patient was lost. At FU, 2 patients were still smokers and 89% had a favorable lipid profile (LDLc < 1 g/l). No patient died, only 3 patients (12%) experienced a new ACS. Younger patients (<40 years) showed a worse compliance with medical treatment (p = 0.04). All patients had their professional activity (mean delay: 2.6 months); 21 patients took up sport again (mean delay: 6.8 months) but only 32% amongst them rediscovered their original level. QOL was worse than before ACS, but was better in those who resumed sport (p = 0.01). The evaluation of QOL was not related to age or original level.

Conclusions: Patients with ACS related to sport are younger and appear to have a better outcome than conventional coronary patients, partly due to their favorable lipid profile and etiology.

P1787

Regular supervised exercise training improves endothelial function, early atherosclerosis, arterial stiffness and endothelial progenitor cells in PCI patients

J.H. Park1, J.S. Kim1, H.J. Nam2, S.J. Jung3, C.M. Ahn1, S.J. Hong1, D.S. Lim1, 1Korea University, Anam Hospital, Seoul, Korea, Republic of; 2Asan Medical Center, Seoul, Korea, Republic of

Backgrounds: A disrupted balance between endothelial injury and repair induces endothelial dysfunction and endothelial progenitor cells (EPC) augment vascular repair. So, exercise training improves endothelial function through increased numbers of circulating EPC. We investigated the effect of training on vascular health by measuring the number of circulating EPC, and assessing flow-mediated dilation (FMD), brachial-ankle pulse wave velocity (baPWV) and carotid intima-media thickness (IMT) in patients with percutaneous coronary intervention (PCI).

Methods: Fifty-nine patients who were done PCI recently were randomized to full exercise training group and control group (pre exercise: 30 ± 8% vs. post exercise: 45 ± 7%; p = 0.04) whereas they were reduced in control group (pre exercise: 59 ± 5% vs. post exercise 51 ± 6%; p = 0.03). Thus, the exercise response was different between the groups (ΔCT group: +15 ± 7% vs. ΔCR group: -8 ± 3%; p = 0.01). There were no differences between the groups in the control session (p = 0.05).

Results: Three months regular supervised exercise training improved FMD, ba-PWV, carotid IMT and waist to hip ratio in PCI patients, and it augmented numbers of circulating EPCs. Our results showed that exercise training contributes to additional improvement of vascular health in PCI patients with optimal medical treatments.

SOCIO-ECONOMIC AND CULTURAL ASPECTS ON PREVENTIVE CARDIOLOGY

P1788

Educational, occupational and socioeconomic status and cardiovascular risk facAfis in Asian Indians

R. Gupta1, P.C. Deedewaria2, K.K. Sharma1, A. Gupta1, S. Guptha1, R. Gupta1, 1Fortis Escorts Hospital, Jaipur, India, 2University of California San Francisco VA Medical Center, Fresno CA, United States of America, 2University of Rajasthan, Jaipur, India

Background: Influence of socioeconomic status (SES) on cardiovascular risk factors has not been well studied in low income countries. To determine correlation of education, occupation and social class on cardiovascular risk factors we performed study in India.

Methods: The study was performed at eleven cities using cluster sampling. Subjects (n=4198, men 3426, women 2772) were evaluated for socioeconomic, demographic, biophysical and biochemical factors. They were classified into low, medium and high SES based on educational level (<10, 10-15 and >15 yr formal education), occupational class and socioeconomic scale. Differences in risks in various groups were evaluated using multivariate logistic regression.

Results: Age-adjusted prevalence (%) of risk factors in men/women was overweight or obesity 41.1/45.2, obesity 8.3/15.8, high waist circumference 10.4/23.5, high waist-hip ratio 40.0/72.6, hypertension 32.5/30.4, hypercholesterolemia 24.8/25.3, low HDL cholesterol 34.1/53.0, high triglycerides 41.2/31.5, diabetes 16.7/14.4 and metabolic syndrome in 17.2/22.7. Lifestyle factors were smoking 12.0/0.5, other tobacco use 12.7/6.3, high fat intake 51.2/48.2, low fruit/vegetables intake 60.2/64.6, and low physical activity 78.6/83.4. There was significant correlation of educational status with occupation class (men 0.35, women 0.31) and SES (men 0.15, women 0.15) (p = 0.001). Prevalence of ≥3 risk factors was significantly greater in low (22.4%) vs. middle (17.8%) or high (15.7%) education (p = 0.01). Compared with high educational status, in low educational status there was greater prevalence of age- and sex-adjusted low HDL cholesterol (1.51, 1.27-1.80), total high/low cholesterol ratio (1.18, 0.98-1.43), hypertension (1.16, 0.99-1.37), metabolic syndrome (OR 2.37, 2.66-4.01) and physical activity (1.15, 0.97-1.37), and lower prevalence of alcohol abuse (0.51, 0.39-0.66), high fat diet (0.55, 0.38-0.80), smoking/tobacco use (OR 0.70, 0.55-0.99) and physical inactivity (1.37, 1.20-1.58).

Conclusions: Low educational status Asian Indian subjects have greater prevalence of low HDL cholesterol, high total/HDL cholesterol, hypertension, metabolic syndrome, smoking/tobacco use, low physical activity and clustering of ≥3 major risk factors.

P1789

Patient preferences for chronic treatment for stroke prevention: results from the European Patient Survey in Atrial Fibrillation (EUPSY)

J.L. Zamorano1, W. Greiner2, N. Leach3, A. Sandberg4, A.M.S. Oberdiek5, A. Bakhai6 1University Clinic Ramon y Cajal, Madrid, Spain, 2University of Bielefeld, Health Economics & Health Care Management, Bielefeld, Germany, 3Oxford PharmaGenesis Ltd, Oxford, United Kingdom, 4DaichI Sankei Europe GmbH, Munich, Germany, 5Barnet and Chase Farm Hospitals NHS Trust, London, United Kingdom

Purpose: To assess treatment preferences in different European countries for patients with atrial fibrillation (AF) receiving long-term anticoagulation treatment for stroke prevention of stroke.

Methods: The 2008 Commonwealth Fund International Health Policy Survey of Chronically Ill Adults was adapted for patients with AF. Computer-assisted digital telephone dialing was used to screen a random sample from the entire adult pop-
Influence of socioeconomic status on Acute Myocardial Infarction (AMI) in China population: the Interheart China study

J. Guo1, W. Li1, Y. Wang1, T. Chen1, D. Xie1, K. Too2, L. Liu1, S. Yusuf2. 1Cardiovascular Institute & Fuwai Hospital, Beijing, China; People’s Republic of; 2Population Health Research Initiative, McMaster University, Hamilton, Canada

Objectives: This study aimed to determine whether levels of education, family income and other socioeconomic status (SES) were associated with acute myocardial infarction (AMI) in a Chinese population. A secondary aim was to compare the difference of this association between northern and southern regions in China.

Methods: We conducted a case-control study. Cases were first AMI (n=2909). Controls (n=2947) were randomly selected and frequency matched to cases on age and sex. SES was measured using education, family income, possessions in the household and occupation.

Results: Low levels of education (8 years) were more common in cases compared to controls (53.4% vs. 44.1%; p=0.0001). After adjusted all risk factors, the levels of education was associated with AMI risk in Chinese population (Global P value, 0.0005). The odds ratio (OR) associated with education 8 years or less, compared with more than 12 years (trade school/college/university) was 0.95 (95% CI: 1.21-1.59), and for education 9-12 years 1.04 (95% CI: 0.88-1.33). The proportion of higher income population was in controls more than cases (39.4% and 33.5%, respectively). Numbers of possessions and non-professional occupation were only weakly or not at all independently related to AMI. The adjusted OR associated with the lower education was 2.38 (95% CI: 1.67-3.39) in women, and 1.18 (95% CI: 1.40) in men (p value for heterogeneity 0.0001). The interaction between levels of education and different regions was significant (p value for interaction, 0.0026).

Conclusions: Several socioeconomic factors including levels of education, income were closely associated with increase of AMI risk in China, most markedly in northeast and southern area. The effect of education was stronger to AMI in the women than men.

P1791 Socioeconomic position and marital status as independent predictors for cardiovascular mortality in western Siberia, Russia: a prospective cohort study

V.A. Kuznetsov1, G.S. Pushkarev1, E.V. Akimova2, V.V. Galafarov2. 1Tyumen Cardiology Center, Tyumen, Russian Federation; 2International Laboratory of Cardiovascular Diseases Epidemiology in Siberia, Novosibirsk, Russian Federation

Background: Socioeconomic factors and marital status of individuals are associated with risk of cardiovascular mortality in developed societies but in our country this problem has not been studied sufficiently.

Purpose: To assess the relationship between socioeconomic factors, marital status and risk of cardiovascular mortality in working-age male population of Western Siberia.

Methods: A representative sample of 795 men aged 25-64 years living in Tyumen, Russia, was examined with standard epidemiological methods in 1996. Cardiovascular death rate was studied during 12-year prospective follow-up (from 1996 till 2008). The relationship between cardiovascular mortality and education, occupation, and marital status was evaluated using Cox proportional hazards model. Hazard ratio (HR) was calculated after adjustment for the following confounders: age, systolic and diastolic blood pressure, body mass index, smoking status, hypertension, diabetes mellitus, total cholesterol, total triglycerides, high-density-lipoprotein cholesterol, history of coronary artery disease, and social risk factors.

Results: Over 12 years of prospective study in the male cohort 85 deaths (10.6%) from cardiovascular diseases were recorded. Compared to men with higher education, HR was higher for men with low education level - 1.92 (95% confidence interval (CI) 1.14-3.22). After adjusting for all mortality risk factors HR was significantly higher in manual workers - 2.72 (95% CI 1.42-5.23) compared to professionals. Compared to married men, HR was higher in single - 4.08 (95% CI 2.17-8.3) widowed - 3.19 (95% CI 1.22-8.34) and divorced men - 3.18 (95% CI 1.90-5.34).

Conclusions: Our results showed that socioeconomic position (low education level and manual occupation) and marital status (widowed, divorced or single) were significant predictors of cardiovascular mortality, independent of other traditional risk factors.
Increased anticoagulant effects of warfarin after a catastrophic earthquake in a stricken area

M. Oda1, H. Watamine2, E. Oda2, T. Ozawa1, Y. Oda1, T. Iizuka1, T. Tobita2, Y. Aizawa2
1 Nippon University Medical and Dental Hospital, Niigata, Japan; 2 Tachikawa Medical Center, Nagakute, Japan

Background: On March 11, 2011, Northeast Japan was shaken by a magnitude 9.0 earthquake followed by a catastrophic tsunami, which damaged nuclear power plants. This disaster displaced a large population and caused severe shortages of food, water, electricity, and fuel. Hypothesizing that the profound life changes caused by the earthquake modified the dietary intake in patients taking warfarin K, we examined its effects on the international normalized ratio (INR) in victims treated with warfarin.

Methods and Results: We compared the INR measurements before and after the earthquake in two cohorts in different areas: 59 victims whose life was affected after the disaster and 155 controls whose life was not so affected. The INR measured within the first 3 weeks after the earthquake was increased (2.29 ± 0.31, p = 0.015) in victims. The INR was not changed early and mid-term cardiac events. The excess burden of risk associated with age ≥ 75 compared to those aged 65-74 years. 75% (42.5% vs. 30.0%, OR 1.51, 95% CI 1.07-2.10, p = 0.023) and 76% (43.3% vs. 31.2%, OR 1.56, 95% CI 1.10-2.21, p = 0.011) of women and men, respectively, were overweight or obese.

Conclusions: The anticoagulant effects of warfarin was increased after the disaster. The modified dietary intake may result in the increased anticoagulant effects of warfarin. 

Increased anticoagulant effects of warfarin after a catastrophic earthquake in a stricken area

P.1795

Age amplifies early to mid-term risks following acute coronary syndrome in elderly asians with low high-density lipoprotein cholesterol


Background: The relationship between high-density lipoprotein (HDL) cholesterol and acute coronary syndrome (ACS) among elderly asian subpopulations has not been explored. The objective of this study was to assess magnitude of risk among elderly asians with low HDL after ACS.

Methods: This was a prospective study of all patients with ACS defined as either unstable angina pectoris or non-ST elevation MI. Baseline characteristics of age, gender, diabetes mellitus, hypertension and TIMI score were analyzed and adjusted for outcomes. Lipid profiles were obtained after 12 hours overnight fasting from index hospital admission for ACS. Primary outcomes were major adverse cardiovascular events (MACE) of MI, target vessel revascularization (TVR) and death up to 12 months.

Results: We analyzed 585 patients with median follow-up of 9 months and median TIMI score of 4. 66% of the cohort had suboptimal HDL level <1.0mmol/L and 22% were aged 75 years or above. Patients with HDL <1.0mmol/L had more 6-month nonfatal MI (32% vs. 8.1%, OR 2.16 95% CI 1.22-3.74, p = 0.003) and 12-month nonfatal MI (32% vs. 12%, OR 3.08 95% CI 1.56-6.42, p = 0.002). Compared to Chinese with HDL <1.0, Indians were more likely to have 1-month TVR (3.6% vs. 0.3%, OR 8.43 95% CI 1.64-62.9, p = 0.041) while the Malays were more likely to have 1-month nonfatal MI (6.5% vs. 1.2%, OR 6.06 95% CI 1.27-22.10, p = 0.031). Indians aged ≤75 years with HDL <1.0mmol/L were more likely to have early cardiac death at 1 month compared those aged >75 years (14.3% vs. 1.0%, OR 16.3, 95% CI 1.70-157, p<0.003). Among the group with HDL <1.0, 6-month nonfatal MI and 12-month MACE rates were significantly higher among the Malays and Indi ans combined who were aged ≤75 compared to those aged >75 years. [33.3% vs. 12.5%, OR 1.95, 95% CI 2.67-94.7, p=0.016, (41% vs. 4.4%, OR 11.1, 95% CI 1.22-101.6), p=0.02].

Conclusions: Elderly Indians and Malays with low HDL have the highest risk of early and mid-term cardiac events. The excess burden of risk associated with age across ethnicity and in association with abnormal lipid profile is warrants further investigation.

PUBLIC HEALTH AND HEALTH POLICIES

P.1796

Waist circumference combined with BMI; a better predictor of childhood obesity? ROI data for 6609 children from the WHO surveillance initiative

P. Heavey1, C. Murfin1, U. O’Dwyer2, C. Hayes2, N. Elder3, C. Kelleher1. 1 SPHPPS, University College Dublin, Dublin, Ireland; 2 Department of Health, Dublin, Ireland; 3 Trinity College Centre for Health Sciences, Dublin, Ireland; 4 Health Service Executive, Dublin, Ireland

The World Health Organisation childhood growth surveillance system was established in 2008 to systematically measure childhood obesity in the European region. The present study provides an assessment of the prevalence of obesity from two sweeps of 6-9 year old Irish children measured in 2008 and 2010. The core objective was to measure weight, height and waist circumference and to examine prevalence of normal weight, overweight and obesity according to the WHO protocol. A nationally representative sample of schools was chosen on a probability proportional to size basis. In large schools the average class size was estimated to be 20, small schools having less than 20 pupils per class. Body mass index (BMI) was standardised by age and sex and overweight and obesity were classified using the International Obesity Taskforce cut-off points. Statistical analysis was carried out using Pearson’s chi-squared test and logistic regression. BMI was the outcome variable and this was dichotomised to normal versus overweight and obese combined. BMI measurements were recorded for 6609 children (3168 boys and 3441 girls, 48% and 52%, respectively) and 23% were classified as either overweight or obese. A significantly greater proportion of girls are overweight or obese compared with boys (25% compared with 20% χ2 =18.48, df=1, P =0.001). The proportion of normal versus overweight and obese children did not change between 2008 and 2010. Logistic regression demonstrated that overweight and obesity were more likely in females (OR 1.277, 95% CI 1.134-1.438), those who attended small schools (OR 1.203, 95% CI 1.063-1.360) and of borderline significance 8 years old (OR 1.262, 95% CI 1.026-1.551). The model was repeated including waist circumference, when adjustment was made for demographics only, for demography and single SES measures, and for demography and multiple SES measures. For example, the hazard ratio for mortality in disadvantaged Sephardic compared with advantaged Ashkenazi was 1.87 (95% CI: 1.40, 2.48) in a model adjusting only for demography; 1.58 (95% CI: 1.18, 2.12) in a model adjusting also for income; and 1.03 (95% CI: 0.74, 2.04) in a model adjusting for multiple SES indicators. Further adjustment for clinical variables did not appreciably change effect size. Findings highlight the importance of using multidimensional models of SES. Over-adjustment as a result of control of intermediate variables such as SES can result in underestimation of the role of ethnicity in health outcomes.
Statin prescription in Europe: the potential conflict between clinical guidelines and healthcare policies

K. Webb1, D. Liew1, J. Van Vuylt2, P. Clemmensen1, J. Bonnet4, C. Phillips1,1University of Melbourne, Department of Medicine, Melbourne, Australia;2Pfizer Ltd, Surrey, United Kingdom;3Righospitalet - Copenhagen University Hospital, Heart Centre, Copenhagen, Denmark;4University Victor Segalen, Bordeaux, France;5Swansea University, Swansea Centre for Health Economics, Swansea, United Kingdom

Purpose: Market data for statins in Europe highlight the potential for conflict between recommendations in clinical guidelines and healthcare policies designed to constrain costs. The potential impact is significant, particularly as statins vary considerably in terms of low-density lipoprotein cholesterol (LDL-C) reduction potency.

Methods: The median doses of prescribed simvastatin, pravastatin and atorvastatin in 17 Western European countries (E17) were derived from IMS data for 2008 and 2009. Clinical guidelines for cardiovascular management in elderly patients and prescribing policies were sourced from the literature. Dose-specific, LDL-C modifying effects of the three statins were derived from published meta-analyses.

Results: In 2009 and 2010, the median prescribed doses of pravastatin, simvastatin and atorvastatin were 40mg, 20mg and 20mg, respectively, for most of E17. However, in France, where clinical guidelines recommend less strict LDL-C targets and patients in both years were 20mg, 20mg and 10mg, respectively. In Sweden, where atorvastatin 10mg was removed from the reimbursement schedule in 2008, the atorvastatin median dose increased from 10mg in 2009 to 20mg in 2010. The opposite occurred in The Netherlands, where following the introduction of an authorization form in January 2009, the atorvastatin median dose declined from 40mg in 2009 to 20mg in 2010. Concurrently, the simvastatin median dose rose from 20mg to 40mg. The simvastatin median dose in the UK is also 40mg, and comprises 69% of the statin market, reflecting NICE guidelines and Quality Outcomes Framework (QOF) policy.

Conclusions: The median statin doses in France, Sweden, The Netherlands and UK are higher than the influence of national clinical guidelines and healthcare policies. Given the superior LDL-C reduction of atorvastatin compared to simvastatin and pravastatin, as well as the current “treatment gap” in many Western European countries, it will be interesting to observe whether the reduction in atorvastatin’s acquisition cost following loss of exclusivity in 2012 will lead to changes in guidelines recommendations and national policies, and how quickly. The availability of generic atorvastatin has potential to further improve cardiovascular outcomes, even without any change in current prescribing patterns.

Implantable cardioverter defibrillator (ICD) in Italy

F. Madotto1, C. Fornari1, S. Corin1, V. Chiodini1, L.G. Mantovani2, G. Cecala1,1Research Centre on Public Health University of Milano-Bicocca, Campus of Monza, Monza, Italy;2Pharma-Economics Research Center, Federico II University of Naples, Naples, Italy

Purpose: We evaluated the trend in ICD therapy from 2000 to 2008 in Lombardy, an Italian region with universal healthcare coverage for more than 9 million people. Secondly we analyzed the consumption of healthcare services and the corresponding direct costs following a first implantation.

Methods: We extracted data from DEnAULI, a database warehouse that organizes administrative healthcare data concerning subjects covered by the Lombardy Health System (HS); demographic information, hospital discharges (HDS), drug prescriptions for outpatient clients. We identified HDS for ICD implantation (first or replacement) occurred between 2000 and 2008. We estimated the annual number of first implants (per million persons) in order to assess the trend time and compare it with European and American ones. We evaluated the substitution annual rate (per hundred implants) estimating the total persons under risk, as the time between the first implantation and its replacement cumulated over population members. In order to assess the economic burden of ICD, we selected subjects who underwent a first ICD implantation between 2000 and 2007 and we followed them from discharge to 31/12/2008. We calculated mean annual total cost per capita, and subdivided it into hospitalizations, drugs and outpatient expenditure.

Results: In Lombardy, the annual number of first ICD implants (per million persons) increased, from 55 in 2000 to 236 by 2008, with higher values in males and in subjects aged between 65 and 74 years. The use of ICD in Lombardy was approximately twice higher than in Europe and 3-4 lower than in US. The replacement rate was around 9 (per hundred implant year) in almost all years with a peak in 2005 (15 per hundred implant year); subjects 75 years-old or older showed the highest replacement rate. 5.814 subjects underwent an hospitalization for first ICD implantation between 2005 and 2007 with a mean expenditure of €23,814 (confidence interval, CI95%: 23,676-23,960) per capita. During the follow-up the HS bore a mean annual cost of €4,354 (CI95%:4,226-4,485) per capita: 17% due to drugs, 12% to outpatient visits and 71% to hospitalizations. Though mean total costs didn’t differ among age classes, younger patients reported lower costs in drug treatments and outpatient visits and a higher expenditure for hospitalizations.

Conclusions: ICD use is growing and it’s important to assess both the efficacy and the burden of this therapy, given the economic implications and differences in use among countries. Administrative databases are a useful tool, as they provide information about large unselected populations.

Sexual Dysfunction in patients with chronic heart failure (CIBIS-ELD Study)

E. Tahirovic1, D. Obrodovic1, T. Tripell1, S. Inkrot1, V. Tscholl1, D. Jahandar Lashki1, M. Osterland1, W. Havermak1, W. Doehner1,40mg, and comprises 69% of the statin market, reflecting NICE guidelines and Quality Outcomes Framework (QOF) policy.

Methods: Data from 780 CHF patients (75.5±5.5 years, 36.9% woman, NYHA II) of the CIBIS-ELD trial, a cross-sectional, observational, multicentre trial in elderly CHF patients were analysed. Self-reported sexual function was assessed using data from question 10 of the MLWHF questionnaire. Dyspareunia, peripheral edema, pulmonary rhonchi were assessed as signs and symptoms of CHF.

Results: 165 patients were measured to use SRF. Chi-square-test and Mann-Whitney-U-Test were performed.

Results: A total of 271 patients (76±5.5 years, 46.5% women) provided sufficient data concerning sexual dysfunction. 33 patients (12.2%, 37% women) have reported changes in sexual function in the CIBIS-ELD trial and were invited to participate in an observational follow-up 1.6 to 5.5 years after the end of up-titration with beta-blockers. As the most frequent reasons for this change shortness the breath (20%), fatigue (13.3%) and medication (10%) have been stated. The presence of sexual dysfunction showed no significant correlation with signs and symptoms of heart failure. There are more changes in sexual function (P<0.003) reported by patients who consume (17.6%) alcohol then those who do not (8.6%). Patients with reported sexual dysfunction have significant lower scores in SF-36 questionnaires vitality (41.1±30.7 vs. 50.1±0.05), psychological wellbeing (68.77 vs. 81.86, P<0.002) and psychological component (43.5 vs. 48.99, P<0.013), as well as a higher PHQ score (8.88 vs. 6.29, P<0.006).

Conclusion: Our data revealed no correlation of CHF symptoms with sexual dysfunction. However, psychological parameters, i.e. especially depression score, and alcohol consumption significantly contributed to sexual dysfunction. There is higher chance for lower scores of quality of life questionnaire and sexual dysfunction occurrence.
Results: Out of 321 445 coronary angiography ± PCI procedures in the ARSIF Database between 2003 and 2008, 11 987 were performed in patients treated in Paris and the small ring was at 11.9%.

Conclusion: Cold weather in addition to influenza epidemic during the winter increased the relative risk of STEMI by 14.5%. Subjects at risk for myocardial infarction may benefit from specific protections against cold temperature and influenza infection.

Validation of a new questionnaire to measure physical well-being in patients with chronic heart failure

E. Tahirovic1, D. Trippe1, O. Obascondoc1, V. Tschiopp1, S. Inoktc1, D. Jahandar Lashj1, M. Osterland1, W. Haverkamp1, W. Doehner2, H.-D. Duen1 on behalf of Competence Network Heart Failure.

Purpose: The validation of the FEW-16 included assessment of data quality, internal consistency and intraclass correlation and correlates well with SF-36 and PHQ-D. Data were collected at baseline.

Methods: The Physical Well-Being (FEW-16) is a short 16 Item Questionnaire using a six-point Likert-scale. Higher scores indicate better physical well-being. The scales consist of 4 scales: resilience, ability to enjoy, vitality, and inner peace. Each scale consists of 4 items. In 234 patients with documented CHF (mean age 73.6, 67 men aged 55%, NYHA II 70%, LVFV 47%) we measured the FEW-16 as well as the SF-36 and questionnaire on depression (PHQ-D).

Results: The validation of the FEW-16 included assessment of data quality, scale assumptions, construct validity and reliability. Cronbach’s α was 0.84 for resilience, 0.80 for ability to enjoy, 0.88 for vitality, 0.87 for inner peace and 0.95 for whole FEW-16 score. Pearson's Correlations of FEW-16 with SF-36 and PHQ-D are displayed in Table 1. The Intra-class Correlation Coefficient is 0.87 (95% CI 0.84–0.89; ICC 1.1).

Table 1. Pearson's CCC of FEW-16 with SF-36 and PHQ-D

<table>
<thead>
<tr>
<th>Resilience</th>
<th>Ability to enjoy</th>
<th>vitality</th>
<th>inner peace</th>
<th>FEW-16 score</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.670*</td>
<td>0.689*</td>
<td>0.714*</td>
<td>0.656*</td>
<td>0.783*</td>
</tr>
<tr>
<td>0.579*</td>
<td>0.631*</td>
<td>0.602*</td>
<td>0.779*</td>
<td>0.745*</td>
</tr>
<tr>
<td>0.520*</td>
<td>0.584*</td>
<td>0.565*</td>
<td>0.612*</td>
<td>0.680*</td>
</tr>
<tr>
<td>0.567*</td>
<td>0.634*</td>
<td>0.645*</td>
<td>0.681*</td>
<td>0.737*</td>
</tr>
</tbody>
</table>

*Indicates significance of p < 0.01 (both ways).

Conclusion: The FEW-16 shows good reliability, internal consistency and intraclass correlation and correlates well with SF-36. FEW-16 scores correlate more strongly with psychological well-being of SF-36 and PHQ-D than with clinical parameters.

European Hospital Benchmarking in Acute Coronary Syndrome: the EURHOBOP project

I. Kirchberger1, A. Azevedo2, M. Davoli3, D. Farmakis4, I. Ferri1, P. Garre1, U. Haekkinen5, J. Marrugat6, M. Torres7, C. Meisinger8, 1KORA Myocardial Infarction Registry, Augsburg, Germany; 2University of Porto Medical School, Department of Hygiene and Epidemiology, Porto, Portugal; 3Health Authority Roma E - Department of Epidemiology, Rome, Italy; 4Hellenic Cardiologic Society, Athens, Greece; 5Association pour l’étude et la prévention des maladies dégénératives du système cardio-vasculaire ; Toulouse, France; 6European Hospital and Federation (HFEPE), Brussels, Belgium; 7National Institute for Health and Welfare - Centre for Health and Social Economics, Helsinki, Finland; 8Municipal Institute of Health Assistance - Municipal Institute of Medical Care, Granada, Spain; 9National Institute for Health Care and Health Promotion, Rome, Italy; 10Italian Agency for Public Health, Rome, Italy; 11EU Member States efforts are aimed at improving the quality of the provided health care systems and at tackling inequalities among European citizens. Coronary heart disease kills more than 2.000.000 people in Europe every year and, if acute cases (≥ 700.000 in age range 35-64 years) are not adequately managed, it may result in a high case fatality. Benchmarking the hospitals performance is a key instrument to improve the quality of the provided health care.

EURHOBOP (European Hospital Benchmarking by Outcomes in Acute Coronary Syndrome Processes) is a project funded by the European Commission, under the Second Programme of Community Action in the Field of Public Health (2008–2013). EURHOBOP seeks to validate a set of predictive mathematical functions that include determinants of in-hospital case fatality outcome indicator, to assess the quality of management of myocardial infarction (MI) or unstable angina (UA) patients, and of the following procedures: coronary angiography, thrombolysis, percutaneous revascularization. The indicators will be adjusted for patient, hospital and country characteristics and will permit hospitals to benchmark their performance in these procedures.

Prehospital case-fatality will be considered as the outcome indicator in patients admitted for an acute coronary syndrome (ACS) who receive a discharge diagnosis of MI or unstable angina (UA) and undergo coronary angiography, thrombolysis, percutaneous intervention. The indicators will be adjusted for patient, hospital and country characteristics and will permit hospitals to benchmark their performance in these procedures. Prehospital case-fatality will be considered as the outcome indicator in patients admitted for an acute coronary syndrome (ACS) who receive a discharge diagnosis of MI or unstable angina (UA) and undergo coronary angiography, thrombolysis, percutaneous intervention. The indicators will be adjusted for patient, hospital and country characteristics and will permit hospitals to benchmark their performance in these procedures.
symptom's interpretation may influence time of hospital admission. We decide to explore illness perception and its predictors among patients with acute coronary syndrome.

Methods: We conducted a cross-sectional study of all consecutive patients admitted to Cardiology department with acute coronary syndrome (ACS) between January to September 2011. Data was obtained from personal patient registries and telephonic interview asking patients about their perception of the symptoms beginning. The question for all was: "Did you consider the possibility of heart infarction diagnosis when you started chest pain?" Patients without constructive chest pain and those who had initial symptoms in hospital were excluded.

Results: One hundred and eighty six patients (mean age 63.99±12.34 years old with ACS were included (12.3% with unstable angina, 38.5% with ST-segment elevation myocardial infarction, 42.8% with no ST-segment elevation and 6.4% with undetermined ECG location). The majority (62.6%) of patients didn't had perception of ACS, until the doctor information. Among those who had perception, 82.6% were men and 56% had previous ischemic coronary disease diagnosis. Patients with arterial hypertension and dyslipidemia had superior illness perception (p=0.04; p=0.013; respectively). Only 27.5% of patients with ST-segment elevation myocardial infarction had perception of cardiac disease. No association was found between ACS perception and age, academic degree and residence (rural vs. urban). Among patients with ACS, only 29% decided to seek a hospital within the first thirty minutes of symptoms. Of those, the illness perception was present in 42%.

Conclusion: The illness perception of patient with acute coronary syndrome needs to be improved, independently of socio-demographic factors. An educational program for the general population, focusing in the alert signs for ACS may be necessary to improve hospital admission time and treatment in this setting.

ENDOTHELIAL DYSFUNCTION IN DIFFERENT HYPERTENSIVE POPULATIONS

P1809 Incidence and clinical significance of hypertension induced by anti-VEGF agents

E. Michalopoulou, P. Stamal, M. Michaliakou, F. Katis, D. Stamatis. METMA HOSPITAL, ATHENS, Greece

Objective: Hypertension has been observed as an on target toxicity to anti-vascular endothelial growth factor therapy (VEGF), reflecting VEGF pathway inhibition. Bevacizumab is a monoclonal antibody approved as first-line treatment of colorectal cancer. We retrospectively analyzed the incidence of bevacizumab induced hypertension and its association with clinical outcomes.

Methods: We consecutively included 156 patients (median age 57 years) with colorectal cancer treated with bevacizumab (7.5 mg/kg every 2 weeks) at our Institute from 2006 to 2010. Office blood pressure monitoring (3 measurements at 3 separate visits) and home blood pressure monitoring (2 measurements morning and evening for 7 days) were performed. Blood pressure was graded according to the European Society of Hypertension criteria.

Results: 34 patients (22%) developed grade 3 hypertension, 27 patients (17%) developed grade 2 hypertension and 14 patients (9%) developed grade 1 hypertension. Home-based measurements detected more cases of hypertension than in-clinic measurements did (61.3% vs 29.4%; p<0.01). Patients with hypertension tended to have a better prognostic rate (82% achieved complete or partial response as compared with 47.3% of patients who did not show this side effect).

Conclusions: Patients with any hypertension grade had an adjusted hazard ratio for death of 0.4 (p=0.02) compared to those without hypertension.

P1810 The association of androgenic alopecia with target organ damage in newly diagnosed and never treated young male hypertensive subjects. A pilot study


Purpose: Several studies have demonstrated the presence of an association between androgenic alopecia (AGA) and cardiovascular disease. The aim of this study was to evaluate any target organ damage in newly diagnosed and never treated young male hypertensive with and without AGA by the incorporation of arterial stiffness (PWV, PP), carotid intima-media thickness (IMT), left ventricular hypertrophy (LVM), microalbuminuria (MAU) and coronary flow reserve (CFR).

Methods: We performed a cross sectional study in 21 newly diagnosed and untreated young male hypertensive with AGA (mean age 41.6±6 years) and 8 ones without AGA (mean age 49.6±12 years) who were matched as controls. Carotid and femoral pulse wave velocity (PWV) and office pulse pressure (PP) were assessed as indices of arterial stiffness. Carotid ultrasonography was used to measure the IMT of the common carotid arteries. ECHO was performed in all subjects in order to estimate LVM and CFR. 24h urine collection was performed for MAU estimation. AGA was classified according to the Hamilton-Norwood scale, age of onset and duration while body height was estimated.

Results: No significant difference was found within groups regarding age, BMI, systolic and diastolic blood pressure, PP, PWV, IMT, LVM, MAU and CFR. However, in AGA patients: a. Hamilton-Norwood scale was related with PP (r=-0.64, p<0.01), b. age of onset of AGA was inversely related with PP (r=-0.48, p<0.05), c. duration of AGA was related with PP (r=0.61, p<0.01) and inversely with CFR (r=-0.55, p<0.05) and d. body hair growth was related with PWV (r=0.48, p<0.05).

Conclusion: Our results support the hypothesis that the severity, the early onset, the long standing of AGA as well as body hair growth are related with target organ damage in young untreated males with newly diagnosed essential hypertension. However, it is pending to be demonstrated with further studies if the release of substances from hair follicles or the over expression of androgen receptors or 5a-reductase in the kidney induce a hypertensive response.

P1811 Role of single-nucleotide polymorphisms in renal function of untreated hypertensives: impact on cystatin-C and classical estimates

E. Androulakis1, D. Tousoulis1, E. Chatzistamatiou, N. Papageorgiou, A. Milou, G. Siasos, G. Moustakas, I. Kalliakaros, G. Latsios, C. Stefanadis. Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: Renin-angiotensin aldosterone system (RAAS) participates in the development of renal impairment. Several genetic polymorphisms of its key components, such as M235T and C-344T may be clinically relevant. We therefore aimed to investigate whether these polymorphisms have effects on quantitative measures of renal function in states of hypertension.

Methods: The study population consisted of 318 untreated essential hypertensives and a control group, consisted of 193 matched subjects. The gene mutation frequency was determined using polymerase chain reaction (PCR) technique and appropriate restriction endonucleases. Plasma glucose, serum creatinine, uric acid and lipid levels were determined by routine methods. Serum Cystatin-C levels were measured by ELISA kit. We also assessed GFR by the Cockcroft-Gault formula and estimated Cystatin-C-dependent GFR (eGFR) using the following equation: eGFR = 127.7×Cystatin-C (mg/L)×1.154× Age (years)×0.742×0.857 for women.

Results: Interestingly, angiotensinogen 235TT genotype showed a trend towards a lower GFR compared with MM and MT genotype in hypertensive patients (104±31 vs 110±48, p=NS) and higher values of uric acid (5.3±1.8 vs 4.7±1.5 mg/dL, p=0.056) but neither genotype was associated with increased creatinine, cystatin-C nor eGFR (p=NS for all). With respect to Cystatin-C levels, TT homozygotes of C-344T polymorphism exhibited a trend for higher values compared to C-allele carriers (82.1±19.4 vs 79.9±20.6 mg/mL, p=0.6) and similarly eGFR did not differ across genotypes (CC: 74.9±23.4, CT: 71.9±15.1, TT: 72.1±17.8, p=NS). Combination of allele variants of these candidate genes was not associated with worse renal estimates and different Cystatin-C levels (p=NS for all).

Conclusions: In the present study we have shown that variations in the angiotensinogen gene may affect uric acid levels, however according to our findings, the single polymorphisms are not capable to affect further renal function in patients with essential hypertension.

P1812 Role of leptin on 24hr heart rate variability in overweight hypertensive subjects

G. Moustaïkas1, D. Tossouli2, E. Chatzistamatiou1, G. Trantsis1, E. Androulakis1, C. Dologliannis2, I. Skikas1, A. Milou1, C. Stefanadis1, I. Kalliakaros1,1. Hippokration General Hospital, Cardiology Department, Athens, Greece, 2Hippokration Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: There is increasing evidence that leptin may have effects beyond the regulation of appetite and body weight. Recently, a possible impact of leptin on autonomic nervous system and cardiovascular function has been hypothesized. The aim of the study was to investigate possible relationship between blood pressure (BP) variability and serum leptin levels in overweight subjects with essential hypertension.

Methods: A cross-sectional study was carried out in a population of 161 consecutive never-treated hypertensive subjects, non-diabetic, aged 51 years, with BMI ≥25 kg/m². Venous blood samples were obtained from each participant after an overnight fasting for the determination of serum leptin. All subjects underwent 24-hr ambulatory BP monitoring. Subjects were categorized in tertiles of plasma leptin concentration.

Results: In the whole group plasma leptin concentration correlated significantly with age and gender (r=-0.450, p<0.001). 24th hour systolic and diastolic BP (r=-0.174, P=0.028, r=-0.170, P=0.033 respectively), 24th hour heart rate standard deviation (HR SD) (r=-0.159, P=0.044) and 24th hour heart rate variability index (r=-0.272, P=0.001). Anova showed that age, gender, plasma glucose, blood pressure were similarly distributed across the tertiles. In contrast, subjects in the third tertile of plasma leptin concentration had significantly higher values of office pulse pressure and 24th average pulse pressure, and lower values of 24th HR SD and 24th HR variability index than subjects in the first tertile (51.5±11 vs. 58.1±13, P=0.005, respectively).
Undiagnosed hypertension trumps trastuzumab as a risk factor for anthracycline cardiotoxicity

P. Kotwinski¹, G. Smith², J. Sanders², J. Cooper², A. Teis², A. Jones³, D. Penrell², H. Montgomery¹, L. Ma³, on behalf of The BETTER-CARE Study Investigators. ¹University College London, London, United Kingdom; ²Royal Brompton Hospital, Cardiovascular Magnetic Resonance Unit, London, United Kingdom; ³Royal Free Hospital and University College London, Centre for Hepatology, London, United Kingdom

Introduction: A growing number of patients are at risk from chronic anthracycline cardiotoxicity (cAC), a result of improving prognosis from cancer. This risk is present even at adjunct doses of chemotherapy. Although the early risk of heart failure immediately treatment is low, the life-time risk of heart failure is significantly increased in survivors of childhood cancer. Furthermore, while risk of AC is known to be highly idiiosyncratic, effective tests to predict susceptibility are lacking. We undertook a study to look for genetic and non-genetic risk factors that predict cAC. Here we present data on the relationship baseline blood pressure, weight and percentage body fat (%BFat), and the cardiac response to anthracycline treatment.

Methods: Patients receiving adjuvant anthracycline-based chemotherapy for early breast cancer were recruited. Those with known cardiovascular disease or SBP>160/100 were excluded. LVEF was measured using cardiovascular magnetic resonance imaging (CMR) before chemotherapy. Follow-up was ≥1 year after the final dose of anthracycline, or ≥3 months after the end of Trastuzumab. Chronic AC was defined as a fall in absolute LVEF<5% (ΔLVEF<5%); Blood pressure, weight and %BFat were measured at baseline.

Results: 164 subjects completed the study. The mean dose of epirubicin was 23.6±8.0mg/m2. Thirty were treated with Trastuzumab. Thirty-four participants (20.7%) of this study were determined to have heart failure with reduced ejection fraction (HFrEF)

Conclusions: Our data demonstrate that plasma leptin concentration is related to the development of essential hypertension needs further investigation.

Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>IgG AECA</th>
<th>IgM AECA</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>0.097±0.05</td>
<td>0.055±0.04</td>
</tr>
<tr>
<td>B</td>
<td>0.105±0.07</td>
<td>0.093±0.08</td>
</tr>
</tbody>
</table>

Conclusions: Our results suggest that subjects with high normal blood pressure and high AECA levels are prone to future development of arterial hypertension. The possibility that high AECA levels may be a driving mechanism for the development of essential hypertension needs further investigation.

The relationship of eNOS gene polymorphisms and cholesterol level at the patient with arterial hypertension in Ukrainian population

D. Shorikova, E. Shorikov. Bucovian State Medical University, Chernivtsi, Ukraine

In our days the polymorphism of genes-candidates of cardiovascular diseases is actively studied as one of potential risk factors of the development of atherosclerotic process and alterations of endothelial nitric oxide synthase (eNOS) enzyme activity. The role of specific polymorphisms of eNOS gene and of borderline hypertension as well.

Purpose: In this study, we determined the prevalence and distribution of the above polymorphism and its relationship with the cholesterol level in the hypertensive patients, Ukrainians of Bucovian region and significance of homozgyotes and heterozygotes mutations in this context.

Methods: The association of variants of eNOS-3 gene polymorphism (normal homozgyotes – T786T, heterozgyotes – C786T and homozgyotes mutations – C786C) were determined by polymerase chain reaction with use of primer pairs. The products of amplification were detected in 2% agaric gel using video documentation system.

Results: The prevalence of normal homozgyotes T786T among hypertensive patients was 92%, homozgyotes with C7 mutation were 10.1%. The most part of the inspected patients were presented with polymorphism G/T – 80.7%. The level of general cholesterol at patients with T-T polymorphism was estimated as 7.0±1.10 mmol/l and 3.3±1.31 mmol/l was level of low-density lipoproteins. At the heterozygous patients with polymorphism C-T the maintenance of general cholesterol arrived at 7.3±1.70 mmol/l and low-density lipoproteins - 3.85±1.16 mmol/l (p<0.05). In case of homozygote’s mutation and C-C polymorphism it was marked the considerably higher levels of both general cholesterol 8.07±1.87 (p<0.05) and lipoproteins of low-density 5.71±1.37 mmol/l (p<0.05).

Conclusion: In addition, relation between carriage of allele C of eNOS-3 gene and higher levels of cholesterol and low-density lipoproteins was found in Ukrainian population of Bucovianian region. By addressing these report, the eventual hope is that we might design better therapeutic strategies to prevent endothelial dysfunction and atherosclerotic vascular disease.

The role of community-based lifestyle intervention on salt intake and blood pressure in Iran

A. Khorasav¹, R. Kelashi², M. Pourmoghadass², N. Sarrafzadeh³, M. Boshin⁴, F. Nouri⁵, S. Zarfshar⁶, A. Esmaillzadeh⁷. ¹Hypertension Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Science, Isfahan, Iran (Islamic Republic of); ²Cardiovascular Research Center, Isfahan Cardiovascular Research Institute, Isfahan University of Medical Science, Isfahan, Iran (Islamic Republic of); ³Isfahan Cardiovascular Research Center, Isfahan, Iran (Islamic Republic of)

Background and aim: Data on the effect of lifestyle intervention programs on salt intake and blood pressure in developing countries are scarce. This study aimed to assess the impact of a healthy lifestyle community-based trial on salt intake and blood pressure among a representative sample of normotensive Iranian adults.

Methods: We compared the data for salt intake, urinary sodium levels and blood pressure from three cross-sectional surveys in time points of 1999, 2001-2002 (beginning of the community interventions), and 2007 (after the community trial) for normotensive adult population of Isfahan, Iran. Using multi-stage cluster sampling method, one of the family members at each household was randomly selected. Dietary salt intake was estimated based on urinary sodium levels. Systolic and diastolic blood pressures were measured according to standard methods.

Results: Dietary sodium intake and urinary sodium levels as well as systolic and diastolic blood pressure were significantly decreased during the 9-year study period. Unlike systolic and diastolic blood pressures that had a consistent decrease between 1999 and 2007, dietary sodium intake and urinary sodium levels were slightly raised from 1999 to 2000-2001 and then reduced between 2001-2 and 2007 evaluations. The same findings were reached when data were analyzed separately by gender or weight status.

Conclusion: A lifestyle community trial was effective in controlling the escalating
trend of blood pressure and salt intake in Iranian population. It can be adopted in other developing countries.

P1817 Assessment of dietary sodium intake among adults in Korea population general by 24 hour urine samples
M.Y. Rhee 1, J.S. Shin 2, C.Y. Lim 3, S.W. Kim 2, D.Y. Nah 4, J.H. Bae 5, Y.S. Kim 6, Y.K. Kim 7, M.M. Lee 1, J.H. Kim 1, Dongguk University Hospital, Gayang, Korea, Republic of; 2Dongguk University, Seoul, Korea, Republic of; 3Dongguk University College of Medicine Gyeongju Hospital, Gyeongju, Korea, Republic of
Aims: Korean Government has started sodium intake reduction policy since 2005. Accurate estimation of sodium intake by reproducible method and assessment of the effects of high sodium intake to cardiovascular health are crucial aspect in performing that policy. The present study was performed in 2011 to test the feasibility of 24 urine collection and to introduce it as a standard method of salt intake measurement in a nationwide survey (granted by Korea FDA, 11162KFD1A162, NCT01438619, NCT01327717).
Methods and results: Representative population aged 20 between 65 years was selected by List-assisted random-digit dialing method (LARDD) from a city with one million population. Sodium and potassium intake (24HUNa, 24HUK, respectively) were measured with 24 hour urine collection. Out of 1623 telephone interviews, 496 adults (30.6%, age range 20 – 65 years) were recruited by LARDD. Among those recruited, 368 subjects completed 24 hour urine sampling using the method. The estimated mean 24HUNa was 166.4 mmol/day, much lower than 208.2 mmol in 1988 (INERSA). 24HUNa was highest in population aged 30 to 49 years, with decrease in 24HUNa after 50 years. Men had higher 24HUNa than women (182.0 vs. 151.4 mmol/day). The estimated sodium intake is higher than that reported from UK and Scotland, solution, and Finland, similar to that of Spain, and lower than that of Portugal and Slovenia. In contrast to 24HUNa, 24HUK was continuously increased as age increased. This trend is different from national health survey 2009, which showed low intake of potassium in population above 50 years. This difference indicates an increased concern about health, leading to ingestion of potassium rich food.
Conclusion: In the estimation of sodium intake, 24 hour urine collection method is feasible, and enables us to compare sodium intake to the result of other surveys expected from other countries. This method will be adopted in nationwide survey of Korea. Although high sodium intake is still a significant problem in population below 50 years, pattern of sodium intake seems to be changing due to high concerns on health.

P1818 The influence of high vs. low sodium intake on blood pressure and hemodynamics in patients with morbid obesity
P.K. Bonlils, M. Taskiran, M. Damgaard, N. Gadsboll. Hospital of Koege, Koege, Denmark
Purpose: Many patients with morbid obesity have hypertension. The complex pathophysiologic abnormalities linking hypertension to obesity have not been fully clarified, but abnormal sodium handling may be an essential mechanism. The purpose of the present study was to examine the hemodynamic responses to a short-term change in dietary sodium intake in patients with morbid obesity and without hypertension.
Methods: Twelve hypertensive patients (5 male, 7 female) and twelve normotensive patients (5 male, 7 female) with severe obesity (BMI > 40 kg/m²) were examined after 5 days of a low-sodium diet (75 mmol/day) and 5 days of a high-sodium diet (250 mmol/day) in a randomized order. Plasma volume, glomerular filtration rate, body compartments, and hemodynamic examinations were performed on day 5 in each diet period. The hemodynamic examinations (non-invasive cardiac output measurements) were performed at rest and during bicycle exercise, whereas blood pressure was measured after 30 minutes of rest and as 24-hour blood pressure measurements.
Results: In hypertensive as well as in normotensive patients, high sodium intake as compared to low sodium intake was associated with an increase in plasma volume (8±2%; p<0.05), cardiac output (17±4%; p<0.05), and stroke volume (27±8% vs. 27±7%; p=0.84) similarly in both groups at rest, with no change in heart rate in either groups (6±3% vs. 4±3%; p=0.684). Twenty-four-hour blood pressure measurements and resting blood pressure was unaltered in both groups, and therefore the total peripheral resistance decreased equally (11±3% vs. 10±3%; p=0.848) during high sodium intake. Similar changes were observed during an incremental bicycle exercise test where cardiac output and stroke volume were higher while mean arterial blood pressure was unchanged at each exercise level during high sodium intake.
Conclusion: Neither hypertensive nor normotensive patients with morbid obesity seem to have a sodium sensitive blood pressure, despite a substantial increase in plasma volume, cardiac output and stroke volume during short term high sodium intake.

P1819 Association of different obesity indices with blood pressure in greek adolescents: the role of familial hypertension burden
S.-M. Kyvelou, C. Tsioufis, V. Tzamou, D. Tsiachris, T. Psaltisopoulos, E. Andrikiou, N. Koufakis, C. Thomopoulous, C. Stefanadis. First Cardiology Clinic, University of Athens.Hippokration Hospital, Athens, Greece
Purpose: To assess the associations between different obesity indices and blood pressure (BP) in Greek adolescent students, while the familial burden of hypertension was also been taken into consideration.
Methods: The study comprised of 496 students who were subjected to repeated BP measurements and anthropometric measurements (i.e. waist circumference, hip, waist-to-hip ratio, waist-to-height ratio, body mass index (BMI) and conicity index) were calculated. By means of a standard questionnaire, developed for the purposes of the study, we retrieved information about age, sex, number of siblings, several indicators of family’s socioeconomic status, smoking habits, time spent on sedentary activities, as well as information on family history of arterial hypertension (one, both or none of the parents) and hospitalizations of the children.
Results: Overall, the study population was divided in two groups according to the presence (n=109) and the absence (n=387) of familial history of hypertension. Adolescents with family history of hypertension presented with significantly higher systolic BP (SBP) (p=0.003) and diastolic BP (DBP) (p=0.021) levels. Further, univariate analysis was conducted assessing correlations between obesity indices and blood pressure levels in the overall population. WHR was strongly associated with SBP and DBP (r=0.27, p=0.001) (r=0.13, p=0.009), respectively, while BMI was strongly correlated with SBP, DBP but not heart rate (r=0.47, p<0.001), (r=0.36, p=0.001), (P=NS), respectively. Finally, CI was positively associated with SBP but not with DBP (r=0.185, p<0.0001) and (P=NS) respectively, while waist-to-height ratio was strongly correlated with SBP; DBP but not HR (r=0.32, p<0.0001), (r=0.24, p<0.0001), (P=NS), respectively.
Conclusion: Young adolescents with familial aggregation of hypertension have higher levels of both systolic and diastolic BP, independently of age, smoking and body weight, while obesity indices are strongly correlated with BP levels in these ages.

P1820 Role of aerobic capacity in inflammation state in diabetes with and without chronic kidney disease
R.J. Franco, F.G.S. Shirasidi, F.S.B. Stringueta-Belik, V.R.O.S. Silva, L.C.M. Martin, J.C.H. Hueb, J.C.T.C. Caramori, P.B. Barretti. UNESP, Botucatu Medical School, Department of Internal Medicine - Sao Paulo State University, Botucatu, Brazil
Our hypothesis is that in patients with both, better aerobic capacity(AC) is associated with less inflammatory state (IS) and arterial stiffness. The aim of this study was to determine if a better AC measured by VO2max is associated with attenuation of chronic IS, arterial stiffness and carotid intima-media thickness (IMT) in CKD DM and non-DM. Thirty-nine CKD patients (17 in hemodialysis program), were clinically and laboratory evaluated. According to CKD etiology 2 groups were obtained: DM (GD) was formed by 11 and non-DM (GND) formed by 28. Central BP and arterial stiffness were evaluated by Sphygmocor. Average and max of left and right MIT by US were also performed. AC was measured by estimated VO2max according to treadmill test by Bruce protocol. The GD showed a higher frequency of CRP above our laboratory cut-off (p=0.044), higher frequency of male gender and a non-significant higher value of VO2max (p=0.009). The IMT was similar. Only better AC was associated with lower frequency of high CRP when adjusted to DM and gender in a logistic regression model. In conclusion, AC was associated with inflammatory state, in CKD patients, independently of DM presence.

Baseline characteristics

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>BMI (kg/m²)</th>
<th>MAP (mmHg)</th>
<th>Fat (%)</th>
<th>st-GFR (ml/min per 1.73m²)</th>
<th>VO2-max (ml/kg/min)</th>
<th>Inulin (mmol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertensive pts (n=12)</td>
<td>43±8</td>
<td>42±3±3.3</td>
<td>103±11</td>
<td>42±7</td>
<td>108±18</td>
<td>2.7±0.8</td>
</tr>
<tr>
<td>Normotensive pts (n=12)</td>
<td>39±8</td>
<td>42±7±5.2</td>
<td>92±6</td>
<td>41±7</td>
<td>108±16</td>
<td>2.5±0.5</td>
</tr>
<tr>
<td>p-value</td>
<td>0.148</td>
<td>0.955</td>
<td>0.008</td>
<td>0.790</td>
<td>0.945</td>
<td>0.589</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation.

Multiple linear regression: C-reactive protein

<table>
<thead>
<tr>
<th>Gender</th>
<th>P</th>
<th>Lower</th>
<th>Upper</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>0.210</td>
<td>0.021</td>
<td>2.335</td>
</tr>
<tr>
<td>Female</td>
<td>0.646</td>
<td>0.107</td>
<td>86.802</td>
</tr>
<tr>
<td>VO2max</td>
<td>0.024</td>
<td>0.701</td>
<td>0.976</td>
</tr>
</tbody>
</table>
Effect of coffee consumption on blood pressure and exercise tolerance


Heart Institute, Univ. of Sao Paulo Medical School, Sao Paulo, Brazil; University of Sao Paulo (USP), Sao Paulo, Brazil

Purpose: Coffee is the most abundantly consumed stimulant worldwide. However, its cardiovascular safety remains controversial. Some studies suggest coffee consumption acutely can determine a slight blood pressure raise and improve exercise tolerance. AIM: We evaluated blood pressure and exercise tolerance before and after daily chronic coffee consumption in a group of healthy volunteers and in patients with coronary artery disease.

Methods: We did a prospective random cross-over trial to evaluate two different types of roasted coffee. All individuals were oriented by the same nutritionist and put on 3 weeks washout for caffeine beverages and foods. Then they were randomly assigned to start drinking filtered coffee first in one style-roasted coffee and then crossed-over to the other style. Ground coffee beans, provided for four weeks each, were medium-dark (MD) and dark (D) roasts. After 4 weeks they were cross-over with a total of 8 weeks of drinking coffee. All individuals were taught the amount of coffee to brew each time. They get instructions to drink 450 to 600ml every single day. In the baseline and after each period of drinking they were submitted to 9 (5min) test and ambulatory blood pressure monitoring (24-h ABPM). We did analyze average systolic blood pressure (SBP) and diastolic blood pressure (DBP) from 24-h ABPM, total exercise time (J-T Exercise) and double productions (DP) from treadmill test. Variables were evaluated by the analysis of variance for repeated measures.

Results: We evaluated 80 subjects (26 with coronary artery disease and 54 healthy volunteers) with 53.4±13.5 years old, 35 men and 45 women (see table).

24-h ABPM and Treadmill Test

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>D</th>
<th>MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>J-T Exercise</td>
<td>619.5±209</td>
<td>658.2±251</td>
<td>664.5±224</td>
</tr>
<tr>
<td>DP (SBP/HR)</td>
<td>2323±7.3</td>
<td>2431.7±3928.8</td>
<td>0.272</td>
</tr>
<tr>
<td>SBP (mmHg)</td>
<td>109.5±10.3</td>
<td>107.9±15.4</td>
<td>126.6±11.7</td>
</tr>
<tr>
<td>DBP (mmHg)</td>
<td>68.6±7.8</td>
<td>66.4±8.4</td>
<td>68.7±8.7</td>
</tr>
</tbody>
</table>

Measures expressed as average ± SD.

Conclusions: Both raised total exercise time capacity, without an increase in double product. Medium dark roasted coffee consumption, but not dark, promoted a slight blood pressure elevation. These findings suggest that there are substances other than caffeine that raises blood pressure and is degraded by roasting.

Muscular endurance and maximal aerobic capacity as determinants of blood pressure in young men

M. Mantysaari, J. Vaara, M. Santtila, H. Kyrolainen. Centre for Military Medicine, Helsinki, Finland; Department of Leadership and Military Pedagogy, National Defence University, Helsinki, Finland; Personel Division, Defence Command, Helsinki, Finland; Department of Biology of Physical Activity, University of Jyväskylä, Jyväskylä, Finland

Purpose: The relationship between blood pressure and physical work capacity as well as short time physical activity was studied. AIM: The study participants were enrolled in 2008 during eight Finnish Defence Forces refresher courses for the army reserve and consisted of 846 young men (25.5±5.0 years). Body weight, height, and waist circumference were measured. Muscular endurance was determined using a score based on the number of repetitions during 1-minute sit-up, push-up and repeated squat tests. Maximal aerobic capacity was measured using a bicycle ergometer test. Blood pressure was measured sphygmomanometrically twice from the arm with the subject sitting after 5 minutes of rest. The study participants also completed a questionnaire about their leisure time physical activity and alcohol consumption. In the statistical analysis, mean and standard deviation were given. Spearman's correlation coefficient was calculated between blood pressure and the other parameters. Results: Mean ±SD systolic blood pressure was 123±12 mmHg, diastolic blood pressure was 77±19 mmHg, height was 176±7 cm, body mass was 81±14 kg, body mass index was 25.4±6 kg/m² and waist circumference was 86±10 cm. Systolic blood pressure was higher than 140 mmHg in 8% of the participants and diastolic blood pressure was higher than 90 mmHg in 7% of the participants. Correlations between blood pressure and other measured parameters are given in the Table below (**p = 0.001, *p = 0.05).

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>6 mo PP</th>
<th>At term</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Mass (kg)</td>
<td>77.5±6</td>
<td>77.3±6</td>
<td>77.5±6</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>24.1±3</td>
<td>24.3±3</td>
<td>24.1±3</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>86±10</td>
<td>86±10</td>
<td>86±10</td>
</tr>
<tr>
<td>Maximal Aerobic Capacity</td>
<td>-0.067</td>
<td>-0.068</td>
<td>-0.067</td>
</tr>
<tr>
<td>Muscular Endurance Index</td>
<td>-0.003</td>
<td>-0.086</td>
<td>-0.003</td>
</tr>
<tr>
<td>Leisure Time Physical Activity</td>
<td>0.046</td>
<td>0.046</td>
<td>0.046</td>
</tr>
</tbody>
</table>

Conclusions: Obesity and lower aerobic capacity were associated with higher blood pressure. Muscular endurance, self-reported leisure time physical activity and alcohol consumption were not associated with blood pressure level. Thus, the present study suggests that even in young adults, measures that combat obesity and low fitness may prove effective in the prevention of hypertension.

Persistent increments in proximal arterial stiffness and peripheral resistance following preeclampsia might contribute to the higher cardiovascular risk in future life

M.-E. Estensen, G. Grindheim, E.W. Remme, O.A. Smieth, P. Segers, T. Henriksen, S. Aakhus. University of Oslo, Faculty Division Rikshospitalst University Hospital, Oslo, Norway; Oslo University Hospital, Department of Anaesthesiology and Intensive Care, Oslo, Norway; Institute for Surgical Research, University of Oslo, Oslo, Norway; Ghenet Institute, University for Biomedical Technology (BioMMeda/IBTech), Gent, Belgium; Oslo University Hospital, Department of Cardiology, Oslo, Norway; Department of Obstetrics, Oslo University Hospital, Rikshospitalet, Oslo, Norway, Oslo, Norway

Purpose: Preeclampsia (PE) is pregnancy induced hypertension and proteinuria, occurring after 20 weeks of gestation. We performed a study of arterial properties and ventriculo-arterial coupling (VAC) at term and 6 months post-partum in women with PE and women with normal pregnancy (NP). Postpartum recordings were compared against non-pregnant values from women with previous preeclamptic pregnancy (PPEP).

Methods: 35 women (37±4 years) with PPEP (3.5±1.0 years), 40 (32±6 years) with PE and 65 (32±5 years) with NP. Aortic root flow and pressure obtained by Doppler (transcatheter echocardiography) and calculated right subclavian arterial pulse traces. Arterial compliance (C), characteristic impedance (Z0), and peripheral arterial resistance (R) were estimated by 3-element Windkessel model (WK) and Fourier analysis of pressure and flow. Arterial elastance, Ea, was calculated as end systolic pressure (Pes) over stroke volume (SV). Ventricular function was assessed by ELVI, which represents left ventricular systolic elastance (Pes/ESVI).

Results: At term, 20, Ea and R were higher and C was lower in PE pregnancy compared to NP. Indicating a higher resistance in the arteriole tree. 20, Ea and R remained elevated 6 months follow-up in PE and after 3 years in PPEP.

Table 1 Results

<table>
<thead>
<tr>
<th></th>
<th>At term</th>
<th>6 mo PP</th>
<th>At term</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAP (mmHg)</td>
<td>85.5±7</td>
<td>86.7±6</td>
<td>85.5±7</td>
</tr>
<tr>
<td>R (mmHg m²/s²)</td>
<td>0.92±0.23</td>
<td>1.10±0.29</td>
<td>1.13±0.23</td>
</tr>
<tr>
<td>Z0 (mmHg m²/s²)</td>
<td>65.24</td>
<td>68.22</td>
<td>68.24</td>
</tr>
<tr>
<td>Z0 (mmHg m²/s²)</td>
<td>0.43±0.23</td>
<td>0.52±0.31</td>
<td>0.58±0.27</td>
</tr>
<tr>
<td>C (mmHg m²/s²)</td>
<td>1.55±0.46</td>
<td>1.40±0.45</td>
<td>1.34±0.43</td>
</tr>
<tr>
<td>Pes (mmHg)</td>
<td>87.9±9</td>
<td>92.8±8</td>
<td>122±11</td>
</tr>
<tr>
<td>Es (mmHg/mg/m²)</td>
<td>3.82±1.76</td>
<td>5.40±1.88</td>
<td>7.13±2.52</td>
</tr>
<tr>
<td>Es/El (m²/mg)</td>
<td>0.64±0.23</td>
<td>0.45±0.14</td>
<td>0.51±0.19</td>
</tr>
</tbody>
</table>

*p<0.05 vs 6 months, *p<0.05 vs normal pregnancy.

Conclusions: PE is characterized by increased proximal arterial stiffness and peripheral resistance at term, 6 months post partum, and at 3 years follow up. These results indicate that the cardioprotective disturbances in PE extend beyond pregnancy and might explain the higher risk of hypertension and cardiovascular disease in future life.

PREVALENC OF HYPERTENSION IN DIFFERENT POPULATIONS

Could microinflammation explain the relationship between low diastolic blood pressure and mortality in hemodialysis patients?


1Univ. Estadual Paulista (UNESP), Botucatu Medical School; Sao Paulo State University, Botucatu, Brazil; 2Faculdade Educave Avare, Avare, Brazil

There are an inverse paradoxical relationship between diastolic blood pressure and mortality in hemodialysis patients. It means that the higher the diastolic blood pressure the lower the mortality rate. This has induced some institutions the need for antihypertensive treatment in this subset of patients. But others confounding factors, besides hemodynamic load, could act to explain this relationship. So the aim of this work is to verify the role of microinflammatory state in the excess of mortality of low diastolic blood pressure hemodialysis patients. We performed a longitudinal analysis of 113 hemodialysis patients of the Nephrol-colog)).
Increased prevalence of a hypertensive response to exercise in male patients with obstructive sleep apnea and essential hypertension


First Cardiology Clinic, University of Athens, Hippokration Hospital, Athens, Greece

Purpose: Obstructive sleep apnea (OSA) is characterized by increased sympathetic activity that serves as a possible pathophysiologic mechanism for a hypertensive response to exercise (HRE). We sought to investigate the association of OSA with HRE in the setting of hypertension.

Methods: We studied 37 male patients with essential hypertension (age: 52±8 years, mean office BP: 134/91mmHg) and untreated OSA diagnosed with polysomnography (PSG) (apnea-hypopnea-index>5) and 39 hypertensive control subjects with OSA (negative PSG) matched for age and body mass index. All patients underwent office and ambulatory BP measurements, echocardiography, routine blood testing and exercise treadmill testing according to the Bruce protocol. A HRE was defined as peak systolic BP (>210mmHg).

Results: The two groups did not differ significantly regarding office and ambulatory blood pressure, metabolic profile and left ventricular mass index. However, peak systolic and diastolic BP were significantly higher in patients with OSA compared to controls (190±21 vs. 188±22mmHg, p<0.031 and 93±11mmHg, p=0.023 respectively). Furthermore, a HRE was significantly more prevalent in hypertensives with OSA compared to those without (46% vs. 20%, p<0.034). In a model of multiple logistic regression analysis, HRE was independently predicted by logAHI (OR=2.24, CI: 1.06-4.72).

Conclusions: HRE is more prevalent in hypertensive patients with OSA compared to their non-OSA counterparts. This finding may have important diagnostic and prognostic implications.

The relationship between additional markers of cardiovascular risk and the complex metabolic and haemodynamic parameters in hypertensive patients with obesity

O. Pionova. Kharkiv National Medical University. Kharkiv, Ukraine

Objective: The objective is to evaluate the relationship between indicators carbohydrate metabolism, serum apolipoprotein B (apo B) and apolipoprotein A1 (apo A1) level and blood pressure in hypertensive patients with obesity.

Materials and methods: 102 patients on average age 54.9±9.4 with hypertension and obesity were examined. They were matched in age and sex. Control group consisted of 21 healthy men aged on average 53.40±11.80 years. All patients underwent clinical examination that included anthropometric examination, assessment of carbohydrate metabolism (fasting glucose, insulin, glycated hemoglobin (Hb A1c) levels) and determine the level of apolipoproteins (apo B and apo A1) level. We statistically tested the criteria of the IDF 2005 was diagnosed abdominal obesity and to definition the glomerulotoxic effects. Oral glucose tolerant test and glucated hemoglobin was used to exclude patients with type DM.

Results: In hypertensive patients with obesity revealed a positive significant association between rate of waist circumference and insulinemia (R=0.24; p<0.01), apo B (R=0.21; p<0.02), and negative significant association with level apo A1 (R=0.29; p<0.002). For 57.84% of them identified insulin resistance (IR). In individuals with IR glycemia was associated with DBP (R=0.41; p<0.05), but not with SBP. In hypertensive patients without IR reliable relationship between metabolic and haemodynamic parameters haven't been identified. In hypertensive patients with obesity and IR revealed an association between levels of apo B and total cholesterol (TC) (R=0.29; p<0.05), high density lipoproteins cholesterol (HDL-C) (R=0.35; p<0.05), low-density lipoprotein cholesterol (LDL-C) (R=0.33; p<0.05), and triglycerides (R=0.46; p<0.05), but no relationship with levels of apo A1. On the other hand, hypertensive patients with obesity and without IR revealed the relationship between levels of apo B and TC (R=0.53; p<0.05), LDL-C (R=0.49; p<0.05). At the same time antihypertensive marker (apo A) is negative associated with TC (R=0.46; p<0.05), and LDL-C (R=0.48; p<0.05).

Conclusion: This study showed that in hypertensive patients with obesity the relationship between the levels of additional atherogenic markers in the presence of higher insulin resistance. Probably haemodynamic factors, together with insulin resistance contribute to the formation of athrogenic potential, especially if they have abdominal obesity.

Associations of blood pressure and cognitive function in the adolescents: the population-based study

A. Sukhanov, D. Denisova. Institute of Internal Medicine. Siberian Branch of the Russian Academy of Medical Sciences, Novosibirsk, Russian Federation

Purpose: To assess the influence of BP on the cognitive domains in adolescents in Western Siberia, exemplified by the Novosibirsk city.

Methods: Cross-sectional population-based study of 302 randomly representative sample of school students aged 14-17 of both sexes in Novosibirsk was implemented. For inclusion in this survey the informed consents from parents and from the participants had taken. BP was measured two times within 5 min in sitting position at the right upper arm. The mercury sphygmomanometer with a cuff of 13 x 23.5 cm was used. Tones listened to within 2 mm of mercury. The mean from 2 BP measurements was included in the statistical analysis. Cognitive domains were determined by standardized screening methods. Letter cancellation test (modified Bourdon’s test), Luria’s 10-words test and test of excluded of incorrect words were used. The statistical package “for Windows” was used. Normality of distribution was determined by the Kolmogorov-Smirnov method. Student’s t-test for normal distribution or Mann-Whitney U-test for distributions other than normal were used. Pair correlation analysis (by Spearman) and the multiple linear regressions were used. Hypothesis testing for the level of probabilities 95% (p<0.05) in all cases was carried out.

Results: The sample consisted from 231 boys (42.1%) and 171 girls (57.9%). Average age: 15.66±0.9 years. Statistically significant gender differences (p<0.01) of attention/concentration in the letter cancellation test and of abstract/conceptual reasoning in the test of excluded of incorrect words were observed. Differences in Mann-Whitney U test between two extreme BP groups (below 10 percentile and above 90 percentile values of BP) by the average ranks values of cognitive tests revealed the following data. Higher scores corresponding to better fulfill tasks were at the group below 10 percentile for SBP (with lower SBP): 79.69 and 65.51, respectively. Greater numbers of errors were at the group with lower DBP (below 10 percentile): 68.75 and 54.87, respectively. Weak negative correlation between Luria’s 10-words test and DBP were found (r=-0.136 and -0.122 for immediate and delayed recall, respectively). Low BP group had greater numbers of errors. This is confirmed by the results of pairwise correlation analysis and multiple linear regressions.

Conclusions: Statistically significant associations (p<0.05) between higher BP especially DBP, and cognitive dysfunction in adolescents were revealed. This study suggests an influence of hemodynamic factors such as BP on memory, attention/concentration and abstract/conceptual reasoning in adolescents.

Prevalence of hypertension in different populations

V. Katsi, G. Souretis, I. Vlasseros, D. Vrachatis, D. Tousoulis, C. Stefanadis, I. Kallikazaros. Hippokration General Hospital, Athens, Greece

Purpose: Much of the variance in hypertension-related sequelae across ethnic groups, is highly related to deficits in accurate health-related data. We sought to evaluate the burden of migration on health-related quality of life (HrQol) in the setting of essential hypertension (EH). We hypothesised that immigrants would indicate lower scores in the most dimensions of HrQol than natives, reflecting differences in social-economic status.

Methods: We studied 67 Eastern European immigrants with newly diagnosed untreated stage I-II EH (aged 51±15 years, 35 male, office blood pressure (OBP)=159/92 mmHg), who immigrated to Greece within the previous two years and 61 hypertensives natives matched for age, gender and OBP. The validated Greek version of the Short Form SF-36 (SF-36) General Health Survey questionnaire was administered to all participants. The subscales were further grouped into two summary scales: the physical component summary (PCS) and the mental component summary (MCS). Non parametric Mann-Whitney tests were performed.

Results: Hypertensive immigrants scored significantly lower in all dimensions of SF-36 when compared to natives. (Table)

SF-36 scoring

<table>
<thead>
<tr>
<th>SF-36 scales</th>
<th>Immigrants</th>
<th>Natives</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Role physical</td>
<td>38±13</td>
<td>68±24</td>
<td>0.007</td>
</tr>
<tr>
<td>General health</td>
<td>41±15</td>
<td>67±26</td>
<td>0.05</td>
</tr>
<tr>
<td>Vitality</td>
<td>39±12</td>
<td>72±27</td>
<td>0.001</td>
</tr>
<tr>
<td>Social functioning</td>
<td>28±12</td>
<td>75±28</td>
<td>0.001</td>
</tr>
<tr>
<td>Role emotional</td>
<td>31±13</td>
<td>74±28</td>
<td>0.001</td>
</tr>
<tr>
<td>Emotional health</td>
<td>32±12</td>
<td>74±27</td>
<td>0.001</td>
</tr>
<tr>
<td>PCS</td>
<td>41±16</td>
<td>69±26</td>
<td>0.06</td>
</tr>
<tr>
<td>MCS</td>
<td>31±14</td>
<td>74±27</td>
<td>0.001</td>
</tr>
<tr>
<td>Total SF-36</td>
<td>35±17</td>
<td>74±27</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusions: In conclusion, immigration process and resettlement experience jeopardizes HrQol in the setting of EH. It is crucial for primary health care units and other social services to conduct screening programmes for hypertension and its impact to the psychological well-being of the migrating people.
**Prevalence of cardiovascular risk factors in students**

**F. Aguirre** on behalf of INPETU, Military Hospital, Guayaquil, Ecuador

**Purpose:** P.C.R.F. Study is a prospective, observational study designed to evaluate the prevalence of hypertension and the presence of cardiovascular risk factors in young people aged 11 to 13 years of age.

**Methods:** The study was conducted in two schools in Guayaquil chosen at random. Consent was obtained from school authorities and participating students, who were also informed of the reasons behind the study, in accordance with the Helsinki criteria. In total, 623 students were examined. This examination included collection of anthropometric data and measurement of blood pressure (BP) in the first phase of the study. In the second phase, students with elevated BP were re-examined and classified according to their BP response. They also underwent tests for microalbuminuria using turbidimetric methods. Central tendency (mean, median, and mode) and dispersion values (standard deviation, standard error, 95% CI) were calculated for data analysis. Relative risk was also evaluated using Medcalc software. Body mass index (BMI) and BP was calculated in percentiles in order to define ranges in accordance with their weight, height and age.

**Results:** Of the sample population, 54.4% were men and 45.58% were women. The average BMI was 19.96 ± 0.175 kg. Underweight was found in 3.6% of the sample, overweight in 63.7%, obesity in 17.6%, and obesity grade I in 4.7%. Systolic SBP averaged 109 ± 11 mmHg, diastolic BP was 60 ± 9 mmHg, and mean arterial pressure (MAP) was 77.3 ± mmHg. Participants were classified as BP of 121-129 and 130-139 in the first measurement as white coat hypertension when there was subsequent normalization of the values in two subsequent measurements, and BP ≥ 140 mmHg as hypertension (HTA).

Conclusions: Most young participants with elevated BP were classified as having pre-HTA, followed by white coat HTA and finally HTA. 9.3%, 3.2% and 0.8% respectively. The percentage was higher in men (54%) and overweight and obese youth. A correlation was not found between microalbuminuria values and BP. Of the 8.2%, with microalbuminuria, 4.7% were obese as determined by BMI, 23.8% were overweight, and 28.5% had normal weight. This finding could serve as a practical tool to investigate metabolic disorders such as diabetes, obesity, or HTA. Finally, we found that there is a relationship between family cardiovascular history and the presence of HTA in youth, in contrast to the use of energy drinks, which showed no association.

**Prevalence of arterial hypertension and risk factors in man organized population of Armenia**

S.V. Gurgenyan. Institute of Cardiology, Yerevan, Armenia

**Purpose:** To evaluate the prevalence rate of arterial hypertension (AH) subject to influence of exogenous risk factors (RF), climatic and geographic patters in man urban and rural organized population working at a factory in two different regions of Armenia.

**Methods:** Descriptive cross-sectional study performed in a primary care setting, involving 4782 man of general population (at the age of 20-60 years) of two regions of Armenia. AH was estimated in BP ≥ 140/90 mm Hg. The urban population (I group) involved 2960 persons living in hilly countryside located at 901 m above - sea level, the rural (II group) – 2050 persons living in mountain terrain located at 1600 m above - sea level. We estimate the relationship of AH from age, body mass index (BMI), and excessive intake of salt (EIS). EIS is evaluated by the threshold of sensitivity taste (TST) to NaCl. This test is estimated by NaCl concentration in distilled water from 0.1 to 1.2%, the concentration increases in each 4 consecutive days (as in group A). One drop applies at the apex of the tongue in ascending order. NaCl concentration. The threshold was estimated under minimal concentration when the patient feels the salt taste.

**Results:** Geographic variation in AH prevalence was found: the higher in the I gr - 15.5%, the lower in the II - 4.9%. The risk of AH increases with age in two gers (I gr - in man at the age of 60 years old - 23.7%, II - 7.4%) and obesity class (I gr - 30.3-34.9% of men, II gr - 24.4% of men, and obesity grade I 19.18%, II gr - 15.1%. Systolic SBP was classified in three groups: II group <140 mmHg, III group <160 mmHg, and II group ≥ 160 mmHg. We estimate the relationship of AH from age, body mass index (BMI), and excessive intake of salt (EIS). EIS is evaluated by the threshold of sensitivity taste (TST) to NaCl. The test is estimated by NaCl concentration in distilled water from 0.1 to 1.2%, the concentration increases in each 4 consecutive days (as in group A). One drop applies at the apex of the tongue in ascending order. NaCl concentration. The threshold was estimated under minimal concentration when the patient feels the salt taste.

**Conclusions:** Prevalence of hypertension in different populations / Controversial issues on thrombotic and antithrombotics treatment 303

**Effect of rivaroxaban with or without acetylsalicylic acid on thrombus formation in an ex vivo perfusion chamber: an open-label, randomized study in healthy subjects**

M. Woitzl,1 G. Gouya, S. Kaplitz1, M. Becka,2 M. Wueck,2 D. Kubitzke,1 Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria; 2Bayer HealthCare Pharmaceuticals, Department of Biometry, Pharmacometry, Wuppertal, Germany; 3Bayer HealthCare Pharmaceuticals, Clinical Pharmacology, Wuppertal, Germany

**Purpose:** Although the pathogenesis differs between arterial and venous thrombosis, fibrin formation and platelet activation have important roles in thrombogenesis. This study investigated the effect of rivaroxaban, an oral, direct Factor Xa inhibitor, with or without acetylsalicylic acid (ASA), on thrombus formation in an ex vivo perfusion chamber at both low (as in the venous system) and high (as in stenosed arteries) shear rates.

**Methods:** Fifty-one healthy subjects were enrolled in this randomized, two-way cross-over trial of rivaroxaban with and without ASA. The study design is a parallel-subject study for comparison between the different dosing regimens of rivaroxaban and ASA plus clopidogrel. The treatment groups were: (A) rivaroxaban plus ASA: rivaroxaban 15 mg twice daily and ASA 75 mg once daily on day 1; rivaroxaban 10 mg plus ASA 75 mg on day 2; rivaroxaban 10 mg plus ASA 75 mg on day 3; rivaroxaban 5 mg plus ASA 75 mg on day 4. (B) ASA plus rivaroxaban: clopidogrel 300 mg loading dose followed by 75 mg on day 1; rivaroxaban 15 mg twice daily on days 2 to 4. (C) ASA plus rivaroxaban: clopidogrel 300 mg loading dose followed by 75 mg on day 1; rivaroxaban 15 mg twice daily on days 2 to 4.

**Results:** Rivaroxaban reduced fibrin deposition in the perfusion chamber thrombus as measured with D-dimer levels (for fibrin deposition) and P-selectin content (for platelet deposition), which were performed at the time of Cmax of rivaroxaban and at the maximum effect of ASA or clopidogrel. Pharmacodynamic parameters measured from plasma included inhibition of Factor Xa activity, prothrombin time, activated partial thromboplastin time and endogenous thrombin potential.

**Conclusions:** Rivaroxaban reduced fibrin deposition in the perfusion chamber thrombus as measured with D-dimer levels, which were decreased by 9%, 84% and 65% at low shear rate and 37%, 73% and 74% at high shear rate after rivaroxaban 5, 10 and 20 mg, respectively. Steady-state ASA with rivaroxaban 5 mg caused a greater reduction in D-dimer levels (63%) at low shear rate. Co-administration of rivaroxaban and clopidogrel was associated with a 30% decrease at low shear rate and a 14% decrease at high shear rate. No conclusive effect was observed for thrombus P-selectin content across the treatment groups. The effects of rivaroxaban on the pharmacodynamic parameters measured in plasma were similar to previous studies, and co-administration of ASA and rivaroxaban had no additional influence.

**Prevalence of hypertension in overweight and obesity by gender and age in North Indian diabetic punjabi population**

R. Kapoor, S. Chopra. Carewell Heart & Superspecialty Hospital, Amritsar, India

**Purpose:** To determine the prevalence of Hypertension in Overweight and Obese Type 2 diabetic patients.

**Method:** 2644 Type 2 DM subjects, aged between 20 – 80 yrs. were enrolled for this study which is a cross-sectional and co-relational study.

**Results:** From total sample of 2644 subjects with T2DM, 52.83% were overweight and 35.39% obese. There was a increase prevalence of overweight in male patients whereas women had increase prevalence of obesity. According to BMI, it was noted that there is a increase prevalence of overweight and obesity grade I to subjects among the age group of 51- 60 yrs., while obesity grade II in subjects from 41-50 yrs. age group.

SBP was elevated in 70% in overweight and obese subjects. SBP is slightly high in male but there is no significant difference between genders (P = 0.84). Regarding to elevated DBP, it affects 35.4% subjects, presenting a greater proportion in males with 42.2% compared to 36.3% females. DBP has highly significant association with respect to gender (P < 0.009). DBP affects in greater proportion the subjects ranging from 51- 60 yr.

**Conclusion:** Prevalence of hypertension in overweight and obese subjects from a hospital setting was 82.8 and 67.7% in men and women respectively. This is a matter of great concern due to increasing prevalence of overweight and obesity in our society. It is to be noted that although there is no significant difference between genders in prevalence of hypertension, there is a gender difference in the type of overweight and obesity. Prevalence of overweight and obesity was significantly higher in men, specifically when they are in between 51- 60 yrs.
Use of proton pump inhibitors and the risk of coronary events in patients receiving low-dose acetylsalicylic acid in UK primary care

L.A. García Rodríguez1, L. Cea Soriano1, H. Bueno1, L. Frasquet1, J. S. Johansson1, A. Centreo Español de Investigación Farmacoepidemiológica (CEIFE), Madrid, Spain; 2Department of Cardiology, Hospital General Universitario ‘Gregorio Marañón’, Madrid, Spain; 3University Hospital ‘La Fe’, Zaragoza, Spain; 4Astellas. Spain

Purpose: To estimate the risk of coronary events associated with proton pump inhibitor (PPI) use in patients taking low-dose acetylsalicylic acid (ASA).

Methods: Two patient cohorts were identified aged 50–84 years with a first prescription for low-dose ASA (75–300 mg/day) between 2000 and 2007. The first included patients in The Health Improvement Network (THIN) primary care database prescribed low-dose ASA after an acute coronary event or coronary artery revascularization (acute coronary syndrome [ACS] cohort; N = 42 542). New cases of non-fatal myocardial infarction (MI)/coronary heart disease (CHD) event (event date for cases and random date for controls). Patients were considered continuous low-dose ASA users if they did not have a gap in treatment of more than 30 days. Logistic regression analyses were performed to estimate the risk of the non fatal MI/CHD death associated with current continuous use of both low-dose ASA and a PPI.

Results: Compared with non-use of ASA, there was a suggestion of a decreased risk of coronary events associated with continuous use of low-dose ASA monotherapy in both the CVD cohort (relative risk [RR]: 0.78; 95% confidence interval [CI]: 0.60–1.02) and the ACS cohort (0.84; 95% CI: 0.69–1.04). In current continuous users of low-dose ASA monotherapy, current continuous use of a PPI was not associated with a significant change in risk of coronary events compared with non-use of a PPI in either the CVD cohort (RR: 1.15; 95% CI: 0.83–1.56) and the ACS cohort (RR: 0.73; 95% CI: 0.43–1.23). No statistically significant changes in risk were seen regardless of whether PPI use was started at or before the time of MI/CHD event.

Conclusions: A PPI does not confer a significant clinical benefit to patients taking low-dose ASA. Further research is needed to explore the potential mechanisms underlying any observed associations.

Multiple thrombogenic and atherogenic markers were investigated in a rat arteriovenous shunt model. Bleeding times were measured in a rat tail transection model. TF-induced platelet aggregation; their combination increased the inhibition synergistically (H:W 33.1% vs T: 26.9%, p < NS). Pts prescribed at least one medication known to inhibit CYP2C9 activity sometime during the study were 30% of the total (181412). TTR for pts on W before study improved to 73.2% for W and 74.0% for T (p = 0.51). No significant difference in the outcome of the Cls was found (371, 53.2% vs 317, 49.2%; p = 0.14). The total number of dose adjustments was not significantly different between the Cls.

When INR values during an intercurrent medical event were excluded, the percent of TTR was significantly worse on W on T (66.4% vs 70.7%, p = 0.0099). Significant differences were seen using INR values with a lower percent of TTR on W vs T both for warfarin experienced switchers (64.2% vs 67.0%, p = 0.0022) and patients with the CYP2C9 wild type genotype (62.5% vs 66.1%, p = 0.0162). For CYP2C9 heterozygotes taking drugs that inhibit CYP2C9, the mean TTR for W was 66.9% vs 76.1% for T, p = 0.01; the difference in patients exhibiting good control was even more marked: W:64.3% vs T:89.5%, p<0.0001. The total number of dose adjustments was not significantly different between the Cls. Conclusions: A PPI does not confer a significant clinical benefit to patients taking low-dose ASA. Further research is needed to explore the potential mechanisms underlying any observed associations.
tibility to CAD. LTA mutant was risk marker for CAD only in male without the traditional risk factors.

Conclusions: Worse traditional risk factors profile and atherothrombogenic markers were associated with susceptibility to premature CAD. LTA mutant allele was independently associated with premature CAD in the absence of traditional risk factors. Premature CAD was associated with worse clinical and laboratory markers.

**P1838**

D-dimer, plasmin-antiplasmin complex and matrix metalloproteinase 2 as markers of cardiovascular events in patients with stable coronary disease

A. Komarova1, T. Ryuschenko1, A. Dobrovolsky1, E. Titaeva1, Shmatkova1, A. Deev1, E. Paranchenko1,1 Russian Research Center for Radiology of Cardiovascular System, Moscow, Russian Federation;2Institute of Preventive Medicine, Moscow, Russian Federation

Purpose: A series of biomarkers have been recently proposed as potential novel risk factors for the development of cardiovascular events (CVE). We examined markers of fibrinolytic function (D-dimer, plasminogen activator inhibitor (PAI-1) activity, tissue plasminogen activator (tPA)/PAI-1 complex, plasmin-antiplasmin (PAP) complex) and circulating matrix metalloproteinases (total MMP-9 and free MMP-2). Aim of the study was to determine their predictive ability in pts with stable coronary artery disease (CAD) after accounting for conventional risk factors.

Methods: 503 pts with stable CAD (male 77%, mean age 59 yrs) were included (n=300) and in some observational study at a mean follow-up of 5.4 yrs. The primary outcome was the occurrence of major CVE: death, acute coronary syndrome (ACS) or stroke/transient ischemic attack.

Results: The frequency of major CVE was 21.1% (3.9/100 patient years). Strong interrelationships between the variables were noted: e.g., D-dimer and PAI-1 complex (r=0.65), tPA/PAI-1 activity and PAP complex (r=-0.48), D-dimer and tPA/PAI-1 complex (r=-0.23), MMP-2 and PAP-1 activity (r=0.34), MMP-2 and PAI-1 complex (r=-0.38), MMP-2 and PAI-1 complex (r=0.24). On univariable analysis (age- and sex-adjusted), only D-dimer, PAP and MMP-2 were associated with risk of CVE. Their plasma levels were strongly associated with total load of conventional factors, which has prognostic impact in our study, i.e. severity of angina, history of ACS, three vessel disease and other comorbidity (cerebrovascular or peripheral disease, obesity, chronic kidney disease): F value for D-dimer = 4.2 (p for trend = 0.01); F value for PAP = 7.4 (p for trend = 0.001); F value for MMP-2 = 7.0 (p for trend = 0.001). The multivariable relative risks (RR) for the four higher vs lowest quintile were 2.1 (1.1-4.1) for MMP-2, 1.8 (1.3-2.5) for PAP and 3.1 (1.1-8.7) for D-dimer. The age- and clinical-adjusted risk of CVE significantly increased with simultaneous elevations of both MMP-2 and PAP: RR = 3.6 (1.1-11.5).

Conclusion: D-dimer, PAP and MMP-2 were identified as independent predictors of major CVE in patients with stable CAD.

**P1839**

Correlation of platelet reactivity and C-reactive protein levels to occurrence of peri-procedural myocardial infarction in patients undergoing Percutaneous Coronary Intervention


Background: The incremental predictive value of high inflammatory status and platelet reactivity in those with both CKD and elevated CRP is unknown.

Methods: Five-hundred consecutive patients treated with clopidogrel and undergoing PCI had pre-procedural measurement of C-reactive protein (CRP) levels and platelet reactivity by the point-of-care VerifyNow P2Y12 assay. Elevated inflammatory status was defined as CRP >3 mg/L and elevated CRP was defined as CRP >2 mg/dl. Patients were categorized by no CKD/no elevated CRP (n=142), coexistence of both CKD and elevated CRP (78%, Figure 1). The association between both CKD and elevated CRP with HRPR remained significant after multivariable adjustment (OR 3.4 [95% CI 1.5 – 7.3; p=0.002).

Results: While mean age and proton-pump inhibitor use increased across groups there were no significant differences in time from clopidogrel load to platelet testing. The frequency of HRPR increased across the highest frequency among those with both CKD and elevated CRP (78%, Figure 1). The association between both CKD and elevated CRP with HRPR remained significant after multivariable adjustment (OR 3.4 [95% CI 1.5 – 7.3; p=0.002).

Conclusions: CKD and elevated CRP exert a synergistic influence on platelet reactivity and may contribute to higher cardiac risk in patients with both abnormalities.

**P1840**

Combined and independent impact of chronic kidney disease and elevated C-reactive protein on residual platelet reactivity

U. Baber1, J. Bander1, R. Mehran2, B.A. Hadi1, R. Karajigak1, G.J. Vlachoiannis1, P. Muntner1, J. Badimon1, S.K. Sharma1, A.S. Kiri1,1 Mount Sinai School of Medicine, Department of Cardiology, New York, United States of America;2Mount Sinai Medical Center and the Cardiovascular Research Foundation, New York, United States of America;1University of Alabama at Birmingham, Alabama, United States of America

Background: Chronic kidney disease (CKD) is characterized by a pro-inflammatory phenotype. C-reactive protein (CRP), an inflammatory biomarker, augments cardiovascular risk in CKD. Whether or not this risk is due to changes in platelet reactivity in those with both CKD and elevated CRP is unknown.

Methods: We studied 401 clopidogrel-naive patients undergoing percutaneous coronary intervention (PCI) who underwent platelet function testing a minimum of 4 hours after a 600 mg clopidogrel load. High residual platelet reactivity (HRPR) was assessed using the VerifyNow P2Y12 Analyzer and defined as P2Y12 Reaction Units (PRU) values ≥ 235. CKD was defined as an estimated glomerular filtration rate (eGFR) < 60 ml/min/1.73m2 and elevated CRP was defined as CRP > 2 mg/dl. Patients were categorized by no CKD/no elevated CRP (n=142), elevated CRP alone (n=144), CKD alone (n=111) and both CKD and elevated CRP (n=64).

Results: While mean age and proton-pump inhibitor use increased across groups there were no significant differences in time from clopidogrel load to platelet testing. The frequency of HRPR increased across the highest frequency among those with both CKD and elevated CRP (78%, Figure 1). The association between both CKD and elevated CRP was highly significant after multivariable adjustment (OR 2.4, 95% CI 1.2-4.5; p=0.002).

Conclusions: CKD and elevated CRP exert a synergistic influence on platelet reactivity and may contribute to higher cardiac risk in patients with both abnormalities.

**P1841**

Magnetoliposomes for targeting activated platelets: development of a human compatible MRI contrast agent for detection of unstable atherosclerotic plaques

S. Meier1, G. Puetz2, U. Massing3, D. V Ellenfeld4, S. Barnert1, K. Peter5, R. Schuber9, C. Bode1, C. V. Muehlen1,1 Albert-Ludwig University of Freiburg, Department of Cardiology and Angiology, Freiburg, Germany;2 Albert-Ludwig University of Freiburg, Department of Clinical Research, Freiburg, Germany;3 Albert-Ludwig University of Freiburg, Department of Radiology/Medical Physics, Freiburg, Germany;4 Albert-Ludwig University of Freiburg, Department of Pharmaceutical Technology and Biopharmacy, Freiburg, Germany;5 Baker Heart Research Institute, Melbourne, Australia;6Baker Heart Research Institute, Melbourne, Australia

Background: Unstable atherosclerotic plaques may easily rupture, which attracts platelets. This can result in a rapid occlusive thrombosis with myocardial infarction or stroke. Early detection of unstable plaques by non-invasive techniques would therefore be helpful to identify patients at risk. We previously demonstrated that activated mouse platelets can be imaged by in vivo magnetic resonance imaging (MRI) using a platelet specific contrast agent. Those consisted of microparticles of iron oxide (MPIOs) bound to an antibody specifically targeting the activated GPIIb/IIIa receptor on platelets. Unfortunately, MPIOs are not suitable for human MRI applications, since they are potentially toxic. In order to develop a human compatible contrast agent, small supramagnetic iron oxide particles (SPIOs) with a median diameter of 10 nm were entrapped into liposomes (magnetoliposomes).

Methods & Results: Magnetoliposomes were prepared by rehydration of lipid films with negatively charged SPIOs in a dual asymmetric centrifuge (DAC). Non- liposomally associated SPIOs were removed by ion exchange chromatography (IEC). To calculate the liposomally associated iron, the iron and phosphatidylcholine amount was analysed before and after IEC. The quality of the magnetoliposome...
Hypertriglyceridemia - a predictor of platelet resistance to acetylsalicylic acid in patients with stable coronary artery disease

T. Wolsko, M. Dominik, J.D. Kasprazk, Medical University of Lodz, Department of Cardiology, Lodz, Poland

Background and purpose: Acetylsalicylic acid (ASA) is commonly used in a daily dose of 75 mg in the population of patients with coronary artery disease (CAD). However, resistance to ASA is reported to occur with a rate of 5-42%. We aimed to determine clinical and biochemical predictors of insufficient response to ASA.

Methods: 360 consecutive caucasian pts with stable coronary artery disease undergoing elective coronary angiography were included in the study (109 women, 251 men; age 62±11.2 years, mean body weight 79.2±7.9 kg, mean BMI 28.0±3.9 kg/m²). All patients have been receiving daily dose of 75 mg ASA for at least 7 days before admission. The study group was divided into two groups: I-resistance group (n=77), II-respondent group (n=289) to the treatment. Resistance to ASA was defined as ARU value ≥550 (aspirin reaction unit) obtained with point-of-care test Rapid Platelet-Function Assay (RPFA).

Results: In the population treated with a daily dose of 75 mg of ASA, 71 patients (19.7%) were resistant (mean age 58.4±9.8 years, ARU=612±34.4), and 289 patients (81.3%) were responsive (mean age 61.4±10.7 years, ARU=449±47). No significant differences were detected in the panel of clinical risk factors for CAD between resistant and responsive groups including: diabetes (28.4% of non-responders vs. 26.3% of responders; p=0.55), hypertension (62% vs. 59.5%; p=0.88), and smoking (56% vs. 22.6%; p=0.74). In logistic regression analysis including laboratory tests, a statistically significant difference between both groups, was found regarding serum triglycerides concentration (TG): 165±91 vs. 129±65 mg/dl, p=0.0035, but not for other lipid or inflammatory parameters. Cutoff value of serum triglycerides>125mg/dl had 66.3% positive and 52.4% negative predictive value of ASA resistance. In patients with the value of TG≥125mg/dl the risk of ASA resistance increased 2.7-fold (95% CI: 1.3;0.4;35; p=0.004).

Conclusion: The prevalence of ASA resistance in the population of patients with stable coronary artery disease treated with a daily dose of 75mg of ASA is 19.7%, and cannot be predicted by medical history or clinical/demographic variables. The only independent factor prognostic to ASA resistance in patients with stable coronary disease is serum triglyceride concentration. This novel finding requires validation in larger scale studies.

Blockade of platelet alpha2B-adrenergic receptors: a novel antiaggregant mechanism

M.E. Marketou1, E. Kintsurashvili2, N.E. Androulakis1, J. Kontarakis1, M.G. Alexandrakis1, L. Gavros3, P.E. Vardas1, H. Gavros1
1Heraklion University Hospital, Heraklion, Greece, 2Boston University School of Medicine, Boston, United States of America

Purpose: Platelets play a vital role in hemostasis and thrombosis. Catecholamines have a profound effect on platelet aggregation and atherothrombosis prevention of atherothrombotic events. ARs show a substantial inhibition in platelet aggregation that had been induced by adenosine diphosphate (ADP), by epinephrine and by arachidonic acid. The presence of alpha2B-ARs in platelets may offer a future therapeutic opportunity in the prevention of atherothrombotic events.

Methods: Pretreatment of human platelets with agents that selectively block alpha2-ARs showed a substantial inhibition in platelet aggregation that had been induced by adenosine diphosphate (ADP), by epinephrine and by arachidonic acid. The percent aggregation decreased from 81.5±1.7% to 35.8±5.5% and to 24±4.6% for ADP with alpha2B-ARs and AR-239 respectively, from 72±2.1% to 29.5±4.3% and to 8.8±1.7% for epinephrine with alpha2B-ARs and AR-239 respectively, and from 87±2.1% to 47.9±6.2% and to 61±2.5±% for arachidonic acid with alpha2B-ARs and AR-239 respectively, p<0.05. Furthermore, collagen/epinephrine closure time increased from 120.8±6.1 sec to 189.5±39.5 sec (p<0.001).

Results: Our results reveal that contrary to previous knowledge, the u2-AR subtype does exist in platelets and is an important regulator of aggregation.

Inhibition of u2-ARs in platelets may offer a future therapeutic opportunity in the prevention of atherothrombotic events.

Markers of endothelial and platelet activation are associated with high on-aspirin residual platelet reactivity

A.A. Pettersen, H. Arnesen, T.B. Opstad, V. Bratseth, I. Seljeflot on behalf of Center for Clinical Heart Research, Oslo University Hospital, Ullevaal. Center for Clinical Heart Research, Department of Cardiology, Oslo University Hospital, Ullevaal, Oslo, Norway

Purpose: Despite COX-1 inhibition by aspirin, platelets in patients with coronary artery disease (CAD) can be activated through other mechanisms. Methods: 1001 stable CAD patients, all on single aspirin treatment, were classified by the PFA100 method as having high on-aspirin residual platelet reactivity (RPR) or not. Markers of hypercoagulability, endothelial and platelet activation as related to RPR, were evaluated to explore the potential mechanisms behind high on-aspirin RPR.

Results: 25.9% (n=259) of the patients had high on-aspirin RPR. S-thromboxane B2 levels were very low in both groups. Patients with high on-aspirin RPR had significantly higher levels of von Willebrand Factor (vWF) (p<0.001), platelet-derived microparticles (p=0.006), total tissue factor pathway inhibitor (TFPI) (p=0.005) and thromboglobulin (p<0.001) compared to patients with low on-aspirin RPR. No significant differences between the groups were observed in levels of endoge-
Paraoxonase-1 (PON1) activity is associated with clopidogrel response and intra-stent thrombus after drug-eluting stent implantation in the CYP2C19 loss-of-function polymorphism carriers

Kobe University Graduate School of Medicine, Department of Cardiology, Kobe, Japan

Background: The impact of paraoxonase-1 (PON1) activity on the efficacy of clopidogrel has not been clarified. The aim of this study was to assess the association of PON1 activity and clopidogrel response in the CYP2C19 loss-of-function polymorphisms carriers (LOF carriers) and non-carriers receiving drug-eluting stent (DES) implantation.

Method: This study included 112 Japanese patients receiving clopidogrel (75mg/day) and aspirin (100mg/day) who underwent optical coherence tomography (OCT) examination for the evaluation of intra-stent thrombus 9 months after DES implantation. The CYP2C19 genotype was analyzed and LOF carriers (*1/*2, *1/*3, *2/*2, *3/*3, *2/*3) were identified. Platelet reactivity was determined by measuring P2Y12 reactivity unit (PRU) with VerifyNow P2Y12 assay and the PON1 activity was evaluated by spectrophotometric assay.

Result: In 112 Japanese patients, 75 patients were LOF carriers (67.9%). The median PON1 activity was 245 U/L. In both LOF carriers and non-carriers, the patients were divided into High PON1 (PON1 activity was equal or above 245 U/L) and Low PON1 (below 245 U/L) groups. PRU was higher in LOF carriers than non-carriers (285.3±39.6 vs. 198.8±25.8, P=0.002) and intra-stent thrombus was observed more frequently in LOF carriers than non-carriers (37.3% vs. 16.2%, P=0.003). Among LOF carriers, PRU was higher in High PON1 group than Non-carriers (245.3±38.2 vs. 227.0±29.3, P<0.001) and intra-stent thrombus was observed more frequently in LOF carrier than Non-carrier group (54.8% vs. 25.0%, P=0.01). Among non-carriers, PRU and incidence of intra-stent thrombus were not different between High and Low PON1 groups.

Conclusion: The PON1 activity might ameliorate responsiveness to clopidogrel only in LOF carriers, but did not influence that in non-carriers.

Optimal thresholds for on-treatment platelet reactivity to predict clinical events after percutaneous coronary intervention are different in patients with and without diabetes mellitus

F. Manjaciaparca1, A.J. Peace1, E. Barbato2, G. Patti1, L. Gatto2, B. De Bruyne3, G. Di Sciascio1, W. Wijns2. 1University Campus Bio-Medico of Rome, Department of Cardiovascular Sciences, Rome, Italy; 2OLV Hospital Aalst, Cardiovascular Center, Aalst, Belgium

Aims: Patients with diabetes mellitus (DM) have increased baseline platelet reactivity (HPR) that predict clinical outcomes after percutaneous coronary intervention (PCI) similar in diabetic compared to non-diabetic patients. Aim of the present study was to investigate whether thresholds for high platelet reactivity (HPR) that predict clinical outcomes after percutaneous coronary intervention (PCI) are similar in diabetic compared to non-diabetic patients.

Methods and results: A total of 640 (32.6% with DM) consecutive patients taking aspirin and clopidogrel undergoing elective PCI were recruited. Platelet reactivity was measured immediately before the procedure with the VerifyNow P2Y12 assay. Primary end points was the 30-day incidence of major adverse cardiac events (MACE) in relation to the presence of DM and to P2Y12 reaction units (PRU) distribution. The optimal cut off to predict 30-day MACE was a PRU value of >256 in diabetics, and a PRU value of >229 in non-diabetics. Accordingly, were defined HPR on the basis of these two specific thresholds (HPR-ST), now including 60/209 (29%) diabetic patients with PRU >256, and 130/431 (30%) non-diabetic patients. HPR-ST was higher in diabetic patients with and without diabetes, with a diagnostic accuracy of 73% (McNemar’s chi-square=5.23, p=0.022 vs. diagnostic accuracy of PRU values >240 [70%]). Patients with HPR-ST had a higher occurrence of MACE compared to those with out HPR-ST both among diabetics (23.3% vs. 5.4%, p<0.001) and non-diabetics (13.9% vs. 3.3%, p<0.001). Moreover, the occurrence of MACE was highest in patients with both DM and HPR-ST and lowest in patients without DM or HPR-ST (p for trend <0.0001).

Conclusion: Redefining HPR based on specific thresholds for patients with and without DM significantly improves prediction of MACE post-PCI. Patients with HPR-ST, especially in the presence of DM, are at increased risk for ischemic events and may benefit from more aggressive antiplatelet strategies.

Acute exposure to diesel exhausts induces immediate platelet activation

A. Wauters1, C. Dreyfuss1, P. Hendrick2, W. Wijns1, O. Pradier3, G. Berkenboom1, P. Van De Borne1, J-F. Argach1. 1ULB Erasme University Hospital, Department of Cardiology, Brussels, Belgium; 2ULB Aero-thermo-mechanic, Brussels, Belgium; 3ULB Erasme University Hospital, Laboratory of Hematology, Brussels, Belgium

Background: Exposure to diesel exhausts was recently identified as an important cardiovascular risk factor by increasing the incidence of thrombo-embolic events. The biological mechanisms underlying this pro-thrombotic effect are unclear. We thought that acute platelet activation could play a role in these observations.

Methods: We tested this hypothesis in a randomized, crossover study in 11 healthy male. Each subject was exposed to ambient and polluted air during 2 hours at rest and 1 hour of moderate exercise (4 different sessions). Blood samples were collected before and immediately after the exposures. The effects of
dielectric exhausts on platelet function were measured by the platelet function analyzer PFA-100 and by whole blood aggregometry (Multiplate). Platelet activation was evaluated by surface expression of CD62P (P-selectin) and CD63, using flowcytometry of labeled platelets and was expressed in Median Fluorescence Intensities (MFI). Diesel exhausts exposure was performed in a computer-assisted inhalation room, where the pollutants produced by the motor engine were under standard conditions.

Results: The diesel particulate matter -2.5 μm (PM2.5) mean concentration was 12.9±0.1 μg/m³ in ambient air and 309.4±1.6 μg/m³ on polluted air. Exercise increased adrenergic ventilation from 7.95±0.10/min to 32.1±1.01/min. Platelet function assessed by PFA-100 and Multiplate was not impaired after polluted air exposure, neither at rest nor at exercise. Acute diesel exhausts exposure had no effect on platelet activation at rest, while exercise in polluted air increased the expression of CD62P from -0.45±0.18MFI to 0.22±0.18MFI and CD63 from -0.09±0.3MFI to 0.06±0.4MFI (all p<0.05). The rise in the expression of CD62P and CD63 was related to the concentration of PM2.5 achieved during exercise (correlation coefficients: 0.51 and 0.52, respectively, both p<0.05).

Conclusion: In healthy subjects, acute experimental diesel exhausts exposure induces a immediate CD62P and CD63 over-expression in platelet, which turn, could set off acute coronary syndromes in patients at risk.

P1850 Fibrinogen alpha chain gene variability alters the prothrombotic state independently of risk factors for coronary artery disease

D. Tousoulis1, N. Papageorgiou1, A. Milios1, M. Kozaritiou1, E. Androulakis1, G. Hatzis1, G. Latsios1, C. Antoniadis1, Z. Pallantza1, C. Stefanadis1. 11st Cardiology Unit Hippokration Hospital Athens, Athens, Greece. 2Hippokratis Hospital, University of Athens, 1st Department of Cardiology, Athens, Greece

Purpose: The G58A polymorphism on fibrinogen alpha (a)-chain gene has been associated with increased fibrinogen levels in healthy individuals, but its effect on thrombosis in patients with coronary artery disease (CAD) remains unknown. In the present study we examined the impact of this polymorphism on fibrinogen and D-dimers levels as well as its interaction with established risk factors in the development of CAD.

Methods: The study population consisted of 339 patients with CAD and 260 healthy controls. The G58A polymorphism was determined according to the biochemical measurements (routinely performed), clinical examination and medical history.

Results: In patients with CAD fibrinogen levels (mg/dl) were not significant higher compared to healthy controls (p=NS). Similarly, in CAD patients smoking as well as gender (p=NS) did not significantly affect platelet aggregation. Although, 58AA homozygotes developed CAD earlier (years) than 58G carriers, this difference was not significant (p=NS). In addition, the expression of CD62p from -0.45±0.18MFI and CD63 from -0.09±0.3MFI to 0.06±0.4MFI (all p<0.05). The rise in the expression of CD62P and CD63 was related to the concentration of PM2.5 achieved during exercise (correlation coefficients: 0.51 and 0.52, respectively, both p<0.05).

Conclusion: In healthy subjects, acute experimental diesel exhausts exposure induces a immediate CD62P and CD63 over-expression in platelet, which turn, could set off acute coronary syndromes in patients at risk.

P1851 Collagen-induced platelet aggregation is specifically suppressed, but coagulation and bleeding time are not altered up to 3 weeks after a single bolus of revecapect (dimeric GPVI-Fc; phase I trial)

G. Muench1, A. Buettmann1, K. Rosport2, K. Uhland2, M. Gawaz2, G. Lang2. 1Department of Cardiology and Cardiovascular Medicine, University Hospital Tuebingen, Tuebingen, Germany; 2Physiology and Regenerative Medicine, University of Tuebingen, Tuebingen, Germany

Background: Blocking of vascular collagen sites promises to become an attractive target for a platelet activation-specific treatment of acute atherothrombotic diseases, such as myocardial infarction or stroke. Preclinical studies showed that the soluble dimeric GPVI-Fc fusion protein (PR-15, Revacept) strongly reduced glycoprotein VI (GPVI)- and von Willebrand factor (VWF)-dependent platelet activation by vascular collagen sites, and that the drug should be critical for thrombosis.

Methods and Results: In a first in man study (Eudra CT 2005-04566-12, NCT 01042964), 30 healthy subjects received a single IV administration of either 10 mg, 30 mg, 40 mg, 80 mg, or 160 mg Revacept. Collagen-induced platelet aggregation was dose dependently inhibited up to 10 days and 3 weeks after higher dose levels. In contrast, ADP- or thrombin (TRAP)-dependent platelet aggregation remained unaltered, and platelet counts did not change significantly. These findings are in clear contrast to prior studies using anti-GPVI or anti-GPIIb-IIIa antibodies. Bleeding times were measured by ear lobe incision (Duke), and did not vary significantly between the groups. Coagulation was determined by assessing PT and INR values, and showed no differences. There were no relevant changes of other laboratory parameters (biochemistry and haematology), nor changes of blood pressures, pulse rates, or 24h ECG monitoring. No anti-Revacept antibodies occurred.

Conclusion: Revacept is a well tolerated new compound which specifically suppresses collagen-induced platelet aggregation without impacting on platelet counts, bleeding time or other coagulation parameters.

P1852 Percutaneous coronary intervention causes increased platelet - derived microvesicle release

K. Vargova1, Z.S. Horner1, E. Faller1, S. Lee1, A. Kovacs1, E. Tothzsmolki1, A. Falus1, I. Preda1, R.G. Kiss1. 1Military Hospital, Department of Cardiology, Budapest, Hungary; 2Semmelweis University, Department of Genetics, Cell- and Immunobiology, Budapest, Hungary

Purpose: Microvesicles (MVs) are membrane-derived micro-particles originating mostly from platelets (platelet-derived microvesicles, PMV). The role of MVs in cardiovascular disease (CVD) or the effect of percutaneous coronary intervention (PCI) on MV release was not elucidated. Accordingly, we aimed to determine the early and long-term MV and PMV release after PCI performed in stable angina (SA) and to assess the effect of combined antiplatelet therapy (clopidogrel, aspirin) on MV and PMV absolute count.

Methods: We recruited 102 patients with SA undergoing elective coronary angiography. The direct and long – term effect of PCI was determined in forty - one stable angiina patients (PC group). Individuals were negative coronary angiography (NC, n= 27) or those with positive coronary angiography, but without PCI (NC, n= 34) served as controls. The total microvesicle count (MV), platelet derived CD41+PMV (CD62P-CD41+ PMV), P-selectin negative PMV (CD62P-CD62P-CD41+ PMV) and P-selectin positive PMV (CD62P+CD41+ PMV) absolute count was determined by flow-cytometry. Blood samples were taken on admission, 24 hours, and 1, 3, 6, 12 months thereafter. In each time point, platelet aggregation was assessed by Born-aggregometry (in-ductors: 6 micromol ADP, 10 micromol ADP, 1 microg/ml collagen, 2 microg/ml collagen, 0.5 microg/ml ascorbic acid, and 10 microg/ml epinephrine), as well.

Results: No significant difference in baseline absolute count of MV, PMV, CD62P-CD41+ PMV and CD62P-CD41+ PMV was detected by p-value between the study groups. After 24 hours the PCI the MV (p<0.05), PMV (p<0.01) and P62+41+ PMV (p<0.05) absolute count showed significant increase compared to baseline levels. Diagnostic coronaryography itself (PC, NC group) had no significant effect on the above parameters assessed at 24 hours. When analyzing patients according to the implanted stent type, the PMV (p<0.01), the P62+41+ PMV (p<0.01) and the P62+41+ PMV (p<0.05) absolute count was significantly higher in the drug - eluting stent (DES) group compared to the bare metal stent (BMS) group. No significant correlation (Spearman correlation analysis) was found between the PV parameters, platelet aggregation values and the antiplatelet therapy.

Conclusion: Percutaneous coronary intervention evokes total microvesicle absolute count and - predominantly - P-selectin negative PMV absolute count elevation. This early systemic and platelet response is independent from platelet aggregagation and is not influenced by combined antiplatelet therapy. At six months after the PCI the PMV was higher in case of DES implantation.

P1853 Serum- and glucocorticoid-inducible kinase 1 (SGK1) regulates platelet granule biogenesis and secretion

O. Bors1, P. Muerroz2, E.M. Schmidt2, E. Schmid2, T. Schoenenberger2, C. Lebrock2, M. Schaller2, D. Kuhl2, M. Gawaz2, F. Lang2. 1Department of Cardiology and Cardiovascular Medicine, University Hospital Tuebingen, Tuebingen, Germany; 2Department of Physiology, University of Tuebingen, Tuebingen, Germany.

Background: Platelet secretion is critical to the development of acute thrombotic occlusion. Platelet dense granules contain a variety of important hemostatically active substances. Nevertheless, the biogenesis of granules in the platelet precursors, the megakaryocytes, is poorly understood. Platelet activation is regulated by phosphoinositide-3-kinase (PI3K) dependent signaling. PI3K-dependent AGC kinases include the serum- and glucocorticoid-inducible kinase 1 (SGK1). SGK1 has been shown to be highly expressed in platelets and megakaryocytes, but its role in the regulation of platelet granule biogenesis and its impact on thrombosis has not been investigated so far.

Methods and Results: To study the functional role of SGK1, platelets were isolated from mice lacking SGK1 (sgk1-/-) and respective wildtype littermates (sgk1+/+). Electron microscopy analysis of platelet ultrastructure revealed a significant reduction in number and packing of dense granules in sgk1-/- platelets. It has not been investigated so far.

Conclusion: Platelet secretion is critical to the development of acute thrombotic occlusion. Platelet dense granules contain a variety of important hemostatically active substances. Nevertheless, the biogenesis of granules in the platelet precursors, the megakaryocytes, is poorly understood. Platelet activation is regulated by phosphoinositide-3-kinase (PI3K) dependent signaling. PI3K-dependent AGC kinases include the serum- and glucocorticoid-inducible kinase 1 (SGK1). SGK1 has been shown to be highly expressed in platelets and megakaryocytes, but its role in the regulation of platelet granule biogenesis and its impact on thrombosis has not been investigated so far.

Methods and Results: To study the functional role of SGK1, platelets were isolated from mice lacking SGK1 (sgk1-) and respective wildtype littermates (sgk1+/+). Electron microscopy analysis of platelet ultrastructure revealed a significant reduction in number and packing of dense granules in sgk1-/- platelets. It has not been investigated so far.
High platelet reactivity by arachidonic acid and increased platelet aggregation and serum risk of cardiac death at a 5-year follow-up.

Results: Patients with previous MI had 65% higher platelet aggregation levels compared with CAD patients without previous MI when evaluated by Multiplate/arachidonic acid (p < 0.0001). In a multiple linear regression analysis, the importance of previous MI remained significant after adjustment for age, smoking, and diabetes (p = 0.0001). Further, MI patients had increased serum thromboxane B2 levels compared with CAD patients (p = 0.01). Multiplate/collagen platelet aggregation levels were 11% higher in MI patients than in CAD patients (unadjusted p = 0.20, adjusted p = 0.11). These findings were not in agreement with the VerifyNow test showing a 3% higher aggregation level in CAD patients compared with MI patients (adjusted p = 0.005). Patients treated with aspirin prior to MI had significantly higher aggregation levels compared with non prior users when evaluated by Multiplate/collagen (p = 0.02) and VerifyNow (p < 0.0001).

Conclusion: Patients with previous MI had a reduced antiplatelet effect of aspirin shown by higher Multiplate aggregation levels and serum thromboxane B2 compared with CAD patients. Prior aspirin users had higher platelet aggregation levels compared with non prior users. Our findings suggest that patients with previous MI may have reduced cardiovascular protection from low-dose aspirin.

P1854

High platelet reactivity by arachidonic acid and elevated c-reactive protein levels identify STEMI patients at risk for 5-year follow-up cardiac death

R. Marcucio1, S. Valente2, A.M. Goransson2, M. Chiotiri2, R. Panici2, C. Lazzere3, B. Giusti2, C. Giglioli2, R. Abbate2, G.F. Gensini2, 3Careggi University Hospital, Florence, Italy; 2Department of heart and vessel, Florence, Italy

Objectives: This study sought to investigate clinical utility of platelet reactivity by arachidonic acid (AA) and C-reactive protein (CRP) in the prognostic stratification of STEMI patients undergoing percutaneous coronary intervention (PCI).

Background: Data on long-term prognostic value of high-on-treatment platelet reactivity by AA or CRP after PCI are limited. On the other hand, it is well known that elevated CRP levels are associated with a worse prognosis in high risk vascular patients.

Methods: We evaluated 436 STEMI patients undergoing PCI. On a blood sample obtained within 24 hrs from PCI, platelet function was assessed using LTA by 1 mM AA and CRP levels by high-sensitivity method. The primary endpoint was cardiac death at 5 year follow-up.

Results: At 5 year follow-up 52 cardiac deaths were registered (11.9%). By receiver operating characteristic curve (ROC) analysis, the optimal cutoff value in predicting cardiac death was 1 mm AA LTA≤18% (HPR) (AUC:0.59 (95%CI 0.52-0.67,p<0.001) and CRP: <12 mg/L (H-CRP) (AUC:0.69 (95%CI 0.62-0.77,p<0.0001). Cardiac death occurred in 7 (13.5%) patients without HPR and H-CRP; in 8 (11.5%) patients with HPR and without H-CRP; in 18 (34.6%) patients without HPR and with H-CRP and in 21 (40.4%) patients with HPR and H-CRP. The Cox regression analysis adjusted for age, diabetes, renal function and LVEF, patients with HPR and H-CRP were at significantly higher risk of cardiac death (HR:4.4 (95%CI 1.8-10.9,p<0.001) with respect to patients with out HPR and H-CRP. On the other hand, in patients with HPR and without H-CRP we did not find a significant increased risk of cardiac death (HR:1.5 (95%CI 0.5-4.5), p=0.48) and in patients without HPR and with H-CRP we did observe a slight association with cardiac death (HR:2.4 (95%CI 0.9-5.9), p=0.05).

Conclusions: These data show that in STEMI patients the addition of platelet reactivity by AA to CRP measurement allows us to identify a subset of patients at risk of cardiac death at a 5 year follow-up.

P1855

Increased platelet aggregation and serum thromboxane levels in aspirin-treated patients with previous myocardial infarction

S. Larsen1, S.B. Neergaard-Petersen1, E.L. Grove1, S.D. Kristensen1, A.M. Hvaal2, 1Aarhus University Hospital, Skejby, Department of Cardiology, Aarhus, Denmark; 2Aarhus University Hospital, Skejby, Department of Clinical Biochemistry, Aarhus, Denmark

Background: Aspirin reduces the risk of cardiovascular events in patients with coronary artery disease (CAD). However, the antiplatelet effect of aspirin displays considerable variability between patients.

Objectives: We investigated the antiplatelet effect of aspirin in stable CAD patients on aspirin mono-therapy with or without previous myocardial infarction (MI). Further, we investigated whether the effect of aspirin differed between patients treated with aspirin before having a MI compared with patients not treated with aspirin before MI.

Materials and Methods: We performed a study on 231 CAD patients, including 171 with previous MI. Among patients with only previous MI (116 patients) 3% were on aspirin treatment at the time of acute MI. All patients were treated with 75 mg non-enteric coated aspirin as single antiplatelet therapy. Platelet aggregation was assessed by multiple electrode aggregometry (Multiplate) using arachidonic acid (1.0 mmol/L) and collagen (1.0 μg/ml) as agonists and the VerifyNow Aspirin Assay. Standardised blood sampling was performed one hour after ingestion of aspirin. Compliance was optimized by face-to-face interviews and pill-counting, and cyclooxygenase-1 inhibition was evaluated by measurement of serum thromboxane B2.

Results: Patients with previous MI had 65% higher platelet aggregation levels compared with CAD patients without previous MI when evaluated by Multiplate/arachidonic acid (p < 0.0001). In a multiple linear regression analysis, the importance of previous MI remained significant after adjustment for age, smoking, and diabetes (p = 0.0001). Further, MI patients had increased serum thromboxane B2 levels compared with CAD patients (p = 0.01). Multiplate/collagen platelet aggregation levels were 11% higher in MI patients than in CAD patients (unadjusted p = 0.20, adjusted p = 0.11). These findings were not in agreement with the VerifyNow test showing a 3% higher aggregation level in CAD patients compared with MI patients (adjusted p = 0.005). Patients treated with aspirin prior to MI had significantly higher aggregation levels compared with non prior users when evaluated by Multiplate/collagen (p = 0.02) and VerifyNow (p < 0.0001).

Conclusion: Patients with previous MI had a reduced antiplatelet effect of aspirin shown by higher Multiplate aggregation levels and serum thromboxane B2 compared with CAD patients. Prior aspirin users had higher platelet aggregation levels compared with non prior users. Our findings suggest that patients with previous MI may have reduced cardiovascular protection from low-dose aspirin.

P1856

Higher thrombus, altered clot kinetics and fibrin architecture in patients with type 2 diabetes mellitus after non ST elevation acute coronary syndrome

G.N. Viseanu1, R. Balasubramaniam2, A.G. Harper3, B. Babawale4, S.M. Marshall2, J.J. Badimon2, A.G. Zaman4, 1Institute of cellular medicine, Newcastle University, Newcastle upon Tyne, United Kingdom; 2Newcastle University, Newcastle upon Tyne, United Kingdom; 3Mount Sinai Medical Center and the Cardiovascular Research Foundation, New York, United States of America; 4Newcastle upon Tyne Hospitals NHS foundation trust, Newcastle upon Tyne, United Kingdom

Thrombotic events following non-ST elevation acute coronary syndrome (NSTE-ACS) are higher in patients with type 2 diabetes mellitus (T2DM) despite optimal medical therapy.

Methods: We prospectively studied 28 patients (14 T2DM and 14 non diabetics), 7 days after troponin positive NSTE-ACS. All patients were treated according to current AHA/ESC guidelines including 75mg of both aspirin and clopidogrel. We assessed thrombus formation using the ex-vivo Badimon chamber, platelet reactivity, thrombus ultrastructure using scanning electron microscopy and thrombus kinetics using thromboelastography.

Results: Baseline characteristics (age, gender, BMI and lipid profile) were similar in both the groups. T2DM patients had increased thrombus (thrombus area, sq.microns/mm: median (IQR), 146 (98) vs 89 (68) to 119 (62), p=0.04), lower visco-elastic tensile strength [clot index: median (IQR), -0.2 (1.7 to 0.7) vs 1.0 (-9.3 to 3.3), p=0.04] and impaired autolysis [rate of thrombus retraction mm/min: median (IQR), 27.8 (11.7 to 70.7) vs 70.8 (68.5 to 109.6) p<0.01]. There was moderate correlation between autolysis and thrombus quantiry (rho 0.450, p=0.02). Platelet reactivity indices, P selectin and CD40 ligand levels were similar. Ultrastructure of the diabetic thrombus showed loosely arranged individual fibrils but with more interlinked fibrin strands compared to twisted and densely packed fibrils with less interlinking in non diabetics.

Conclusion: T2DM patients after NSTE-ACS had more thrombus, altered tensile strength, reduced thrombus retraction and loosely arranged but interlinked fibrin fibres despite optimal medical therapy and treatment, but they lack an effective antidote in the case of urgent medical intervention or bleeding. We have reported the ability of PRT064445 (PRT), a recombinant factor Xa inhibitor antidote, to reverse anticoagulation and prevent blood loss in patients with acute coronary syndrome.
Unlike heparin, newer oral anticoagulants do not interact with HIT antibodies and may be useful in the long term anticoagulant management of heparin compromised patients.

**Materials:** Rivaroxaban was obtained in powdered form from Bayer Healthcare (Wuppertal, Germany). Apixaban and Dabigatran were synthesized. Enoxaparin was obtained from Sanofi-Aventis (Paris, France). All drugs were dissolved in buffered saline at a concentration of 100 μg/ml. Whole blood samples drawn from normal healthy volunteers were incubated with each of these agents at concentrations of 0–100 μg/ml for 60 minutes to determine the release of platelet factor 4 (PF4). To test the interaction of HIT antibody with each of these agents PRP was mixed with HIT positive sera collected from symptomatic HIT patients. Graded concentrations of EV-077 (vehicle, 10, 30, 100, and 300 nM) were added to test the effect of EV-077 on platelet aggregation.

**Results:** In contrast to enoxaparin which produced an increase in the PF4 release upon 60 minute incubation (25.6±3.1 ng/ml), none of the new oral anticoagulants produced an increase in the PF4 (≤15.0 ng/ml). Enoxaparin also produced a strong HIT antibody mediated response, whereas none of the oral agents produced any aggregation responses.

**Conclusions:** These studies demonstrate that unlike enoxaparin, the newer oral anticoagulant drugs do not interact with HIT antibody to mediate platelet aggregation. Moreover, these newer agents do not promote PF4 release. Thus, these agents should be used in the long term anticoagulant management of heparin compromised patients.

**References:**

1. University of Florida College of Medicine, Jacksonville, United States of America
2. Evola SA, Reinsch, Switzerland
3. KeilSa s.a.s, Biella, Italy

**Purpose:** Low dose aspirin inhibits cyclooxygenase-1 and thus prostanooid production. However, some patients may have inadequate aspirin effects leading to persistent prostanooid and isoprostane production increasing atherothrombotic risk, vascular inflammation and oxidative stress. Thromboxane A2 (TXA2) and Thromboxane A2 receptor (TP receptor) antagonists have been developed as a potential treatment of these vascular conditions. The aim of the present study was to describe the intravascular pharmacodynamic effects of escalating concentrations of EV-077, a novel dual TP/TP inhibitor, on human blood.

**Methods:** Blood samples were collected from 10 healthy volunteers aged 35 ± 3.6 years old. Whole-blood heparinized tubes were incubated with escalating concentrations of EV-077 (vehicle, 10, 30, 100, and 300 nM). Citrated platelet-rich plasma (PPP) was incubated with vehicle or 100 μM of EV-077. Platelet aggregation was measured using the Multiplate Analyzer (MEA) on whole-blood and light-transmission aggregometry (LTA) on PRP. Platelet agonists included 1 μM arachidonic acid (AA), 7 μM U46619 (TXA2 analog), and 3 μM collagen for both assays.

**Results:** A dose dependent reduction in platelet aggregation was observed with escalating concentrations of EV-077 with all agonists as measured by MEA (Figure A). Using LTA, in vitro addition of 100 nM EV-077 to PRP led to near complete blockade of platelet aggregation induced by AA and U46619, and showed marked inhibition of collagen-induced platelet aggregation (Figure B).

**Conclusions:** In vitro incubation with escalating concentrations of EV-077 achieves a dose-dependent reduction of platelet aggregation in healthy volunteers. Ongoing in vivo and in vitro studies will provide more insights on the pharmacodynamic effects and safety of EV-077.

**References:**

1. Y. Naruse, N. Satō, N. Takeyasu, T. Hoshii, M. Hayashi, M. Misaki, D. Abe, T. Enomoto, K. Aonuma on behalf of Ibaraki Coronary Artery Disease Study (ICAS) registry. 2. University of Tsukuba, Graduate School of Comprehensive Human Sciences, Division of Cardiovascular, Tsukuba, Japan; 3. Ibaraki Prefectural Central Hospital, Department of Cardiology, Kasama, Japan; 4. Tsukuba Memorial Hospital, Tsukuba, Japan

**Purpose:** An increasing number of patients requiring long-term oral anticoagulation with warfarin have undergone percutaneous coronary intervention (PCI) with drug-eluting stent implantation (DES). However, the benefits and risks of triple antithrombotic therapy (combination of aspirin, clopidogrel, and warfarin) are still unclear.

**Methods:** This study included 1626 patients (69±10 years; 244 male; 382 female) who underwent PCI with DES in the Ibaraki Cardiac Assessment Study (ICAS) registry and received dual antiplatelet therapy with or without warfarin. Clinical primary endpoints were defined as the occurrence of major bleeding complications and major adverse cardiovascular events (MACE) including cardiac death, myocardial infarction, and target vessel revascularization. The major bleeding complications were defined as a cerebral hemorrhage or a gastrointestinal bleeding.

**Results:** Among 1626 patients, 115 (7.1%) patients received warfarin. After a mean follow-up of 16.9±0.7 years, 24 (1.5%) and 232 (14.3%) patients had experienced the episode of major bleeding complications and MACE, respectively. There were no significant differences in age, gender, body mass index, a history of prior PCI, smoking, left ventricular ejection fraction between the patient with and without major bleeding complications. However, a prevalence of hyperlipidemia was lower (38% vs. 59%; p<0.05) and a prevalence of warfarin usage was greater (33% vs. 7%; p<0.001) in the patients with major bleeding complications than in those without. A multivariate Cox regression analysis revealed that triple antithrombotic therapy was the independent predictors for the occurrence of major bleeding complications (hazard ratio (HR) 7.25; 95% confidence interval (CI) 3.05–17.21; p<0.001). The patients with MACE had a greater prevalence of prior PCI (26% vs. 20%; p<0.05), cerebrovascular disease (14% vs. 8%; p<0.01), diabetes mellitus (52% vs. 43%; p<0.01) than those without. The prevalence of MACE was significantly lower in the patients received dual antiplatelet therapy with warfarin than in those without (8% vs. 15%; p<0.05), however, a multivariate cox regression analysis revealed that the prevalence of MACE did not differ between the patient received dual antiplatelet therapy with and without warfarin (HR 0.81; 95% CI 0.46–1.41; p=0.45).

**Conclusions:** Triple antithrombotic therapy predisposes patients to an increased risk of major bleeding complications. We should consider the optimal combination of anticoagulant and antiplatelet therapy to avoid the major bleeding complications following PCI with DES.
**P1861**

**Association of the cytochrome cytochrome 450 2c19 polymorphism monitoring on residual platelet activity after chronic clopidogrel medication by 3 different platelet function tests**

H.Z. Zhang, M.H. Kim, K.I. Park, J.S. Park, T.H. Park, Y.D. Kim, J.Y. Han. College of Medicine Dong-A University, Busan, Korea, Republic of

**Background:** Published data suggests that the presence of at least one CYP2C19*2 or 3 loss-of-function alleles results in increased residual platelet aggregation and are at a higher risk of adverse cardiovascular events despite clopidogrel administration. There is little evidence to show the correlations and agreements between LTA, MEA and VerifyNow data according to the consensus definitions of high residual platelet reactivity (HPR) to ADP. Objective: To assess the correlation and agreement in different devices for the prediction cut-off of for those carrying CYP2C19*2 or 3 loss-of-function allele carriers suggested by MEA, LTA and VerifyNow assays in Korean patients.

**Methods:** We enrolled 231 coronary stenting patients with chronic clopidogrel medication. Platelet inhibition was measured by LTA, MEA and VerifyNow assays and CYP2C19 genotypes were analyzed.

**Results:** Determination of cut-off levels for based on functional CYP2C19 gene carriers indicated LTA=83.3% and VerifyNow=245. The prevalence of HPR was 56.5% by MEA, 38.5% by LTA and 47.6% by VerifyNow. The MEA assay showed a significant correlation (r=0.54, p<0.001) with LTA and a moderate agreement (κ=0.4, p<0.001) with 68.8% of concordant values. A significant correlation was found between MEA and VerifyNow (r=0.39, p<0.001) with mild agreement (κ=0.28, p<0.001) of 63.2% of concordant values. Significant correlation was also found between LTA and VerifyNow (r=0.71, p<0.001) with good agreement (κ=0.51, p<0.001) and 75.3% concordant values (see figure).

**Conclusions:** Important regional differences in the use of AT for the management of ACS were observed, with EE and LA countries showing less aggressive patterns of AT than NE and SE countries.

**P1863**

**On-treatment platelet reactivity as assessed by multiplate analyser in relation to early and long-term risks for ischemic and bleeding events following the stent placement**


**Background:** In pts treated with aspirin (ASA) and clopidogrel(CI) following stenting, the needs for definition of high and low on-treatment platelet reactivity (HOTP, LOTPR) remained unmet. Although multiplate® (MPL) is a novel assay, the long-term efficacy and safety issues of MPL-guided treatment need to be clarified.

**Methods:** In this open, non-randomized and single-center prospective study (614 pts, 59±10.2 yrs), we aimed to investigate whether response (R) to ASA and CL on MPL relates to the risk of events including definite stent thrombosis (dST), myocardial infarction (MI), target lesion re-intervention (TLR), cardiovascular death (CVD) and stroke (S) as well as bleeding after primary, urgent or elective bare-metal or drug-eluting stent (BMS, DES) placement.

**Results:** Mean FU period was 805±257 days, and visits were performed within first 7 and 30 days,3.6,9 and 12 mo after PCI.Two and three-year MPL data were available in 98 and 65% of pts, respectively. Loading CL dose was 600 mg and daily dose was 150 mg for first week, and 75 mg for the rest of treatment. Loading MPL dose was 12 mg for BMS, and 12 mg for DES. ASA dose was 100 to 300 mg a day. TIMI major and minor bleeding were noted in 2 and 3.6% of pts, respectively. The incidence of dST, MI, TVR,CVD, death from any cause and the composite of end-points were 0.9,1.3, 2.6, 0.8,0.7 and 4.7, respectively. All dST episodes observed within the first 22 days of PCI. None experienced S. TIMI major and minor bleeding related with puncture sites were noted in 1.3 and 3.1% of pts, respectively. Median platelet aggregation (PA) (AU min) were MPL were 231±229 and 189±213, respectively. The PA measures were subdivided into quintiles,5th and 1st were regarded as HOTPR and LOTPR, respectively. Lower and upper interquartile borders (AU,min) were 44 and 373 for ADP and 301 for MPL,respectively. Dual HOTPR 5% was 7%. HOTPR for CL and ASA related to a 20 times (p<0.001) and a 4 times (p<0.001) higher risk of dST, respectively. LOTPR was noted in 5% of dual HOTPR subset but in none with dual R (p=0.005). For early dST 309 and 174 AU/min of ADP-PA and MPL-PA were cut-off values, respectively (AUC for ADP 0.91, p=0.001, for ASPi/P=0.68, p=0.01). However,PA to ADP or ASPi were not independent predictor for any end-point(p=NS).

**Conclusions:** HOTPR on MPL predicts only early risk of dST, but not mid and long-term ischemic end-points after BMS or DES placement, regardless of the clinical and procedural characteristics. Moreover, LOTPR was not associated with increased risk of bleeding.

---

Controversial issues on thrombotic and antithrombotics treatment
Evaluation of serum fibronectin degradation processes as an additional factor of acute coronary syndromes course defining and development of thrombotic and hemorrhagic complications

O. Koval1, O. Mararenko2. 1 State Institution "Dnipropetrovsk Medical Academy of Ukrainian Ministry of Healthcare", Dnipropetrovsk, Ukraine; 2 Community Institution "City Joint Emergency Hospital of Dnipropetrovsk Regional Municipality", Dnipropetrovsk, Ukraine.

Fibronectin (FN), the main matrix protein, which degradation causes the appearance of a great number of fragments (FFN) possessing new properties and having great impact upon thrombosis processes and inflammation during acute coronary syndromes (ACS), and hence complications development has not been studied enough yet.

The aim: To study FNF spectrum in patients with different ACS forms and to evaluate their association with thrombotic and hemorrhagic complications development.

Material and methods: 135 ACS patients (pts) who received standard medical treatment, amongst them 40 pts with ACS without ST elevation; 64 ACS pts with ST elevation early admitted (~6 hrs) and received thrombolysis, and 31 pts late admitted with acute QMI without repertusion and 14 normal subjects matched for age and gender as a control group. FN fragmentation was detected by Western blot analysis, using rabbit antibodies to human plasma FN.

Results and discussion: Reliable activation of proteolytic processes has been observed in all pts comparing with the normal subjects irrespective of the pts' gender (p=0.05) and age (p=0.05). Frequency of detection of some important FFN has reliably changed: FFN with molecular mass (MM) 20-38 kDa - binding fibrin and activating metalloproteinases genes (p=0.0001); 100-110 kDa - inducing cardiomyocytes apoptosis and eliminating the excess of FN causing pathological fibrosis and remodeling (p=0.006); 165-175 kDa - defining the activity of anticoagulants interaction with cells (p=0.041) was increased. Frequency of FFN with MM 60-72 kDa - locally actively binding collagen; FFN 75-80 kDa and 90-95 kDa with thrombin activity (p=0.02), simultaneously decreased.

Development of thrombotic ACS complications was associated (p<0.05) with increase of FFN frequency with MM 60-72 kDa - locally actively binding collagen; FFN 75-80 kDa and 90-95 kDa with thrombin activity (p<0.05) with in increase of MACCE. The ideal regimen for duration of triple therapy post PCI in this group is undetermined and large prospective trials are required.

Conclusions: In all forms of ACS an activation of FN degradation processes takes place, confirming their role of an important link connecting mechanisms of thrombosis and inflammation. The FFN spectrum reflects the individual prevalence of thrombotic or inflammatory mechanisms in the ACS pathogenesis; it is also associated with the development of thrombotic and hemorrhagic ACS complications and can be additionally used in early individual evaluation of their risk development.

P1865 Dual antiplatelet and oral anticoagulant treatment of patients discharged after PCI in acute myocardial infarction - current clinical practice and 12-month outcome - analysis from the PL-ACS Registry


The aim of this analysis was to compare clinical presentation and 12-month outcomes of patients discharged after PCI for NSTEMI and STEMI on dual antiplatelet treatment with and without oral anticoagulant.

Methods: All with NSTEMI and STEMI (N=14403), discharged after PCI, registered in the prospective PL-ACS registry from 7.2007 to 11.2009 were included. Follow-up mortality was obtained from the government database.

Results (table): Patients with triple therapy comprised only 1.5% of the analyzed population. They were older and had significantly more comorbidities. More than one-third of them had atrial fibrillation and half of them had severe left ventricle dysfunction. We did not find significant difference in 12-month mortality between the groups. What more, after multivariate adjustment the hazard ratio for dual antiplatelet +/- oral anticoagulant was less than 1 (HR=0.87, 95%CI = 0.56–1.37, P=0.55).

Conclusion: Dual antiplatelet together with oral anticoagulant treatment after PCI for myocardial infarction is rarely given, mostly in high risk patients with adequate comorbidities. Nevertheless, patients on dual antiplatelet together with oral anticoagulant have comparable 12-month mortality to patients on dual antiplatelet therapy.

P1866 Warfarin and dual antiplatelet therapy post percutaneous coronary intervention (PCI) in the elderly (>75 years old)


Purpose: The requirement for anticoagulation following PCI is relatively uncommon (triple therapy). Current guidelines are ambiguous for elderly patients undergoing PCI on anticoagulation. We therefore present the long-term outcomes of a large group of elderly patients undergoing PCI on dual antiplatelet therapy compared to triple therapy.

Methods: All elderly patients (>75) undergoing PCI were enrolled. The primary endpoint of this study was bleeding events in patients on dual vs. triple therapy according to BARC (Bleeding Academic Research Consortium) and TIMI major and minor criteria. Secondary endpoints were MACCE (cardiac death, myocardial infarction, target lesion and vessel revascularization, stroke) and ARC definite and probable stent thrombosis (ST).

Results: 624 lesions from 596 patients were identified with 99% clinical follow-up (31±4 months). Indications for anticoagulation (6%, 37/595): 89% AF, 5% DVT, 3% Valve and 5% LV thrombus. BARC and TIMI bleeds were significantly greater in the triple therapy group (BARC:22.6±vs.6.5%; p=0.01). There was no difference in MACCE and ST. There was one sub-acute stent thrombosis in a patient taking triple therapy. There were concerns of underdeployment of a drug eluting stent (DES) during the index PCI. Triple therapy regimens varied significantly between operators despite 50% use of DES. Combinations included Triple therapy for 12 months then Warfarin and Aspirin (50%) and triple therapy for 1 month then aspirin and warfarin (23%).

Figure 1. Impact of anticoagulation on bleeding and MACCE post PCI.

Conclusion: This study demonstrates that bleeding is significantly higher in the elderly on triple therapy. However, bleeding does not appear to translate into increased MACCE. The ideal regimen for duration of triple therapy post PCI in this group is underdetermined and large prospective trials are required.

Table 1

<table>
<thead>
<tr>
<th></th>
<th>ASA + Clopidogrel</th>
<th>ASA + Clopidogrel</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, %</td>
<td>14 198 (96.6%)</td>
<td>205 (1.4%)</td>
<td></td>
</tr>
<tr>
<td>STEMI, %</td>
<td>64.1</td>
<td>57.6</td>
<td>0.052</td>
</tr>
<tr>
<td>Mean age, years ± SD</td>
<td>63.0±11.5</td>
<td>66.2±10.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Diabetes, %</td>
<td>31.0</td>
<td>35.1</td>
<td>0.21</td>
</tr>
<tr>
<td>Prior myocardial infarction, %</td>
<td>19.8</td>
<td>26.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Prior cerebrovascular disease, %</td>
<td>15.3</td>
<td>25.9</td>
<td>0.0001</td>
</tr>
<tr>
<td>History of stroke, %</td>
<td>3.0</td>
<td>2.4</td>
<td>0.64</td>
</tr>
<tr>
<td>History of congestive heart failure, %</td>
<td>4.0</td>
<td>8.3</td>
<td>0.0018</td>
</tr>
<tr>
<td>History of hypertension, %</td>
<td>7.3</td>
<td>7.3</td>
<td>0.044</td>
</tr>
<tr>
<td>Atrial fibrillation, %</td>
<td>3.3</td>
<td>35.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Left ventricular ejection fraction &lt; 30%, %</td>
<td>25.2</td>
<td>51.4</td>
<td>0.0001</td>
</tr>
<tr>
<td>In-hospital major bleeding, %</td>
<td>3.0</td>
<td>4.4</td>
<td>0.23</td>
</tr>
<tr>
<td>30-days major bleeding, %</td>
<td>2.0</td>
<td>1.5</td>
<td>0.55</td>
</tr>
<tr>
<td>12-months major bleeding, %</td>
<td>7.2</td>
<td>9.8</td>
<td>0.16</td>
</tr>
</tbody>
</table>

1 St Antonius Hospital, Department of Cardiology, Nieuwegein, Netherlands; 2 St Antonius Hospital, Department of Clinical Pharmacology, Nieuwegein, Netherlands; 3 St Antonius Hospital, Department of Clinical Chemistry, Nieuwegein, Netherlands.

Background and relevance: Despite the use of dual antiplatelet therapy with aspirin and clopidogrel, approximately 10% of patients suffer from atherothrombotic events in the first year after PCI. Multiple risk factors, including high on-treatment platelet reactivity (HPR) and carriage of CYP2C19 gene polymorphisms, have been identified. Recently developed point-of-care tests allow rapid evaluation of platelet reactivity and CYP2C19 metabolizer status in routine clinical practice.

Novel antiplatelet drugs – like prasugrel and ticagrelor – reduce atherothrombotic events in acute coronary syndrome (ACS) patients and are not influenced by CYP2C19 metabolizer status. However, the use of prasugrel or ticagrelor leads to a higher bleeding risk and more cost.

P1867 POPular Risk Score for individualized antiplatelet therapy following non-urgent PCI

T.O. Bergmeijer1, P.W. Janssen1, T. Oribans1, T.C. Godschalk1, R. Rozemeijer1, V.H. Demeer2, C.M. Hackeng1, J.M. Ten Berg3 on behalf of St. Anthony’s centre for platelet function research

1 St Antonius Hospital, Department of Cardiology, Nieuwegein, Netherlands; 2 St Antonius Hospital, Department of Clinical Pharmacology, Nieuwegein, Netherlands; 3 St Antonius Hospital, Department of Clinical Chemistry, Nieuwegein, Netherlands.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790 by guest on 11 March 2019
Objective: To develop a risk score for tailoring antplatelet therapy for non-urgent PCI patients.

Methods: Based on recent literature and clinical relevance the following scoring system was developed: platelet function (6 points for HPR, measured by VerifyNow P2Y12), CYP2C19 gene polymorphisms (1 point for each ‘2’ or ‘3’ allele), clinical risk factors (DM, LVEF <30%, connecting stent length >30mm; 0.5 point for each factor) and ACS in the previous 14 days (1 point, platelet function was scored in these patients). Patients with a risk score ≥2 scored received prasugrel or ticagrelor, otherwise clopidogrel was prescribed.

Results: In total, 1069 elective PCI patients were included. Patients with a risk score of ≥1.5 points had a 6.6% event rate for the combined endpoint of myocardial infarction, CVA, stent thrombosis and all-cause mortality in 1 year following PCI, compared to 12.0% for patients with ≤2 points (p=0.003).

Implementation into clinical practise: the POPular Risk Score was performed in >1000 consecutive non-urgent PCI patients. Tailoring antplatelet drug advice based on the POPular risk score was achieved within 24 hours in 98% of patients. Clopidogrel was switched to prasugrel or ticagrelor in 31.3% of patients. Follow-up for atherothrombotic and bleeding events will be achieved by May 2012.

Conclusion: The POPular Risk Score can discriminate between patients with a high or low risk for atherothrombotic events in a large cohort of non-urgent PCI patients. Prescribing antplatelet drugs based on platelet function and CYP2C19 genotype results is feasible in daily clinical practice. Follow-up for atherothrombotic and bleeding events will be achieved by May 2012.
Contemporary pre-hospital management of ACS patients: results from the EPICOR study

P. R. Simmae1, H. Bueno2, N. Danchin3, J. Sanchez-Covita4, M. Licour5, L. Annemans6, J. W. Jakema6, R. F. Storey6, F. Van De Walle7, U. Zeymer8, M. Licour8, 1Department of Cardiology, Leuven, Belgium; 2Hospital General Universitario Gregorio Maranon, Madrid, Spain; 3AP-HP - European Hospital Georges Pompidou, René Desentes University, Paris, France; 4AstaZenaeca Farmaceutica, Madrid, Spain; 5AstaZenaeca Medical Europe, Zaventem, Belgium; 6CHR Interuniversity Centre for Health Economics Research, Ghent, Belgium; 7Leiden University Medical Center, Leiden, Netherlands; 8University of Sheffield, Sheffield, Sheffield, United Kingdom; 9Institut für Herzinfarktforschung Ludwigshafen, Ludwigshafen, Germany

Purpose: Little is known about current pre-hospital management in ACS patients from a global perspective. EPICOR is a multicentre, international study designed to describe the current use of antithrombotic therapies in a broad ACS population, including pre-hospital, hospital and post-discharge management. In this initial subanalysis, we report on baseline pre-hospital management patterns.

Methods: EPICOR (NCT01171445) enrolled 10,568 patients with STEMI (47%) or NSTE-ACS (53%) in 555 centers in 20 countries across Europe and Latin America.

Results: Overall, 31% of patients (35% STEMI, 28% NSTE-ACS) received pre-hospital care. Drug treatment was started in 21% of patients before hospitalization (27% of STEMI and 15% of NSTE-ACS patients). Pre-hospital fibrinolysis was initiated in 3% (12% of STEMI patients vs. 10% in-hospital). Pre-hospital aspirin was given in only ~20% of patients, clopidogrel in fewer than 10% patients, and prasugrel very rarely. Pre-hospital antiplatelet therapy was more frequently initiated in STEMI patients: 72% for aspirin and 36% for coronaryangiography, among those receiving pre-hospital care. Among patients who had a pre-hospital ECG (36%), pre-hospital aspirin and clopidogrel were given to only 50% and 28% of STEMI patients, respectively, and to 31% and 9% of NSTE-ACS patients. In contrast, pre-hospital clopidogrel was only given to 2% of STEMI patients without a pre-hospital ECG. There were no differences in pre-hospital antithrombotic treatment between hospitals with or without on-site cath facilities.

Conclusion: Pre-hospital initiation of antiplatelet agents remains relatively infrequent, even in patients who do receive pre-hospital care. Further follow-up of these patients will help to determine whether these practice patterns affect outcome.

Reticulated platelets predict the risk of cardiac death in acute coronary syndrome patients independently of mean platelet volume: data from AMI-Florence 2 study

P. R. Simmae1, H. Bueno2, N. Danchin3, J. Sanchez-Covita4, M. Licour5, L. Annemans6, J. W. Jakema6, R. F. Storey6, F. Van De Walle7, U. Zeymer8, M. Licour8, 1Department of Cardiology, Leuven, Belgium; 2Hospital General Universitario Gregorio Maranon, Madrid, Spain; 3AP-HP - European Hospital Georges Pompidou, René Desentes University, Paris, France; 4AstaZenaeca Farmaceutica, Madrid, Spain; 5AstaZenaeca Medical Europe, Zaventem, Belgium; 6CHR Interuniversity Centre for Health Economics Research, Ghent, Belgium; 7Leiden University Medical Center, Leiden, Netherlands; 8University of Sheffield, Sheffield, Sheffield, United Kingdom; 9Institut für Herzinfarktforschung Ludwigshafen, Ludwigshafen, Germany

Introduction: Elevated mean platelet volume (MPV) has been associated with AMI and mortality/following myocardial infarction. Reticulated platelets (RP) are newly formed and larger in size platelets containing residual amount of RNA. Large platelets could be a reflection of the number of RP, although not all large platelets are young platelets. To date, there are no studies that investigated the possible association of RP in predicting the risk of cardiovascular death among acute coronary syndrome (ACS) patients.

Aim: To evaluate the impact of RP on the occurrence of cardiovascular death in ACS patients.

Methods: On the frame of the AMI-Florence 2 study, we investigated 229 ACS (154 M; 76 F) patients. RP were measured using the Sysmex XE-2100 haematology analyzer (Sysmex, Kobe, Japan). RP were expressed as the percentage of RP of the total optical platelet count (immature platelet fraction; IPF) and as the percentage of RP high fluorescence (H-IPF) on a venous blood sample obtained within 24 hrs from coronary angiography. Among those receiving pre-hospital care. Among patients who had a pre-hospital ECG (36%), pre-hospital aspirin and clopidogrel were given to only 50% and 28% of STEMI patients, respectively, and to 31% and 9% of NSTE-ACS patients. In contrast, pre-hospital clopidogrel was only given to 2% of STEMI patients without a pre-hospital ECG. There were no differences in pre-hospital antithrombotic treatment between hospitals with or without on-site cath facilities.

Conclusion: Pre-hospital initiation of antiplatelet agents remains relatively infrequent, even in patients who do receive pre-hospital care. Further follow-up of these patients will help to determine whether these practice patterns affect outcome.

ANTIPATELET AGENTS

In-hospital outcomes of patients treated with clopidogrel or prasugrel for acute myocardial infarction in the real world: Results from the FAST-MI 2010 registry

L. Bella1, F. Schiele2, E. Puymirat3, G. Rouf4, G. Vanzetto5, R. Morice4, B. Ritz7, J. Ferrieres7, T. Simon6, N. Danchin2, 1Hospital, Annecy, France; 2University hospital, Besançon, France; 3University hospital, Nancy, France; 4University hospital, Toulouse, France; 5University hospital, Toulouse, France; 6University hospital, Toulouse, France; 7University hospital, Toulouse, France

Background: The TRITON trial showed that prasugrel was superior to clopidogrel in reducing rates of ischemic events in ACS patients planned for PCI, but increased the risk of major bleeding. In practical routine, however, many patients receive thienopyridine treatment before coronary angiography, and the impact of prasugrel treatment in this setting is poorly documented.

Purpose: To assess the baseline characteristics and in-hospital outcomes of AMI patients treated with either clopidogrel or prasugrel in real world practice.

Methods: FAST-MI 2010 is a nationwide registry that included 4169 patients with AMI in 213 centers representing 76% of French centres managing AMI patients at the end of 2010. Of those, 4115 received thienopyridines: 2856 clopidogrel only (C) (69%), and 1259 received prasugrel (P) (31%) of whom 44% received the first dose prior to coronary angiography.

Results: Both groups differed markedly: age (69±14 vs 71±11, P<0.001), sex (%women: 33 vs 14%, P<0.001), GRACE score (147±37 vs 126±28, P<0.001), %STEMI (49% vs 74.5%, P<0.001) in the C and P groups respectively. CV risk factors, history of CAD, stroke CKD or non-CV comorbidities were all more fre-
High frequency of CYP2C19*2 carriers in PCI-treated patients initially treated with clopidogrel and switched to prasugrel therapy based on a platelet function testing guided approach


Purpose: Among patients undergoing PCI, subjects with high on-clopidogrel treatment platelet reactivity (HTRP) exhibit a high risk for post-procedural thrombotic events. Both non-genetic and genetic variables impact on clopidogrel response. The aim of the current study was to investigate the common variant of CYP2C19 (rs4149056) in PCI-treated patients with stable CAD on 10mg prasugrel, more often presented with STEMI and were at a lower risk than those receiving clopidogrel. After adjustment for baseline differences, no difference was noted in the risk of bleeding or ischemic events.

Methods: Prevalence of the CYP2C19*2 allele was compared between two consecutively recruited cohorts. One cohort (n=1274) of patients with an adequate response to clopidogrel and without a switch of treatment stems from a trial including 1608 patients that we conducted between 2007-2008. A second cohort (n=124) was consecutively recruited between 2009-2011 and includes HTRP patients with a switch of treatment from clopidogrel to prasugrel in a setting of routine platelet function testing. Platelet aggregation (in AU x min) was tested on a Multiplate analyzer and repeated clopidogrel loading doses (LD) were given in the majority of patients (76/124) before switching over to prasugrel treatment. Genotypes were determined by TaqMan assay.

Results: The rate of CYP2C19*2 allele carriers was significantly higher in HCRP patients switched to prasugrel as compared to patients showing an adequate response to clopidogrel (43.5% vs. 22.3%, P<0.001). Following prasugrel LD administration, the ADP-induced platelet aggregation (median, interquartile range) was similar in carriers (n=54) vs. non-*2 allele carriers (148 ±26.1 vs. 137 ±23.6 AU x min, respectively; P=0.94).

Conclusions: The frequency of the CYP2C19*2 allele variant is very high in HCRP patients with a switch of treatment from clopidogrel to prasugrel in a setting of individualized and platelet function testing guided antiplatelet treatment. On-treatment platelet reactivity is not influenced by this genetic variant. The clinical impact of these findings warrants further investigation.

Pharmacokinetics and pharmacodynamics of prasugrel 5 mg in low body weight patients and prasugrel 10 mg in higher body weight patients

T.O. Bergmejer1, D.J. Angiolillo2, S. James3, H. Wagner4, P.B. Brown5, C. Zhou6, J.A. Jakubowski7, B.A. Moser8, D. Eringe9, J.M. Ten Berg1. 1Department of Cardiology, St. Antonius Hospital, Nieuwegein, Netherlands; 2University of Florida College of Medicine, Center for Thrombosis Research, Jacksonville, United States of America; 3Uppsala Clinical Research Center, Department of Medical Sciences, Uppsala, Sweden; 4 Lund University Hospital, Department of Cardiology, Lund, Sweden; 5 Eli Lilly and Company, Indianapolis, United States of America

Purpose: The TRITON-TIMI 38 study showed that following PCI, low body weight (LBW) patients on 10mg prasugrel had an increased bleeding risk. Reducing the prasugrel dose to 5mg in patients ~60kg is recommended but not extensively investigated. The purpose of the present study was to investigate pharmacokinetics (PK) and pharmacodynamics (PD) of 5mg and 10mg prasugrel in LBW and higher body weight (HBW) aspirin-treated patients with stable coronary artery disease (CAD).

Methods: In 3 periods (12 days each), randomized, cross-over fashion, 34 LBW (56.4±3.7kg) and 38 HBW (84.7±14.9kg) patients received a daily dose of 5mg prasugrel, 10mg prasugrel, or 75mg clopidogrel on top of 75-100mg aspirin. We calculated the area under the plasma concentration-time curve (AUC) for prasugrel active metabolite (AM) based on 5 measurements (0.5, 1, 2, 3, and 4 hours). For PD analysis, light transmission aggregometry (LTA), using 5 and 20µM ADP, VerifyNow P2Y12 (VN-P2Y12, VASP-PRI), and vasodilator-associated stimulated phosphoprotein (VASP-PRI) were performed.

Results: LBW patients on 5mg prasugrel had lower prasugrel AM concentrations than HBW patients on 10mg prasugrel (mean AUC0-τ 29.0 vs. 46.7 ng*h/ml, LS mean difference 27.8%, 90% CI 0.53-0.72). Figure 1 shows that there were no significant differences in platelet reactivity between LBW patients on 5mg prasugrel and HBW patients on 10mg prasugrel for either VN-P2Y12 (Figure), VASP-PRI, or LTA (not shown).

Conclusions: While prasugrel AM concentrations in LBW aspirin-treated patients with stable CAD on 5mg prasugrel were lower compared to HBW patients on 10mg prasugrel, no significant differences were found in platelet reactivity measured by LTA, VN-P2Y12, or VASP-PRI. These data support the recommended dosing for 5mg in LBW patients.

Clopidogrel and prasugrel non-responder in patients undergoing therapeutic hypothermia after cardiac arrest

K. Ibrahim1, M. Christoph1, S. Schmeidler1, S. Kolschmann1, C. Wunderlich1, R.H. Strasser1. 1Dresden University of Technology, Heart Center University Hospital, Dresden, Germany; 2Department of Internal Medicine II, Pirmah Hospital, Pirmah, Germany

Summary: Background: In acute coronary syndromes the percutaneous coronary intervention with implantation of a coronary stent is the recommended treatment. Afterwards administration of ASS and a thienopyridine like clopidogrel or prasugrel is necessary to prevent thrombotic complications like stent thrombosis. High residual platelet reactivity after administration of platelet inhibitors is related to an increased risk of thrombotic complications. Objectives: To determine the effect of thienopyridines in patients in therapeutic hypothermia after cardiac arrest.

Patients/Methods: 83 patients with acute coronary syndromes were enrolled in a single center, prospective observational study (40 Patients in hypothermia, 43 in normothermia). All patients received a loading dose of 600 mg clopidogrel or 60 mg prasugrel and platelet reactivity index (PRI-VASP) was measured 24 h after administration. A PRI-VASP above 50% was defined as high residual platelet reactivity. Major adverse cardiac events were recorded in the following.

Results: Mean values showed a significant higher PRI-VASP in the hypothermia group compared to the normothermia group, indicating a worse response to thienopyridine (61.1%±23.8% vs. 36.1%±22.3%, p<0.01). The number of patients with thienopyridine non-responder in the hypothermia-group was higher compared to normothermia group (70.0% vs. 29.3%). Comparing prasugrel and clopidogrel in patients in hypothermia mean PRI-VASP was significantly lower in the prasugrel group (37.5%±28.3 vs. 68.9%±16.0, p<0.01). The non-responder rate in the prasugrel group was lower (30% vs. 83%).

Conclusion: High residual platelet reactivity is common in patients after cardiac arrest in therapeutic hypothermia. Non-responder rate is extremely high in these patients. Novel antiplatelet drugs like prasugrel can ameliorate platelet inhibition significantly. If better platelet inhibition leads to lower rates of thrombotic events has to be investigated in further studies.

Safety and biological efficacy of a second 600 mg loading dose of clopidogrel in elderly patients presenting with high on treatment platelet reactivity

M. Laine1, S. Ammer2, M. Peyrol3, P. Sbraga1, M.P. Jaubert1, O. Helal1, S. Yovora2, F. Paganeli2, L. Bonello1, S.P. Hamad1, W. Varga1. 1AP-HM - Hospital Nord, Marseille, France; 2Centre Hospitalier Général, Martigues, France

Elderly patients have increased thrombotic and bleeding risks following percutaneous coronary intervention (PCI). Studies have shown a high rate of high on treatment platelet reactivity (HTPR) following a 600 mg loading dose of clopidogrel in patients over 75 years old compared to young patients. On the other hand, more potent P2Y12 ADP-receptor antagonists have been associated with increased bleeding risks and may not therefore be optimal to reduce the risk of HTPR in such patients. Trials have suggested that repeated LD of clopidogrel can overcome HTPR and reduce the rate of ischemic events in all comers without increasing the bleeding risk. The aim of the present study is to evaluate the safety and biological efficacy of a second 600 mg loading dose of clopidogrel in elderly patients with HTPR undergoing PCI.

Methods: We included consecutive patients ≥ 75 years with HTPR following a first 600mg loading dose (LD) of clopidogrel undergoing PCI. Platelet reactivity (PR) was assessed with the Vasodilator-Stimulated Phosphoprotein index (VASP) at least 6 hours after the LD. A VASP index ≥ 50% defined HTPR. Patients received a second 600 mg LD of clopidogel in order to improve PRI inhibition. Non-CABG bleeding events during hospitalization were recorded as safety endpoint and the VASP index after the second LD was the biological efficacy endpoint.

Results: 107 elderly patients with HTPR following 600mg were included. In most
patients, PCI was performed for acute coronary syndrome (65.4%). PR was significantly decreased after the 2nd LD (mean VASP after first LD = 66.8±1.0% vs 49.6±1.8% after second LD, p<0.0001). The second LD overcame HTPR in 47.7% of patients. The rate of in-hospital non-CABG bleeding was low with only one BARC 3 event.

Platelet reactivity after loading doses

\[
\begin{array}{l|c|c}
\text{Mean VASP} & \text{Mean VASP} & \text{Patients with VASP} \\
\text{after 1st LD} & \text{after 2nd LD} & \text{after 50\% of 2nd LD} \\
\hline
\text{Mean VASP} & 66.8\pm1.0\% & 49.6\pm1.8\% \\
\text{Mean VASP} & 71.3\pm1.0\% & 51.2\pm1.9\% \\
\end{array}
\]

Data are expressed in Mean ± SD. *p<0.0001 between mean VASP index after 1st LD and VASP index after 2nd LD. LD: loading dose.

Conclusion: HTPR can be overcome in a significant number of elderly patients treated with PCI thanks to a second 600mg loading dose of clopidogrel with a very low rate of bleeding events.

### P1879 Baseline or platelet reactivity on clopidogrel as predictor for clinical outcome

M. Kerneis1, J. Abtan1, J. Silvain1, O. Connor1, G. Cayla2, S. O’Connor1, O. Barthelemy1, F. Begu1, J.P. Collet1, D. Brugier1.

Centre Bad Krozingen, Bad Krozingen, Germany

Purpose: To evaluate the impact of body weight on the influence of body weight on the outcome of patients undergoing PCI. Body weight was measured before and after PCI. The rate of in-hospital non-CABG bleeding was low with only one BARC 3 event.

Body weight and on-treatment platelet reactivity

\[
\begin{array}{l|c|c|c}
\text{Body weight} & \text{Baseline platelet reactivity} & \text{On-treatment platelet reactivity} \\
\text{in kg} & \text{PRU} & \text{PRU} \\
\hline
\text{Baseline} & 49.6 \pm 3.2 \% & 30.1 \pm 2.8 \% \\
\text{After PCI} & 39.8 \pm 2.7 \% & 23.1 \pm 3.1 \% \\
\end{array}
\]

Correlations between the above variables were determined both as a function of the individual study drugs and irrespective of study drug. Overall, we confirmed that body size was a determinant of residual platelet reactivity irrespective of the type and dose of thienopyridines used (Figure). Of the 3 body size measures, BW and BSA demonstrated the highest correlation with on-treatment platelet reactivity; and of the 3 platelet reactivity tests, VerifyNow-P2Y12 had the highest correlation with body size indices. Correlation coefficients ranged from a high of 0.64 (BW vs. PRU on Pr-5) to a low of 0.34 (BMI vs. LTA on Pr-10), but all were significant (p<0.0001).

Conclusion: Using a comprehensive selection of body size indices, platelet function tests, and thienopyridine doses, we demonstrate the continuous relationship between body size and response to clopidogrel and prasugrel.
Profile and in-hospital outcomes of patients treated with a high (600 mg) clopigrel loading dose versus prasugrel for acute myocardial infarction. The FAST-MI 2010 registry

E. Puymirat1, L. Borrello2, G. Ducrocq3, J. Boschat4, C. Robin4, C. Le Ray4, N. Delarche5, G. Mulak6, T. Simon7, N. Danchin8 on behalf of the FAST-MI 2010 investigators. 1AP-HP - European Hospital Georges Pompidou, Paris, France; 2AP-AM - Hospital Nord, Marseille, France; 3AP-HP - Hospital Bichat-Claude Bernard, Department of Cardiology, Paris, France; 4University Hospital of Brest, Department of Cardiology, Brest, France; 5Clinique Convent, Bourg en Bresse, France; 6Hospital of Vannes, Vannes, France; 7Hospital of Pau, Pau, France; 8French Society of Cardiology, Paris, France; 9AP-HP - Hospital Saint-Antoine, Faculty of Medicine Pierre & Marie Curie Paris 6, Paris, France

Background: In real-life, many AMI patients receive high doses of clopidogrel (>600 mg loading dose) as an alternative to newer P2Y12 inhibitors.

Aim: To compare baseline profile and outcomes of patients receiving a high clopidogrel dose, vs those getting prasugrel in AMI.

Methods: Nationwide French registry including 4169 AMI patients in 213 centres: 4115 with thienopyridines, 808 (High-C group: 20%) with ≤600 mg loading dose of clopidogrel (no later switch to prasugrel) and 391 (P group: 9.5%) with prasugrel only (no switch from clopidogrel). We compared baseline profile, bleeding and ischemic complications in High-C and P groups, and then used propensity-score matching to compare outcomes in 2 cohorts with similar baseline characteristics.

Results: High-C pts were older than P-group pts (65 vs 77 years; P < 0.001), with a higher rate of high-risk characteristics (141/36 vs 107/36; P < 0.001): there was more diabetes (29% vs 11%; P < 0.001), obesity (18% vs 12%; P < 0.007), hypertension (57% vs 37%; P < 0.001), stroke/TIA (5% vs 1%, P < 0.001), or renal failure (3.5 vs 1.0%, P < 0.01) in the high-C group. P group had more death (7% vs 61%, P < 0.001) and more often had PCI (93% vs 85%; P < 0.001), but less often fibrinolyis (5% vs 10%). None of the complications differed significantly after multivariate adjustment.

Conclusion: This real-world registry, patients receiving high-dose clopidogrel had a more severe risk profile than those receiving prasugrel. In-hospital complications were uncommon and there was no significant difference between high-dose clopidogrel and prasugrel after adjustment for potential confounders.

Ticagrelor vs prasugrel in diabetic patients: a pharmacodynamic study

I. Xanthopoulou, E. Maounasiou, K.F. Theodoropoulou, G. Kassisimis, V. Gizas, A. Moulias, P. Theodorou, P. Davlouros, G. Hahalis, D. Alexopoulos. Patras University Hospital, Cardiology Department, Patras, Greece

Purpose: Among diabetic patients, prasugrel reduced ischemic events compared to clopidogrel without increasing the bleeding risk. Ticagrelor resulted in a non-significant reduction in ischemic events compared to clopidogrel, in the diabetic subgroup. We aimed to compare the antplatelet effect of ticagrelor vs prasugrel in diabetic patients with acute coronary syndrome (ACS) undergoing percutaneous coronary intervention (PCI).

Methods: This was a prospective, randomized, single-center, single blind, investigator-initiated, two-arm, crossover study. Patients aged ≥75 years or <60 kg, at increased risk for bradyarrhythmia events, strong CYP45A inhibitors or inducers, severe uncontrolled obstructive pulmonary disease and severe hepatic impairment were excluded from the study. PR was assessed with the VerifyNow assay in platelet reactivity units-PRU with a value ≥230 indicating high on-treatment platelet reactivity (HTPR).

Results: There was no difference in patient's demographic and clinical characteristics between ticagrelor (N=11) and prasugrel (N=11) group. Baseline PR did not differ significantly between groups (239.4 PRU±46.6 for ticagrelor vs 241.3±81.5 for prasugrel, p=0.9). The primary end point of PR assessed at the end of the two (precrossover and postcrossover) periods was lower for ticagrelor compared to prasugrel (46.9 ± 11.2% vs 64.5 ± 9.9%, p<0.05 respectively). HTPR rate at baseline was 59.1% (13/22) and was eliminated both by ticagrelor and prasugrel. No deaths or strokes occurred in either treatment group.

Conclusions: In diabetic patients with ACS ticagrelor produced a significantly higher platelet inhibition compared to prasugrel. However, both agents effectively treated HTPR.

Superior pharmacodynamics of ticagrelor BID to clopidogrel QD in terms of inhibition of platelet aggregation (IPA): IPA projections based on patient adherence data from the TWICE project

B. Vrijens1, M.J. Claey3, E. Vandenbussche2, F. Van De Werf2, 1AARDEX Group, Ltd., Sion, Switzerland; 2Antwerp University Hospital, Edegem, Belgium; 3AstroZeneca, Brussels, Belgium; 4University Hospitals (UZ) Leuven, Leuven, Belgium

Purpose: Twice-daily dosing (BID) is often perceived as being inferior to once-daily (QD) dosing due to higher likelihood of missing a dose with a BID regimen. However, the pharmacological superiority of a drug should be evaluated based on both patients' (pts) adherence and PK/PD characteristics. This project compared the anticipated inhibition of platelet aggregation (IPA) of ticagrelor (T) BID to clopidogrel (C) QD using pts adherence data.

Methods: A review of 1354 described cardiovascular medications (primarily hypertension drugs) with QD (337) and BID (1017) regimens were taken from a commercial database that electronically archives pts dosing histories. Based on the onset/offset IP IPA characteristics (20 µmol/L ADP, final extent) of the loading and maintenance dose of both T and C and the independently retrieved BID and QD dosing histories, IPA level was simulated for each patient dosing history for a period of 30 days (QD) after a loading dose.

Results: While many BID pts missed 1 dose at least once in 30D, only 26% of BID pts had at least 1-day dose-free interval (2 sequentially omitted BID doses) does not lower the IPA below the 24h trough levels of fully adherent C-QD patients. Missing 1 day dose of T-BID obtains comparable IPA levels as missing 1 day dose of C-QD. Simulations based on observed pt adherence over time showed that the mean IPA-averages for T-BID (81%) remains significantly higher than for C-QD (55%; p<0.001).

Conclusions: Although BID patients more frequently miss 1 dose as compared to QD patients, the level of platelet inhibition remains higher in T as compared to C, mainly due to higher IPA level achieved with T and the relatively low likelihood of missing 2 consecutive BID doses.

Low prasugrel vs high clopidogrel dose in patients aged greater than or equal to 75 years with ACS and high on clopidogrel platelet reactivity post PCI

I. Xanthopoulou, T-E. Plakomylt, K.F. Theodoropoulou, G. Kassisimis, E. Maounasiou, A. Moulias, A. Damelou, P. Davlouros, G. Hahalis, D. Alexopoulos. Patras University Hospital, Cardiology Department, Patras, Greece

Purpose: In patients ≥75 years of age, if treatment with prasugrel is deemed necessary, a reduced maintenance dose (MD) of 5 mg is suggested, after a careful individual benefit/risk evaluation. We aimed to compare the antplatelet action of prasugrel 5mg versus clopidogrel 150mg in patients ≥75 years of age with acute coronary syndrome (ACS) and high on-treatment platelet reactivity (HTPR) post percutaneous coronary intervention (PCI).

Methods: This was a prospective, randomized, single-center, single-blind, investigator-initiated, two-arm, crossover study. Patients aged ≥75 years with HTPR (≥235 platelet reactivity units-PRU by VerifyNow assay) 24 hours post PCI, were randomized in a 1:1 ratio to prasugrel 5mg or clopidogrel 150mg for 15 days, followed by crossover directly to the alternate therapy for an additional 15 days without an intervening washout period. Patients attended a pharmacodynamics study, on hemodialysis, prior stroke, age ≥75 years or <60 kg, at increased risk for bradyarrhythmia events, strong CYP45A inhibitors or inducers, severe uncontrolled obstructive pulmonary disease and severe hepatic impairment were excluded from the study. PR was assessed with the VerifyNow assay in platelet reactivity units-PRU with a value ≥230 indicating high on-treatment platelet reactivity (HTPR).

Results: There was no difference in patient's demographic and clinical characteristics between ticagrelor (N=11) and prasugrel (N=11) group. Baseline PR did not differ significantly between groups (239.4 PRU±46.6 for ticagrelor vs 241.3±81.5 for prasugrel, p>0.9). The primary end point of PR assessed at the end of the two (precrossover and postcrossover) periods was lower for ticagrelor compared to prasugrel (46.9 ± 11.2% vs 64.5 ± 9.9%, p<0.05 respectively). HTPR rate at baseline was 59.1% (13/22) and was eliminated both by ticagrelor and prasugrel. No deaths or strokes occurred in either treatment group.

Conclusions: In diabetic patients with ACS ticagrelor produced a significantly higher platelet inhibition compared to prasugrel. However, both agents effectively treated HTPR.
There was no difference in patient’s demographic and clinical characteristics between the 2 groups. The primary end point of platelet reactivity (PR) assessed at the end of the two (precrossover and postcrossover) periods, did not differ significantly between the 2 groups (382.2 PRE, 251.2–303.9% vs. PRU for clopidogrel 150 mg vs. 245.4 PRE, 205.6–285.3% for aspirin 75 mg, p = 0.50). HTTR rates remained high in both groups (76.9% for clopidogrel 150 mg and 57.1% for aspirin 75 mg). No deaths or strokes occurred in either treatment group.

**Conclusions:** In patients ≥75 years old with ACS, exhibiting HTTR 24 hours post PCI, the antiplatelet effects of aspirin 75 mg and clopidogrel 150 mg do not differ significantly. HTTR rates remained high with both agents, perhaps suggesting the need of using an alternative antiplatelet agent.

---

**P1886**

Clopidogrel is associated with weaker platelet inhibition, lower active metabolite concentration and more poor responders in higher body weight patients compared with lower body weight patients


1Lund University Hospital, Department of Cardiology, Lund, Sweden; 2Eli Lilly and Company, Indianapolis, United States of America; 3University of Florida College of Medicine, Center for Thrombosis Research, Jacksonville, United States of America; 4St Antonius Hospital, Department of Cardiology, Nieuwegein, Netherlands; 5Upstate Clinical Research Center, Department of Medical Sciences, Upstate, Sweden

**Purpose:** Body weight is a predictor of clopidogrel response. However, no prospective studies have compared pharmacodynamic (PD) and pharmacokinetic (PK) data from higher vs. low weight patients. We compared the PD and PK effects of clopidogrel 75 mg in lower (LBW, <60 kg) and higher (HBW, >60 kg) body weight subjects with stable CAD.

**Methods:** LBW (n=44, 54±3.7 kg) and HBW subjects (n=38, 84±14.9 kg) on aspirin were given clopidogrel 75 mg for 12 days. The area under the plasma concentration-time curve from dosing through last measurable concentration (AUC0-120 min) of clopidogrel active metabolite (AM) was calculated by noncompartmental methods. For PD analysis, light transmission aggregometry (LT A, using 5 μM ADP), VerifyNow P2Y12 (VN-PRU), and vasodilator-associated stimulated phosphoprotein (VASP-PRI) were performed.

**Results:** Mean AUC0-120 min of clopidogrel AM was lower in HBW than in LBW subjects, 12.7 and 18.4 ng*hr/ml, respectively (Figure). In PD analysis with VN-PRU and VASP-PRI, HBW subjects had higher platelet reactivity for both tests: PRU 207±68 vs. 102±57 (Figure), p <0.001, and PRI 56±18 vs. 29±6, p<0.001 (not shown).

More subjects exhibited high on-treatment platelet reactivity (HPR) using con-

**Conclusions:** Platelet transfusion restored completely ASA-dependent aggregability in all study groups.

---

**P1887**

Effects of ex vivo platelet transfusion on platelet aggregability in patients treated with clopidogrel or ticagrelor

E.C. Hansson, C. Hakimi, K. Astrom-Olsson, P. Albertsson, A. Jepsson, Sahlgrenska University Hospital, Gothenburg, Sweden

**Purpose:** Antiplatelet therapy reduces morbidity and mortality in patients with coronary disease but is also associated with an increased risk for bleeding. Platelet concentrate transfusion is often tried to restore platelet function when bleeding occurs but there is scarce knowledge about the efficacy. We as-

**Methods:** Platelet aggregability was investigated ex vivo with multielectrode impedance aggregometry with ADP and arachidonic acid as initiators in whole blood samples from healthy subjects without antiplatelet therapy (n=10), and in coronary artery disease patients treated with ASA (n=10), ASA+clopidogrel (n=10) or ASA+ticagrelor (n=8). Aggregability was measured before and after three doses of fresh platelet concentrate (+48, +96 and +144 h). The aggregability (mean ±SEM) is reported in arbitrary aggregation units (AU*min).

**Results:** ADP-induced aggregability was significantly reduced in ASA+clopidogrel and ASA+ticagrelor at baseline compared to healthy subjects and ASA. Baseline aspirin acid-induced aggregability was reduced in all three patient groups compared to healthy subjects. Addition of platelets had no effect on ADP-induced aggregability in healthy subjects and ASA-treated patients. In contrast, ADP-induced aggregability improved significantly in patients treated with ASA+clopidogrel and ASA+ticagrelor but the effect was limited, also with the highest dose of platelets (+144 h). HTPR rates remained high with both agents, perhaps suggesting the need of using an alternative antiplatelet agent.

---

**P1888**

Which component of the composite endpoints in P2Y12 inhibitor trials drives the benefit: a meta-analysis of randomized controlled trials with 136,117 patients

Z. Sergie1, U. Baber1, J. Yu1, N. Gukathasan1, P. Beam2, J. Collins2, J. Tamias3, R. Mehran2, Mount Sinai School of Medicine, Department of Cardiology, New York, United States of America; 1Gardner Caldwell Communications, Secaucus, NJ, United States of America; 2AstraZeneca, Welington, DE, United States of America; 3Mount Sinai Medical Center and the Cardiovascular Research Foundation, New York, United States of America

**Purpose:** Multiple randomized trials have shown that platelet P2Y12 receptor inhibitors significantly lower several cardiovascular endpoints in the setting of acute coronary syndromes (ACS). Traditionally combined endpoints have been used to evaluate the safety and efficacy of these agents. Whether or not the benefi-

**Methods:** We conducted a meta-analysis of all ACS randomized trials comparing a P2Y12 antagonist versus active control or placebo. We searched MEDLINE, EMBASE, Scopus, and Cochrane Controlled Trials Register (Central) databases from inception to December 2011 without language restriction. Data on the protocol-defined composite endpoints of major adverse cardiovascular events (MACE) were extracted, in addition to rates of death and myocardial infarction. Analysis were performed using an inverse variance weighted random-effects model.

**Results:** From a total of 2,347 articles, 179 underwent full-text review, and 13 met our inclusion criteria. Of these, 3 trials compared clopidogrel to placebo, 5 compared high dose vs. low dose clopidogrel, and 5 compared new vs. standard P2Y12 inhibitors. All patients received aspirin. The analysis included 136,117 pa-

**Conclusions:** P2Y12 antagonism is associated with significant reductions in MACE in ACS patients. This benefit is mostly driven by reduction of myocardial infarction rates, although a more modest concordant benefit is also observed in reducing mortality.
SAFETY AND EFFICACY OF ADJUVANT GLYCOPROTEIN 2B/3A INHIBITORS DURING PRIMARY PERCUTANEOUS CORONARY INTERVENTION (PCI) PERFORMED FROM THE RADIAL APPROACH FOR ST ELEVATION MYOCARDIAL INFARCTION (STEMI)


1 New York Beth Israel Medical Center, Newark, United States of America; 2 Pennsyvania Hospital, Philadelphia, United States of America; 3 SAMU, CHU, Lille, France; 4 Herzentrum Klinikum Ludwigshafen, Medizinische Klinik B, Ludwigshafen, Germany; 5 Wilhelminen Hospital, 3rd Department of Internal Medicine, Cardiovascular and Emergency Medicine, Vienna, Austria; 6 AP-HP - Hospital Lariboisiere, Clinical Research Unit, Paris, France; 7 SAMU Centre Hospitalier Carémeau, Nîmes, France; 8 AP-HP - Hospital Pitié Salpêtrière, Université Paris 6, Dept Cardiology-Medical ICU, Paris, France

Purpose: Use of glycoprotein 2b/3a inhibitors (GPI) in high risk acute coronary syndrome patients has demonstrated reduction in ischemic events with increase in bleeding complications. The role of GPI in patients who have PCI by transradial approach (TR) is not well studied. We conducted a post hoc analysis from the randomized prospective ATOLL trial (Intravenous enoxaparin or unfractionated heparin in primary percutaneous coronary intervention for ST-elevation myocardial infarction) to assess the safety and efficacy of GPIs performed TR.

Methods: 910 patients were enrolled in ATOLL. 592 (67%) had PCI via TR. We conducted two comparative analyses: 1) Patients with TR, with GPI vs. NO GPI. 2) TR with GPI vs. Transfermal (TF) with GPI. Composite endpoints of net clinical benefit, ischemic outcomes, and safety consisting of bleeding and transfusion at one month are illustrated in Table 1. We constructed a propensity score and made weight adjustment for variables including but not exclusive to: age, weight, gender, renal function, concomitant use of other medications, Killip class, and past medical history, when analyzing the endpoints.

Results: There was no significant difference in net clinical benefit or ischemic outcomes between: 1) TR patients with vs. without GPI, NOR 2) TR with GPI vs. TF with GPI. However, TR with GPI had the fewest ischemic events. Additionally, there were significantly less major bleeds and blood transfusion in TR with GPI vs. TF with GPI.

Conclusions: Addition of GPI in the setting of primary PCI by transradial approach adds no liability. Use of GPI with transradial approach is safer than transfemoral. Our study is limited by being a non-randomized retrospective analysis.

REGIONAL TRENDS IN DUAL ANTIPATELET THERAPY AMONG PATIENTS UNDERGOING PERCUTANEOUS CORONARY INTERVENTION: INSIGHTS FROM THE PARIS REGISTRY

G. J. Vlachojannis1, U. Baber1, S. Sartori1, D. Cohen2, D. J. Mokien3, P. G. Steg4, G. Weiss3, B. Wittenkeller3, A. Colombo4, R. Mehran5

1 Mount Sinai School of Medicine, Department of Cardiology, New York, United States of America; 2 St. Luke’s Mid America Heart Institute, Kansas City, United States of America; 3 University of Kentucky, Lexington, United States of America; 4 AP-HP - Hospital Bichat-Claude Bernard, Department of Cardiology, Paris, France; 5 Columbia University Medical Center, New York, United States of America; 6 Charlie - Campus Benjamin Franklin, Cardiology & Pneumology, Centre 11 (Cardiovascular Medicine), Berlin, Germany; 7 San Raffaele Hospital (IRCCS), Milan, Italy; 8 Mount Sinai Medical Center and the Cardiovascular Research Foundation, New York, United States of America

Purpose: Dual antiplatelet therapy (DAPT) is the cornerstone of medical therapy in patients with acute coronary syndromes or after intraocular surgery. Geographic patterns in the prevalence, modes and factors associated with non-adherence to DAPT in the US versus amongst patients undergoing percutaneous coronary intervention (PCI) with stent placement is not well characterized.

Methods: The PARIS registry is an ongoing multicenter, multinational, observational study following 5,033 patients who underwent PCI with bare metal or drug eluting stents. Modes of non-adherence were defined as discontinuation (per recommendation of physician who felt that therapy is no longer needed), interruption (e.g. surgery; physician-guided; DAPT must be reinstituted within 14 days) and discontinuation due to bleeding. We compared differences in the prevalence, modes and factors of 6-month DAPT non-adherence among US and European participants.

Results: The overall non-adherence rate was 9.2% at 6 months. Non-adherence was significantly more common among US (n=3666) compared to European (n=1367) participants (10.09% vs. 6.73%, p < 0.0001). Non-adherence mode also differed by region as discontinuation (5.6% vs. 1.5%, p < 0.0001) and interruption (1.94% vs. 95%, p < 0.0001) were more common in the US while patients in Europe showed a higher rate of DAPT disruption (4.24% vs. 2.59%, p < 0.0001).

Conclusion: DAPT non-adherence at 6-months post PCI is not uncommon, observed in 9% of patients. The incidence and modes of non-adherence also differ significantly between European and US patients. Whether or not these results reflect clinical, economic or socio-demographic differences between countries merits further evaluation.

GASTROINTESTINAL COMPLICATIONS WITH CLOPIDOGREL: A NATIONWIDE POPULATION-BASED COHORT STUDY

E. L. Grove1, M. Wurtz1, P. Schwarzw., N. R. Jorgensen2, P. Vestergaard3, 1 Aarhus University Hospital, Skejby, Aarhus, Denmark; 2 Glostrup Hospital, Copenhagen University Hospital, Glostrup, Denmark; 3 Aarhus University Hospital, THG, Aarhus, Denmark

Background: Clopidogrel prevents cardiovascular events and remains the second most prescribed drug worldwide. The use of clopidogrel has been linked with gastrointestinal complications, particularly bleeding events. We aimed to investigate the risk of gastritis, gastrointestinal ulcer or bleeding in patients treated with clopidogrel.

Methods: We conducted a nationwide population-based cohort study based on the Danish National Patient Registry.
on linkage of three administrative registries in Denmark. All individuals who re-
dezied at least one prescription of clopidogrel from 1996 to 2008 were included as exposed subjects (n=77,553). For each exposed subject, three matched con-
trols were randomly selected from the background population (n=332,510). The study population thus consisted of 310,013 subjects. Follow-up began on Jan-
uary 1, 1996, and was censored on December 31, 2007, or if patients emigrated 
or died. The study endpoint was any event of gastritis, gastrointestinal ulcer or 
bleeding. Analyses were adjusted for comorbidity and medication.

Results: Regardless of dose, adjusted odds ratios associating clopidogrel use with 
the study endpoint were statistically significant and followed a dose-response 
pattern. Accordingly, increasing doses of clopidogrel yielded increasing odds ra-
tios of suffering gastritis or gastrointestinal ulcer or bleeding (odds ratios 1.3-1.9, 
p<0.01). Depending on the dose, numbers needed to harm ranged from 33 to 58 
patients receiving 12 months of clopidogrel treatment.

Conclusions: Clopidogrel is associated with an increased dose-dependent risk 
of gastritis, gastrointestinal ulcer or bleeding. The well-known cardioprotective ef-
fect of clopidogrel must be carefully weighed against an increased risk of gas-
trointestinal complications.

**P1893** Can platelet function test predict safety of prasugrel 
after an ACS?

G. Cayla1, T. Cuisset2, J. Silvain3, S. O'Connor3, M. Kerneis3, 
J. Quilici1, J.L. Bonna2, M.C. Alessi2, J.P. Collet2, G. Montalescot2
1University of Nimes, Department of Cardiology, Nimes, 
France; 2AP-HM - Hospital La Timone, Marseille, France; 3UMR 5956, 
Inserm, University Pierre & Marie Curie (UPMC) Paris 6, Paris, France

Objectives: To evaluate platelet reactivity 30 and 60 day bleeding events in patients 
treated with prasugrel 10 mg after an acute coronary syndrome (ACS).

Methods: In two high volume centers, 444 ACS patients revascularized with 
PCI were treated with a maintenance dose of prasugrel 10mg/day. On-treatment 
platelet reactivity was measured 2 to 4 weeks after discharge by the Vasodilator-
stimulated phosphoprotein (VASP) index. Additional measures with the VerifyNow 
P2Y12 assay and Light Transmission Aggregometry were also performed. Bleed-
ings events (Bleeding Academic Research Consortium (BARC) definition) and is-
chemic events (death, myocardial infarction, and definite stent thrombosis) 
were collected over 30 days of follow-up.

Results: Two thirds of the patients presented with an ST-segment elevation my-
cardial infarction, 28.8% were diabetics and 12.4% were more than 75 y/o. PCI 
was performed through a radial access in 96.4% of patients. High on-treatment 
platelet reactivity (HPR) according to three prespecified definitions (VASP≥50%, 
P2Y12 reaction units (PRU)≥235, residual platelet aggregation (RPA) ≥46.2%) 
was found in 6.8%, 3.4% and 3.2% of patients, respectively.

Conclusion: These data suggest test predictive safety of prasugrel after ACS.

**P1895** Interaction between the effect of abciximab plus 
unfractionated heparin therapy versus bivalirudin 
therapy and the extent of preprocedural myocardial 
injury among patients with non-ST-segment elevation 
myocardial infarction (NSTEMI) undergoing percutaneous coronary intervention (PCI) 
as compared to bivalirudin. However, the interaction of these antithrombotic drugs 
with the severity of the heart attack was not fully elucidated.

Methods: In the patient cohort from ISAR-REACT-4, a double-blind randomized 
trial comparing antithrombotic therapy with abciximab plus unfractionated heparin 
to the therapy with bivalirudin, we divided the patients into quartile groups accord-
ing to the preprocedural Troponin-T level (Q1: 403 patients, Q2: 444 patients, Q3:
438 patients, Q4: 436 patients) and compared outcome. The primary endpoint 
was a composite of death, large recurrent MI, urgent target- vessel revascular-
ization (TVR), or major bleeding within 30 days. Secondary endpoints included 
the composite of death, any recurrent MI (efficacy endpoint) and major bleeding 
(safety endpoint) within 30 days.

Results: There was no significant interaction regarding the primary endpoint be-
tween troponinlevel and antithrombotic therapy (Q1: 7.4% vs 6.1%, p=0.61, Q2: 
9.1% vs 7.5%, p=0.55, Q3: 10.6% vs 14.0%, p=0.29, Q4: 16.1% vs 16.4%, 
p=0.94, for patients treated with abciximab plus unfractionated heparin and 
the patients treated with bivalirudin, respectively). The results regarding the sec-
dary endpoints are shown in the figure.
Conclusions: In patients with NSTEMI undergoing PCI, the extent of preprocedural myocardial injury does not affect the relative merits of the abxicimab plus unfractionated heparin versus bivalirudin observed in the overall cohort.

P1896 Surgery after coronary stenting: the role of antiplatelet therapy on ischemic and hemorrhagic complications

R. Rossini, G. Musumecci, D. Capodanno, P. Calabria, U. Limbruno, C. Lettieri, D. Iaccarino, N. Russo, A. Inashvili, G. Gaggioli, E. Ginibelli, I. Belfrondi, M. Ferri, C. Giordano, F. Angiolini, S. Greco, F. Baccarani, M. Umani, G. Iaccarino, T. Krima. 1Ferrara Hospital - Institute for Cardiology, Department of Cardiovacular, Catania, Italy; 2Messicordia Hospital, Department of Cardiology, Grosseto, Italy; 3Ospedale Carlo Poma, Mantova, Italy

Purpose: Interruption or maintenance of oral antiplatelet therapy (OAT) during an invasive procedure may result in ischemic or hemorrhagic complications, respectively. Currently, there is limited guidance on management of OAT during surgical procedures. The aim of this study is to evaluate the rate of major adverse cardiac and cerebrovascular events (MACCE), as well as major or minor bleeding complications, and their associated independent correlates in coronary stented patients undergoing urgent or planned non-cardiac or cardiac surgery.

Methods: This study included 393 consecutive patients with coronary stents undergoing surgery from March 2003 to July 2011. The primary safety endpoint consisted of the incidence of in-hospital MACCE, defined as death, acute myocardial infarction, acute coronary syndrome (ACS) leading to hospitalization, stent thrombosis, acute heart failure, and stroke. Major bleeding was defined according to TIMI criteria.

Results: The rate of DES use was 59%, with an average of stent length of $22 \pm 5$ mm (52% of PCI were performed during ACS). 37% of patients were on dual antiplatelet therapy at the time of surgery and time from PCI to surgery was $510 \pm 468$ days. At the time of surgery, 57.7% of patients discontinued any antiplatelet therapy $\geq$ 5 days (16.4% of patients discontinued both antiplatelet drugs; 7% discontinued only clopidogrel and 34.3% discontinued only aspirin). The mean time of withdrawal was 5.0 days. At 30-day, the overall incidence of MACCE and TIMI major bleeding was 9.1% and 13%, respectively. The incidence of MACCE in patients who discontinued antiplatelet therapy $\geq$ 5 days was 12.1% versus 8.2% in patients who maintained the antiplatelet therapy (p=0.41). The incidence of TIMI major bleeding was 14.3% in patients who discontinuated antiplatelet therapy $\geq$ 5 days versus 11.0% in those who maintained the antiplatelet therapy (p=0.07). Prior myocardial infarction was identified as independent predictor of MACCE. There was no independent correlate of TIMI major bleeding.

Conclusions: Patients with coronary stents remain at high risk for surgery even if surgery is performed $\geq$ 1 year after PCI. The maintenance of the oral antiplatelet therapy might play a protective role, without increasing bleeding complications.

P1897 Spaced administration of PA32540 and clopidogrel results in greater platelet inhibition than synchronous administration of enteric-coated aspirin, enteric-coated omeprazole, and clopidogrel

P.A. Gretel, K.P. Bilden, J.G. Fort, Y.-H. Jeong, G. Shulderiner, T. Geshelli, M. Antonino, M. Geshelli, Y. Zhang, U. Tarnett, S. Paul. 1Sinai Center for Thrombosis Research, Baltimore, United States of America; 2Pzen Inc. Chapel Hill, NC, United States of America; 3University of Maryland School of Medicine, Baltimore, United States of America

Background: A common regimen for patients requiring dual antiplatelet therapy who are at-risk of gastrointestinal complications is the synchronous administration of enteric-coated (EC) aspirin, a proton pump inhibitor (PPI), and clopidogrel, although PPIs have the potential for pharmacodynamic interaction with clopidogrel. Spaced administration of a clopidogrel and a single tablet formulation of aspirin and immediate-release omeprazole (PA32540) was considered as an alternative that might reduce this pharmacodynamic interaction.

Methods: A randomized, open-label, crossover study was conducted in healthy subjects (n=30). Two 7-day treatments were separated by 14-day washout periods: A) PA32540 + clopidogrel (300 mg loading/75 mg maintenance), 10 hours later B) EC ASA (81 mg) + EC omeprazole (40 mg). The primary endpoint was the inhibition of platelet aggregation (IPA, 20, M ADP, maximal extent) after 7 days. CYP2C19 and ABCB1 genotypes were determined.

Results: IPA was greater with spaced PA32540 + clopidogrel therapy vs. synchronous clopidogrel + EC ASA + EC omeprazole therapy (p = 0.004). There was no difference in day 7 arachidonic acid-induced aggregation. The effect of spacing on pharmacodynamics was independent of genotype.

Conclusions: PA32540 and clopidogrel spaced 10 hours apart had greater antiplatelet effects than synchronously administered EC aspirin (81 mg), clopidogrel (75 mg), and EC omeprazole in healthy volunteers. These findings are directly relevant to the treatment of patients with high gastrointestinal risk who require dual antiplatelet therapy and gastroprotection.

P1898 The efficacy of high dose clopidogrel for the patient with stable coronary artery disease in Japanese population: the primary result from the choice trial

J. Tazaki, H. Horuchi, A. Hirayama, M. Ito, S. Oshima, T. Morimoto, T. Kimura. 1Keio University Graduate School of Medicine, Department of Cardiovascular Medicine, Tokyo, Japan; 2Tokoh University, Institute of Development, Aging and Cancer, Sendai, Japan; 3Niho University School of Medicine, Department of Cardiovascular Medicine, Division of Cardiology, Tokyo, Japan; 4Me University Graduate School of Medicine, Department of Cardiology and Nephrology, Tsu, Japan; 5Gunnja Percutaneous Cardiovascular Center, Division of Cardiology, Nara, Japan; 6Kinki University, School of Medicine, Osakasayama, Japan

Backgrounds: Dual antiplatelet therapy of aspirin and clopidogrel is most commonly used to prevent cardiovascular events after percutaneous coronary intervention (PCI). Clopidogrel is a produgucitated by CYP enzyme families. Several studies have reported the activity-defective CYP2C19 polymorphisms reduce the antiplatelet effect of clopidogrel and associate with cardiovascular event, and CYP2C19 polymorphism is more common in Asian population. Standard dose of clopidogrel is 300 mg loading dose (LD) and 75 mg maintenance dose (MD). High LD and MD had been reported to inhibit platelet aggregation more rapidly and strongly, and prevent thrombotic event around the PCI for Western population. The efficacy of high dose clopidogrel for Asian population is still unclear.

Objective: The aim of this study is to evaluate the efficacy of high dose clopidogrel in Japanese patients.

Methods and Results: CHOICE trial (ClopidogrelHigh dose evaluation for the patient with Coronary artery disease in Japan) is a multicenter, prospective, randomized trial undertaken 4 centers in Japan between March 2010 and December 2011. Patients with low dose aspirin and scheduled PCI due to stable coronary artery disease were randomly assigned to High dose-LD (600 mg on day 1) versus standard-dose LD (300 mg on day 1), and high-dose MD (150 mg on days 2-7, then 75 mg daily) versus low-dose MD (75 mg daily). The primary endpoint is inhibition of platelet aggregation (IPA) at 24 h after LD and secondary endpoint is IPA on 7 day with MD. Among 102 patients enrolled in study, 49 patients assigned to High LD and MD and 53 patients to standard LD, and 44 patients to high MD and 42 patients to standard MD, and 62 patients (61%) had activity-defective CYP2C19 polymorphisms. The IPA at 24 h were significantly higher in High LD group (25.8±15.6% vs. 16.4±25.0, p=0.0087: 5 μM ADP, 20.7±14.7% vs. 14.7±17.7, p=0.032: 20 μM ADP). The IPA at 7 day were also higher in High MD group (28.3±19.0% vs. 22.2±14.7, p=0.09: 5 μM ADP, 25.9±16.0% vs. 18.6±13.4, p=0.034: 25 μM ADP).

Conclusions: Consistent with other randomized trials, high dose clopidogrel was effective in Japanese population, which have more activity-defective CYP2C19 polymorphisms than Western populations.

P1899 Differential impact of omeprazole, pantoprazole and CYP2C19 on clopidogrel pharmacokinetics and pharmacodynamics in stable coronary artery disease patients

J.-P. Collet, N. Simon, J. Finzi, G. Cayla, J. Silvain, G. Montalescot, J.-S. Huluot on behalf of ACTION. 1AP-HP - Hospital Pitie-Salpetriere, Paris, France; 2AP-HM - Hospital La Timone, Marseille, France

Background: PPI use and CYP2C19 LOF alleles are associated with reduced responsiveness to clopidogrel and increased cardiovascular events.

Objectives: To evaluate the interaction between PPI and PK and PD responses to clopidogrel loading doses (LDs) according to CYP2C19*2 allele.

Methods: Young post-MI patients heterozygous (wild type [wt]/*2, n= 43) or homozygous (*2/*2, n= 8) for the CYP2C19*2 LOF were matched with patients not carrying the variant (wt/wt, n=58). All patients were randomized to a 300- or 900-mg clopidogrel LD, 48 patients were receiving PPIs (26 on omeprazole [OPZ] or esomeprazole [EPZ], and 22 on pantoprazole [PTZ]). The relative reduction in residual platelet aggregation (RR-IPA, %) and the area under the plasma concentration time-curve of active metabolite from baseline to 6 h after loading (AUC0-6) were compared according to PPI use and CYP2C19*2 allele.

Downloaded from https://academic.oup.com/eurheartj/article-abstract/33/suppl_1/19/430790 by guest on 11 March 2019
Results: After a 300 mg clopidogrel LD, the maximal clopi-H4 concentrations and the AUC0-6 were significantly lower in PPI users vs. non-users. This reduction was only observed in patients exposed to OPZ/EPZ (p<0.01 for both Cmax and AUC0-6 but not PTZ (p=0.26 and p=0.38 for Cmax and AUC0-6 respectively). Similar trends were observed with the 900mg LD.

In multivariable linear regression, the use of OPZ/EPZ and CYC2019’2 allele were significant predictors of clopi-H4 Cmax and AUC0-6 (AUC0-6: p<0.05; AUC0-6 900mg: p<0.01). A sigmoid function with a gamma exponent best described the relationship between IPA (%) and the Clopi-H4 AUC (%g/L). There was no significant interaction between CYC2019’2 and PPI status.

Conclusions: Both CYC2019’2 and PPI status independently affects clopidogrel active metabolite generation and its antiplatelet effect which correlate as a sigmoid function with a cut-off value of 16 %g/L.

P1900
Third generation P2Y12 antagonists inhibit platelet aggregation more effectively than clopidogrel in a real world myocardial infarction registry

C.B. Olivier1, C. Brandt1, Q. Zhou1, P. Weik1, P. Diehl2, C. Bode1, M. Moser1, 1Albert-Ludwig University of Freiburg, Department of Cardiology and Angiology, Freiburg, Germany; 2Baker IDI Heart and Diabetes Institute, Melbourne, Australia

Introduction: The current standard of secondary prevention of atherothrombotic events includes acetylsalicylic acid (ASA) accompanied by the P2Y12 receptor antagonist with or without co-clopidogrel. In the real world myocardial infarction registry MITAP (registry for patients after Myocardial Infarction Treated With Antiplatelet agents - DRKS00003146) we analysed the antiplatelet effect of ticagrelor, prasugrel and clopidogrel in patients after myocardial infarction and coronary stenting.

Methods: Multiple electrode aggregometry was performed in whole blood of patients on day 3-5 after myocardial infarction. To specifically quantify the effect of P2Y12 antagonists, whole blood was stimulated with 6.4 μM ADP. To assess the overall capacity the platelet aggregation was quantified by stimulation with TRAP (final concentration 32 μM). Relative ADP induced aggregation (r-ADP-agg) was defined as the ADP-TRAP-ratio to reflect an individual degree of P2Y12 dependent platelet inhibition. Patients were grouped as follows: (1) 180 mg ticagrelor per day, (2) 10 mg prasugrel per day and (3) 75 mg clopidogrel per day.

Results: From July 2011 to February 2012 MITAP recruited 118 patients after myocardial infarction and percutaneous coronary intervention. Patients were grouped according to the antiplatelet medication: ticagrelor (n=49), prasugrel (n=38) and clopidogrel (n=31). Women were more frequent in the clopidogrel group (61% vs. 37% with ticagrelor and 42% with prasugrel), p<0.001. A sigmoid function with a gamma exponent best described the relationship between IPA (%) and the Clopi-H4 AUC (%g/L). There was no significant interaction between CYC2019’2 and PPI status.

Conclusions: Both CYC2019’2 and PPI status independently affects clopidogrel active metabolite generation and its antiplatelet effect which correlate as a sigmoid function with a cut-off value of 16 %g/L.

P1901
High-dose atorvastatin enhances antiplatelet effects of double-dose clopidogrel

A. Tosa1, M. Leoncini1, M. Maccini1, R. Marucchi2, B. Giusti2, R. Abbate2, D.J. Angiolillo3, F. Bellandi1. 1Misericordia e Dolce Hospital, Department of Cardiology, Prato, Italy; 2Department of Medical and Surgical Critical Care, University of Florence, Florence, Italy; 3Division of Cardiology, Department of Medicine, University of Florida College of Medicine, Jacksonville, United States of America

Purpose: Patients with high residual platelet reactivity (HRPR) are at increased risk of adverse cardiovascular events after PCI. High-dose statins improve prognosis in high-risk patients by lipid and non-lipid related mechanisms including the antithrombotic effect. This study investigates the enhancing effects of atorvastatin on platelet responsiveness to high-dose (150 mg) clopidogrel in stable CAD patients presenting pre-PCI HRPR on standard-dose clopidogrel.

Methods: The ACHIDOC (Atorvastatin and Clopidogrel High DOSE in stable patients with residual high platelet activity; ClinicalTrial.gov: NCT03135048) study was a randomized study of platelet inhibition by high-dose (80 mg) atorvastatin in addition to high-dose (150 mg) clopidogrel (Atorvastatin group, n=48) versus high-dose (150 mg) clopidogrel alone (Control group, n=38) in patients with HRPR (P2Y12 reaction units (PRU) ≥ 235; VerifyNow assay). Platelet reactivity was evaluated immediately before PCI and at 10 and 30 days.

Results: Atorvastatin presented significantly lower platelet reactivity and HRPR rate at 30 days than controls (Table). Statin treatment was found to be an independent predictor (OR 6.38, p =0.01) of full responsiveness at 30 days, on par with baseline PRU < 298 (OR 14.97, p <0.001) and non-carrier status of HRPR (p<0.05 versus Pre-PCI values; p=0.05 Atorvastatin versus Control group).

Conclusions: Aggressive statin treatment significantly potentiates platelet response to double-dose clopidogrel in stable CAD patients presenting pre-PCI HRPR on standard-dose clopidogrel.

P1902
Clinical characteristics associated with major bleeding in NSTEMI ACS and the relationship between bleeding risk, ischemic events, and the vorapaxar effect: analysis from the TRACER trial

P. Tricoci1, Z. Huang1, H.D. White1, F. Van De Weer2, L. Wallentin1, P. Aylward1, P.W. Armstrong3, E. Chen4, D.J. Moliterno5, R. Harrington6, 1Duke Clinical Research Institute, Durham, NC, United States of America; 2Green Lane Cardiovascular Service, Auckland City Hospital, Auckland, New Zealand; 3University of Leuven, Leuven, Belgium; 4Uppsala Clinical Research Center, Uppsala, Sweden; 5Finders Medical Centre, Adelaide, Australia; 6University of Alberta, Edmonton, Canada; 7Merck Research Laboratories, Kenilworth, New Jersey, United States of America; 8University of Kentucky, Lexington, United States of America

Purpose: Potent antiplatelet therapy is associated with increased major bleeding. In TRACER, we observed modest efficacy and significant increased bleeding with vorapaxar when added to standard of care. We sought to understand clinical characteristics predicting bleeding in the TRACER population and the relationship between bleeding risk, ischemic event risk, and vorapaxar effect.

Methods: TRACER included 12,966 pts with NSTEMI ACS. Inclusion criteria aimed to include high-risk groups (elderly, elevated biomarkers, and prior CV disease). Using 34 pre-randomization characteristics, a Cox model was developed to predict major bleeding (composite of TIMI major, GUSTO severe, or moderate bleeding), Association of predicted bleeding risk with the risk of ischemic events (CV death, MI, stroke) and with vorapaxar efficacy was investigated.

Results: 9 variables were independently associated with risk of major bleeding (p<0.01): age (7.1), PAD history (7.3), tobacco use (past, 4.4; current, 6.2), creatinine clearance (5.5), hemoglobin at presentation (12.4), T-wave inversion on ECG (3.3), Killip class 3-4 (9.4), use of GP IIb/IIIa inhibitor (10.6) (c-index, 0.70). Using the model, we predicted pts’ risk of bleeding at 1 year. Risk of ischemic events increased with increased risk of bleeding. However, there was no evidence of enhanced efficacy of vorapaxor antiplatelet with increased bleeding and ischemia risk (Figure).

Figure 1. Key secondary efficacy endpoint event rate by randomized treatment by risk of bleeding.

Conclusion: A model based on clinical variables may help identify NSTEMI ACS pts who have a high risk of major bleeding, which correlates with more ischemic events. Despite the concomitant increase risk of ischemic events, the addition of vorapaxor to standard of care did not show incremental benefit in pts at high risk of bleeding, suggesting the need for careful selection of pts for this strategy.
Prasugrel versus clopidogrel in daily clinical practice in patients undergoing primary PCI in the Austrian acute PCI registry

J. Doerfer1, F.X. Roithinger2, M. Juhász2, W. Benzer2, R. Zweker2, P. Szoterek1, J. Auer2, H. Schuchert2, O. Pachinger3, F. Weidinger3 on behalf of The Austrian Acute PCI Investigators. 1Innsbruck Medical University, Department of Internal Medicine III, Cardiology, Innsbruck, Austria; 2Hospital Moeding, Department of Cardiology, Moeding, Austria; 3Hospital Barmherzige Brüder, Department of Medicine, Eisenstadt, Austria; 4Academic Hospital, Department of Interventional Cardiology, Feldkirch, Austria; 5Medical University of Graz, Department of Cardiology, Graz, Austria; 6Hospital Barmherzige Schwarzenberg, Department of Internal Medicine/Cardiology, Linz, Austria; 7St. Josef Hospital, Department of Medicine, Braunaun, Austria; 8LKH Gmunden, Department of Cardiology and Intensive Care Medicine, Graz, Austria; 9Rudolfstiftung Hospital, Department of Internal Medicine II, Vienna, Austria

Background: Prasugrel is recommended as first line drug for dual antiplatelet therapy after primary PCI (PPCI) in St-Elevation myocardial infarction (STEMI). There are few data on its use in daily practice of PPCI and clinical outcome in comparison with clopidogrel.

Methods: 2454 consecutive patients with STElevation myocardial infarction undergoing PPCI between January 2010 and December 2011 and receiving either prasugrel or clopidogrel before arrival in the catheter laboratory were enrolled. Evaluation included baseline characteristics and in-hospital outcome. In addition, logistic regression analyses were performed to determine indicators for prasugrel treatment.

Results: 2017 (82.2%) patients received clopidogrel and 437 (17.8%) received prasugrel. The mortality on prasugrel was younger (56.0 vs. 69.6 years), p=0.01), more often male (71.1% vs. 80.8%, p<0.01) and current smokers (58.4% vs. 43.3%, p<0.01), but had less previous PCI (9.2% vs. 12.5%, p<0.01). Direct field triage was more common in the prasugrel group (73.7% vs. 63.8%, p<0.01) resulting in a shorter delay to PPCI (3.98h [1.93–5.71] vs. 3.57h [2.23–6.69], p<0.01). In-hospital mortality was lower in the prasugrel group (1.8% vs. 4.7%, p<0.01) with no difference in TIMI major bleedings between prasugrel (0.2%) and clopidogrel (0.9%, p=0.24). Multivariable logistic regression analysis revealed that age (HR 0.97 95% CI 0.96-0.98 per year; p<0.01), sex (male HR 0.69 95% CI 0.51-0.94; p<0.01) and direct field triage (HR 1.59 95% CI 1.21-2.09; p<0.01) were independent predictors of prasugrel treatment.

Conclusion: In clinical practice prasugrel is predominantly used in younger male patients transferred directly from the field to PCI. These factors may result in lower in-hospital mortality with similar TIMI major bleeding rates compared to clopidogrel.

Clopodogrel plus indobufen in patients with hypersensitivity to aspirin undergoing percutaneous coronary intervention

F. Barilla, T. Dominici, G. Pamarale, F. Giordano, I. Jacomelli, E. De Vito, C. Gaudio on behalf of Francesco Barilla, et al., Sapienza University of Rome, 1st Faculty of Medicine, Dept of Heart & Great Vessels ‘A. Reale’, Rome, Italy

Background: Aspirin (ASA) in combination with a thienopyridine represents the standard antiplatelet treatment. Following revascularization by percutaneous coronary angioplasty (PCI) with the goal of reducing life-threatening stent thrombosis. However, the prescription of ASA could be harmful in a small, but significant number of patients with a history of severe hypersensitivity to the drug.

Purpose: The aim of the study was to assess the antiplatelet activity and safety of a combined antiplatelet treatment with indobufen and clopidogrel in acute coronary syndrome (ACS) patients with hypersensitivity to aspirin, undergoing coronary stenting.

Methods: Between April 2005 and December 2008, among 1045 ACS patients treated with PCI and stent implantation, we identified 42 (4%) consecutive patients known to be hypersensitive to ASA. Of them, 30 male and 12 female (mean age 61.6±10.9 years), 19 patients had a NSTEMI and 23 patients a STEMI. Definition of allergy to aspirin included: cutaneous sensitivity (urticaria in 23 patients, angioedema in 12 patients, wheezing and/or rhinitis in 10 patients (oral, contact and/or inhalation) in 3 patients (21.5%), bronchospasm and/or rhinitis in 1 patient (7.1%), anaphylactic reaction in 5 patients (11.9%) and Quincke’s edema in 4 patients (9.6%). The patients were randomly assigned to receive clopidogrel 75 mg daily (loading dose 300 mg) plus indobufen 100 mg twice a day (group A), or clopidogrel 75 mg daily, after 300 mg of loading dose (group B). Platelet activity and safety were monitored in both groups at 1, 3, 6, 12 and 18 months with laboratory and clinical evaluation. Platelet aggregation activity was tested by the Born’s method.

Results: A lower value of Max % platelet aggregation to arachidonic acid and col-lagen at a dosage of 4-5 pg/ml in group A compared to group B (31.7±27.33 vs 73.67±19.92; p<0.001 and 28.53±21.32 vs 73.68±17.71; p=0.001, respectively). There was no difference in Max % of platelet inhibition to ADP between the two groups (14.23±19.92 vs 10.30±18.97; p=0.23). Three patients (14.3%) in group B (2 with DES and 1 with a BMS) developed an ACS within the first 6 months of follow-up. The coronary angiography documented a sub-occlusive stents thrombosis. No patient developed a cardiovascular event in group A. The combined treatment was well tolerated in group A patients.

Conclusion: This study suggests that the combined antiplatelet treatment with Clopidogrel and indobufen could be an alternative medication in ACS patients with hypersensitivity to aspirin undergoing coronary stenting.

Antiplaete agents / Novel data on cardiomyopathies 323

P1905 Fetal stem cells in combined treatment of chronic heart failure with left ventricular systolic dysfunction: results after 6 months

M.O. Klunyuk, N.S. Sych, O.V. Ivankova. Embryonic Tissues Center EmCell, Kiev, Ukraine

Background: Chronic heart failure (CHF) is one of the topical health issues in all the developed countries calling for novel treatment methods. Conventional medical treatment does not disregard cardiacomyocyte reduction as one of CHF causes, and only transplantation of poorly differentiated cells with high proliferative and differentiation capacity can affect pathogenesis of this disease.

Goal of the study was study effect of fetal stem cell transplantation (FSC) in CHF. Materials and Methods: Study group included 7 patients (M:6, F:1, mean age 63.6±8.7 years) with Class III-IV CHF caused by ischemic cardiomyopathy (72.7%), alcohol-induced cardiomyopathy (13.6%), dilatation cardiomyopathy (13.6%). CHF was diagnosed on the basis physical examination, laboratory (BNP) and in-recovery findings (Echo-CG, EF,EFF).

All patients underwent transplantation of fetal hematopoietic mesenchymal and endodermal cells harvested from germ layers of internal organs of 5-8 weeks old cadaverous fetuses. 1, 3 and 6 months after the treatment, patients underwent physical examination, Echocardiography and BNP test.

Results and Discussion: FSC resulted in • NYHA Class downgrading • Higher quality of life score • Improved tolerance (6-minute test) • Reliable serum BNP reduction by 33.75% 1 month after FSC, 57.17% after 3 months • No reliable LVED volume increase after 1 month, 10.5% increase after 3 months, 20.92% - after 6 months • Reliable LVED reduction 1 months after FSC – 7.85%, 3 months – 11.49%, 6 months – 20.51%. Myocardium function restoration can be achieved through the increase of functional reserve of cardiomyocytes and, probably, their number increase through stimulation of hyperplasia, neoangiogenesis, and apoptosis inhibition.

Conclusions: FSC transplantation is safe and effective way of treatment that can be used as supportive treatment in patients waiting for heart transplantation, as preparation for reconstructive heart surgery and as substitution of post-infarction fibrous tissues with viable cardiomyocyte-like cells.

P1906 Left ventricular dysfunction is induced shortly after the deprivation of dietary choline in adult rats

A. Strilakou1, I. Mourouzis1, A. Perelas1, A. Lazaris2, I. Doulias2, A. Stylianaki1, C. Pantos1, C. Liapi1, P. Stamatelos1, I. Douzis2, N. Tzagarakis2, K. Psaltides1, I. Chalepas1, I. Lazopoulou1, M.O. Klunnyk, N.S. Sych, O.V. Ivankova. Embryonic Tissues Center EmCell, Kiev, Ukraine

Background: Choline is an essential nutrient that is involved in a variety of vital bi- logical functions. Choline deficiency seems to impair heart function and ani- mals consuming inadequate amounts of choline develop significant cardiovascular morbidity. Taking into consideration that choline deficiency is frequently ob-served in the clinical setting such as in patients depending on parenteral nutrition and in patients with cirrhosis or renal failure, the investigation of its effect on heart mechanical properties would be of clinical importance. The present study evalu- ated the effects of choline deficiency on the functional parameters of the heart in adult rats.

Methods: Wistar Albino male rats, about 3 months old, were randomly separated into two groups: a) rats receiving standard laboratory diet (control-CA) and b) rats receiving choline deficient diet (CD). Water and food were provided ad libitum; the duration of the dietary manipulation was four weeks. All animal procedures were carried out in accordance with the principles of the “Guide to the Care and Use of Experimental Animals”. After four weeks of treatment, cardiac function was assessed under isometric conditions in the Langendorff preparations. Left Ventricle Developed Pressure (LVPD), Positive and Negative first derivative of LVPD (+/dP/dt) and (-/dP/dt) were evaluated. Histopathological evaluation of the hearts specimens was performed using Eosin-Hematoxylin and Masson stains.

Results: Diastolic left ventricular function, assessed by (-/dP/dt), was significantly impaired in the CDG group compared to the control group [1911.42 (229.45) vs 2311.9 (288.56); p=0.026] CA). A trend towards compromised left ventricular function as assessed by LVPD in the CDG group compared to the control group [102.14 (8.7) vs 122.5 (13.5); p=0.07] was noted. Systolic force, represented by (+/dP/dt), showed no statistical difference between groups. Histopathology re-
Infarct size-determined uptake of CD34+ cells in the peri-infarct zone and left ventricular remodeling: Insights from integration of labeled cells SPECT visualization with sequential cardiac MRI

P. Musialek1, L. Tekieli1, M. Kostkiewicz1, T. Miszalski2, W. Sztol3, W. Mazur4, R.P. Banya5, D.J. Kereiakes6, P. Podolska6, W. Wojakowski6, 1Jagiellonian University, John Paul II Hospital, Dept of Cardiac & Vascular Diseases, Krakow, Poland; 2Centre for Diagnosis, Prevention and Telemedicine, John Paul II Hospital, Krakow, Poland; 3Linder Center for Research and Education, Christ Hospital Heart and Vascular Center, Cincinnati, Ohio, United States of America; 4Medical University of Silesia, 3rd Department of Cardiology, Katowice, Poland

Infarct size (IS) is a well-established determinant of adverse LV remodeling. Experimental evidence indicates that attenuation of LV remodeling is critically dependent on salvage of apoptosis-prone myocytes in the peri-infarct zone. Objectives: To investigate relationships between myocardial uptake of transcoronary-delivered autologous bone marrow CD34+ cells in recent MI, IS and LVEF in the context of chronic LV remodeling.

Methods and Results: Thirty-one subjects (age 36-69 years) with pPCI-treated anterior STEMI, peak Troponin T (TnT) ≥ 1.6 μg/l (median [range]) and sustained LVEF ≤ 45% were recruited. On day 10 (±3), 1.4-106 [0.7-2.9 x 1011] 99mTc-extametazime-labeled CD34+ cells were administered transcoronary (LAD). Gadolinium late-enhanced total infarct mass (IS, cMRI) was 57 [11-112] g. One hour after administration, 1.7-9.9% labeled cells activity localized in myocardium. LE at 2 years (r = -0.6, p < 0.0001) and severely impaired perfusion segments number (SPECT, O coefficient = 0.83, p = 0.01), IBZ mass correlated with LVEF ≤ 0.6, p = 0.0006) and severely impaired perfusion segments number (SPECT, O coefficient = 0.83, p = 0.01), IBZ mass correlated with LVEF (0.8 vs. baseline LVEF). With the peri-infarct zone cell uptake proportional to IS, IS was not a determinant of ALVESV (p = 0.41) or ALVEDV by cMRI (p = 0.06) (Figure 1, *p < 0.001).

Conclusion: This largest human study with labeled CD34+ cell transplantation after recent STEMI suggests that the higher cell uptake in the peri-infarct zone in subjects with larger infarcts might be associated with improvement of LV remodeling. Further strategies should focus on boosting this effect.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.

Protein lysates from frozen myocardium were analyzed for the expression of calcineurin isoforms by Western blotting and their activation by immunofluorescence.

Conclusions: In the absence of angiotensin II, calcineurin was activated in both CDD and control hearts. In the presence of angiotensin II, calcineurin was activated to a greater extent in the CDD hearts. The activation of calcineurin in the CDD hearts was associated with an increase in the expression of the calcium/calmodulin-dependent kinase II (CaMKII) and protein kinase C (PKC) pathways.

-electronic deposition of labeled cells with anti-CD34 Abs. The labeled cells were injected into the left ventricle through a coronary artery, and the distribution of labeled cells was assessed using SPECT imaging.

Figure 1

Conclusion: This study demonstrated that fibrin-based patch is a suitable substrate for hAMSC proliferation and differentiation towards cardiogenic lineage. Using this patch as a delivery system, the cells would be provided with a firm, flexible support, allowing a direct application onto the infarct site without cell loss and providing a site-directed repair.
Targeted ablation of the plasma membrane calcium ATPase (PMCA) 1 indicates a crucial role in heart failure

M. Shaheen, M. Z., S. Prehar, T.M.A. Mohamed, N. Stafford, Y. Wang, M. Lei, C. Austin, L. Neyses, E.J. Cartwright. University of Manchester, School of Medicine, Manchester, United Kingdom

Currently, up to 14 million people in Europe have heart failure (HF). Since the yearly incidence of heart failure in persons aged 55 years is 15 per 1,000 of the population, it is important to provide new insights into disease development and progression. Recent several genome-wide association studies have identified single nucleotide polymorphisms (SNPs) in the PMCA1 gene as the single strongest association with blood pressure variance in humans. In spite of that, the role of PMCA1, a transmembrane calcium transporter known to eject calcium from the cell, in heart failure remains enigmatic. Our recent experiments have shown that the protein expression of PMCA1 is significantly downregulated in human heart failure patients. Therefore, to further analyze the role of PMCA1 in cardiac disease we have generated mice carrying a cardiomyocyte-specific gene deletion of PMCA1 (PMCA1cko) using αMHC-Cre. PMCA1cko mice subjected to pressure overload induced by transverse aortic constriction (TAC) showed overt HF. TAC decreased fractional shortening (FS) in PMCA1cko in comparison to their age-matched controls (FS: PMCA1cko/TAC 21±2%, PMCA1f/f/TAC 32±3%, PMCA1cko/Sham and αMHC-Cre/TAC 35±2%, p<0.05, n=6). Cardiac relaxation was also impaired (Logistic τ: PMCA1cko/TAC: 8.8±0.8, PMCA1f/f/TAC 6.6±0.3, p<0.05, n=6). This was associated with severe lung congestion shown by elevated lung weight/body weight in PMCA1cko/TAC (11.5±1 vs 7.8±0.8 mg/g in PMCA1f/f/TAC, p<0.05, n=6). Cardiomyocyte cross-sectional area and interstitial fibrosis were also increased in PMCA1cko. Our results show that PMCA1 has an additional role in maintaining cardiac rhythm. At 3 months of age PMCA1cko presented episodes of spontaneous ventricular tachycardia and exhibited downregulation of the expression of the voltage gated sodium channel Nav1.5. A significant reduction in the corresponding sodium current was also observed. In conclusion, these observations point to an important role for PMCA1 in HF following an excessive workload and arrhythmia suggesting that PMCA1 might be a novel target of therapeutic potential in the treatment of heart failure.

Conclusion: This is the first study investigating the clinical profile of TTC in only male gender. The mean age of male patients is slightly lower, however, the clinical presentation and risk factors are similar to reported studies in female literature investigating women.

Differential repolarization dynamics in transient apical and midventricular ballooning

H. Bonnemeier, S. Sandrock, C. Wulf, A. Ziomka, T. Demming. Innere Medizin III, Universitätshospital Schleswig-Holstein, Campus Kiel, Kiel, Germany

The aim of the present study was to assess potential differences in cardiac repolarization dynamics in patients with transient left ventricular apical ballooning syndrome (AB) and the midventricular variant (MB). Even though repolarization abnormalities and QT interval prolongation in the surface electrocardiogram (ECG) have been consistently reported, repolarization dynamics have not yet been investigated in the AB and MB variants. We hypothesized that differences in regional sympathetic denervation may induce differential effects on cardiac repolarization.

Methods: In a prospective single-center study, 49 consecutive patients with transient left ventricular dysfunction syndrome underwent 3-channel-Holter-ECG-recording on the third day after admission. A total of 27 recordings of patients with AB and 10 recordings of patients with MB were valid for beat-to-beat-QT-interval analyses.

Results: There were no significant differences in baseline clinical characteristics between AB and MB patients. Patients with MB showed significantly lower values for mean RR interval (835.1±104 vs 908.1±118 ms; P<0.05). Both, Bazett- and Fridericia-corrected QT-intervals were significantly longer in MB patients (QTb 441.9±38 vs. 483.4±40 ms; P<0.05; QTf 435.0±36 vs. 469.4±36.5 ms; P<0.05). Parameters of QT-interval variability (QTSV) and QT-interval dynamity (QTR-slope) also exhibited significant differences between groups (diagram).

Outcome of patients with left ventricular non-compaction in a single centre


Background: Left ventricular noncompaction (LVNC) has been associated with high morbidity and mortality. ACC/AHA/HRS 2008 guidelines recommended implantable cardioverter defibrillators (ICD) for all the patients (pts) with LVNC to...
reduce the risk of sudden cardiac death (SCD), LVNC is associated with a wide spectrum of presentation and outcomes. The aim of the study is to describe the outcome of pts with LVNC.

Method: In November 1997 to November 2011, 91 pts with LVNC were re-enrolled, 13 pts were excluded from the analysis because 6 pts underwent Status 1 heart transplant (HT), 1 pt died in Status 1 waiting list, 1 pt was lost to follow-up, 2 pts were treated with the ICD and 1 pt had associated CAD. Selected criteria for ICD were secondary prevention (SP): SCD/VT or Primary Prevention (PP): LVEF < 35 or > 2 risk factors (family history of SCD [FH-SCD], syncope or NSTEMI). Results: 78 pts with LVNC were analyzed: mean age 42±15 years (54 men), mean follow-up was 27±31 months. According to the selected risk-stratification criteria 40 pts (52%) received an ICD. ICD Group (pts): 70% men, 50% had NYHA class I-II, mean LVEF was 32±12%. SP (5 pts): During the follow-up none of the pts died, 3 pts (60%) received appropriate shocks (AS) due to VT/VF (all of them with previous SCD) and 2 pts (40%) had inappropriate shocks (15). PP (35 pts): 26 pts (74%) had LVEF < 35% and 13 pts (37%) had > 2 risk factor. During the follow-up none of the pts died, 1 pts underwent HT, 4 pts (11.4%) received appropriate AT/PS and 7 pts (20%) had ICD. Non ICD group (37 pts): Mean age was 41±16 years (36 men), 2.7% had NYHA class III-IV, mean LVEF was 48±17%. There were no deaths during the follow-up. Conclusion: After an immediate follow-up, prognosis of LVNC patients seems to be better than previously reported. Patients with ICD for SP had no death but a high rate of AS; in PP the incidence was much lower. In the non-ICD group there was no death. This registry suggests that pts with LVNC and LVEF <35% or >2 risk factors might be straitly for prophylactic implantation of ICD.

Low incidence and mortality of peripartum cardiomyopathy in a European country: a study of the whole population of Scotland

P.S. Jhund1, J.V. McMurray1, M. Gilles2, J. Dalsell1, L. Waugh3, R.S. Gardner4, J. Chalmers3, M.C. Pietre4. 1University of Glasgow, BHF Glasgow Cardiovascular Research Centre, Glasgow, United Kingdom; 2University of Glasgow, Department of Public Health and Health Policy, Glasgow, United Kingdom; 3NHSS National Services Scotland, Information Services Division, Edinburgh, United Kingdom; 4Golden Jubilee National Hospital, Scottish National Advanced Heart Failure Unit, Glasgow, United Kingdom

Purpose: Prior studies of the incidence peripartum cardiomyopathy (PPCM) in the UK have been based on local referral populations. This study was carried out to examine the incidence and short-term mortality of PPCM in a whole European country.

Methods: The whole Scottish population (5.2 million) receives care from the National Health Service (NHSC) and each person has a unique NHSC electronic record. We screened all hospitalizations for a diagnosis of PPCM or any other form of heart failure (HF) and linked these to birth/maternity records and death registrations over the same period. An incident hospitalization for PPCM was defined by the ICD-10 code O90.3 in a primary or secondary position between the year 2000 and 2009 (with no prior discharge with a diagnosis of PPCM or HF in the prior 5 years). Further potential PPCM cases were defined by a diagnosis of HF found in the 1 month prior to birth and up to 5 months after. An expanded definition was also explored, looking for diagnoses of heart failure from 3 months prior to birth to 12 months after. The incidence of PPCM was calculated using the total number of births as the denominator.

Results: During the study period there were 550,206 live births. There were 50 diagnoses of PPCM, a rate of 1 per 11,004 live births. The median age at discharge was 32 (IQR 29-37). There were further 30 cases of HF within 1 month prior to and up to 5 months after birth (i.e. a total of 80 potential PPCM cases and a rate of 1 in 6,678 live births) suggesting a number of potential cases are not labelled as having PPCM. Median age at discharge was 32 (IQR 29-37) for both extended definitions. The proportion of those with a definite diagnosis of PPCM dead at 30 days was 0%, there were no further deaths by 6 months and 1 year. When the additional cases of HF in the period before and after birth (using both definitions) were included, the proportion dead at 30 days was 1.3% with no further deaths by 6 months and 1 year.

Conclusions: The incidence mortality of PPCM in a predominantly white European population is low. The rate is in keeping with studies of the white population in the US and Canada. There is continued need for outreach efforts to understand the epidemiology of this rare disease.

Lowest LV and RV function in patients with lyme disease compared with endomyocardial biopsy-a long term follow-up

A.I. Gizzi1, R.J. Gei2, A. Pawlak1, O. Mozenska1. 1Department of Invasive Cardiovasc, Warsaw, Poland; 2Institute of Experimental & Clinical Medicine, Polish Academy of Science, Warsaw, Poland

Cardiac manifestation of the Lyme disease is rather rare (0.3-4%) and clinically varying disease caused by Borrelia Burgdorferi (BB) spirochaete. The aim of the study was to echocardiographically assess the LV and RV function in patients with cardiac manifestation of the Lyme disease.

Methodology: Between 02.2000 and 12.2009 we performed 270 endomyocardial biopsies. In 13 patients (4.81%) (mean age 52±7.4 yrs) in the tissue samples BB spirochaete were present (Warrin-Starck staining). Biopsies were obtained in patients with a history of a tick bite (2 yrs prior to the study) and with a diagnosis of erythema migrans. With echocardiography we analyzed LV and RV end-diastolic diameters (LVd, Rvd), LV ejection fraction (EF), RV function (TAPSE), LV diastolic function was also assessed. All parameters were obtained during initial hospitalization (cardiac Lyme disease diagnosis), after 6 months and 2 yrs after finishing therapy with antibiotics (AT).

Results: In 8 patients (61.5%) conduction abnormalities were present, in 3 cases (23.07%) we observed only heart failure symptoms, in 5 cases (38.46%) both. In 12 patients (92.31%) LV diastolic dysfunction was present (46.16% abnormal relaxation, 30.77% pseudonormalization, 15.38% restricted filling pattern). In all patients with conduction abnormalities RV dysfunction was present. After finishing AT in 10 cases (76.9%) all the symptoms resulting in endomyocardial biopsy resolved. In all patients initial diastolic dysfunction persisted. All assessed echocardiographic parameters are presented in Table.

Conclusions: In the majority of patients with cardiac manifestation of the Lyme disease LV systolic and diastolic dysfunction was present. RV dysfunction seemed to be followed by the conduction abnormalities. After finishing AT in over 75% of patients symptoms resulting in cardiac invasive diagnostic process resolved. In echocardiographic assessment permanent LV and RV systolic function improvements were observed, while diastolic dysfunction last.
Diagnosis of cardiac AL amyloidosis: the grey area of LMNA mutations in dilated cardiomyopathy: clinical, ultrastructural and expression studies

**P1919**

**Diagnosis of cardiac AL amyloidosis: the grey area of increased NT-proBNP and normal wall thickness**

F. Salinari1, F. Coppelli2, F. Perfetto2, F. Musca2, M. Boldrini2, R. Masselli3, A. Aloj2, G. Palladino4, G. Martin5, S. Perlini6

1. Foundation IRCCS Polyclinic San Matteo, Medical Clinic II - University of Pavia, Pavia, Italy; 2. Careggi Hospital, Department of Cardiology, Florence, Italy; 3. Niguarda Ca' Granda Hospital, Department of Cardiology, Milan, Italy; 4. Center for Amyloidosis, Biotechnology Laboratories IRCCS San Matteo, Pavia, Italy

**Background:** The amyloidoses constitute a large group of diseases in which aggregates of insoluble toxic protein are deposited in forms of fibrils in several tissues. AL amyloidosis, in which fibrils are composed mainly by the N-terminus of a monomolecular immunoglobulin light-chain, has an incidence of approximately 1 case per 100000 person-years in western countries. Cardiac involvement is not only frequent, but it is also the most common cause of death. The diagnosis of cardiac amyloidosis is relatively simple in AL patients with increased wall thickness (WT) and raised NT-proBNP levels, but it is much more challenging in patients with still normal echo parameters and slightly increased cardiac biomarkers, who do represent a "grey" area. **Objective:** To evaluate cardiac function in patients with normal WT and increased NT-proBNP.

**Methods:** We enrolled 292 consecutive never-treated subjects, in whom a first diagnosis of heart failure leading to heart transplantation was made and cardiac echo-color-Doppler data were evaluated at diagnosis. According to cardiac WT and NT-proBNP values, the cohort was divided into three groups: Group 0: WT <12 mm and NT-proBNP ≤ 332 pg/ml (n=50; i.e. patients with clearcut non-AL); Group 1: WT ≥ 12 mm, NT-proBNP >332 pg/ml and normal renal function (n=27; i.e. patients in the "grey" area); Group 2: WT >12 mm and normal NT-proBNP ≤ 332 pg/ml (n=215; i.e. patients with clearcut cardiac AL).

**Results:** When compared with Group 0, despite comparable WT, chamber volumes and global function, Group 1 patients showed higher prevalence of regional systolic dysfunction and altered diastolic parameters, with lower mitral annulus longitudinal excursion (lateral: 13.4±4.0 vs 15.18±2.67 mm; septal: 10.80±3.08 vs 13.21±2.52 mm), and higher E/E’ ratio (6.81±4.29 vs 6.04±2.83) [p<0.05 for all]. Intermediate values of endocardial shortening fraction, transmural E/A, and pulmonary vein S/D ratios were observed in Group 1 when compared with the other Groups, although these trends fell short of statistical significance. Notably, 1-year survival was 94% in Group 0, 78% in Group 1, and 60% in the other Groups, although these trends fell short of statistical significance. The most discriminative parameter was the mitral annulus longitudinal excursion when compared with Group 0, whereas the other parameters were comparable with Group 1.

**Conclusion:** Beyond confirming NT-proBNP diagnostic value, this study underscores the limitations of the currently used echocardiographic diagnostic criteria (i.e. wall thickness >12 mm). Systolic-diastolic dysfunction is already evident in the "grey" area of patients with amyloidosis and subclinical cardiac involvement.

**P1920**

Impact of dendritic cell-derived interleukin-10 in the post-infarction inflammation and left ventricular remodeling

A. Arzani1, F. Arzani2, S. Nagai3, Y. Maekawa3, Y. Sugano3, M. Saito4, S. Koyada5, K. Fukuda5, 1. Keio University School of Medicine, Tokyo, Japan; 2. National Cerebral and Cardiovascular Center Hospital, Department of Cardiovascular Medicine, Suita, Osaka, Japan

**Purpose:** Inflammation and immune responses play a crucial role in infarct healing and the subsequent left ventricular (LV) remodeling. Recently, we have reported the immunoprotective role of bone marrow (BM)-derived dendritic cell (DC) after myocardial infarction (MI) via controlling monocyte/macrophage homeostasis. The primary aim of this study was to clarify the inhibitory molecule derived from DCs in tissue repair and LV remodeling after MI.

**Methods and Results:** BM chimeric mice were introduced by reconstitution of BM cells from C571cH2Km1/diphtheria toxin receptor/GFP transgenic donor mice into lethally irradiated wild-type (WT) recipient mice. CD11c+ GFP+ DCs were recruted into the heart, peaking on day 7 after MI. Selective DC depletion was induced by diphtheria toxin administration in these mice, and abolition of DCs resulted in increased inflammatory response and LV function after left coronary ligation mainly through enhanced inflammatory monocyte/macrophage infiltration and sustained matrix metalloproteinase (MMP)-9 activation. Seven days after MI, BM cell protein expression analysis revealed that depletion of BM cells from WT mice and IL-10 knock out (KO) mice were concomitant with reburdening mouse granulocyte-macrophage colony-stimulating factor for 6 days and CD11c+ BMDCs were then positively collected by magnetic sorting. We confirmed that intravenously injected CFSE-labeled BMDCs reached infarcted zone based on an immunofluorescent staining. Adoptive transfer of BMDCs from WT mice into DCM-depleted mice restored LV function and negated the increases in myocardial Ly6C+ monocytes and myocardial MMP-9 activity following MI, indicating that DC plays a critical role in healing myocardium. On the other hand, adoptive transfer of BMDCs from IL-10 KO mice did not improve LV function after MI. Furthermore, inflammatory Ly6C+ monocyte infiltration and myocardial MMP-9 activity post-MI were comparable between DC-depleted mice with and without IL-10 KO BMDCs transfer.

**Conclusions:** DC suppresses inflammatory Ly6C+ monocyte-mediated inflammation and subsequent extracellular matrix degradation in the healing process following MI, at least in part, through IL-10 secretion. DC-derived IL-10 plays an important role in the post-infarction healing process, and this could be a novel therapeutic target in heart failure after MI.

**P1921**

LMNA mutations in dilated cardiomyopathy: clinical, ultrastructural and expression studies


1. Institute of Cardiology, Laboratory of Molecular Biology, Warsaw, Poland; 2. Unit for Screening Studies in Inherited Cardiovascular Diseases, Institute of Cardiology, Warsaw, Poland; 3. Department of Heart Failure and Transplantology, Institute of Cardiology, Warsaw, Poland; 4. Faculty of Health Sciences, University of Ottawa, Ottawa, Canada; 5. Department of Congenital Heart Disease, Institute of Cardiology, Warsaw, Poland; 6. Neuromuscular Unit, Mossakowski Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland

**Purpose:** LMNA mutations play a major role in the pathogenesis of dilated cardiomyopathy (DCM) with conduction disease. Once the symptoms develop, the disease often progresses to intractable heart failure leading to heart transplantation. The goal of this study was to identify LMNA mutations, estimate their frequency among DCM patients and characterize their effect.

**Methods:** Between January, 2008 and December, 2012 we collected 148 DCM patients: two patient populations were studied for the presence of LMNA mutations by direct sequencing. Firstly, sixty-six patients from Outpatient Heart Failure Clinic including twenty-seven afibrillary cardiomyopathy (AFDC) patients with clearcut and thirty-nine with DCM due to LMNA heart failure. Secondly, forty-four consecutive patients with DCM were referred for a familial evaluation to Unit for Screening Studies in Inherited Cardiovascular Diseases.

**Results:** We detected nine non-synonymous mutations: Arg82Leu, located in the coiled domain 1B; Gln246Stop and Val256Gly, located in the coiled domain 2A; Gly400ArgfsX11, Ser431Stop, Tyr481Stop, Thr507fsX42, Arg541Cys and Arg541Gly, located in the tail domain of the LMNA. Three mutations are novel to our best knowledge: Ser431Stop, Val256Gly and Gly400ArgfsX11 deletion. Interestingly, five were nonsense-type mutations. There were twenty-four carriers altogether in seven families. The carriers were mostly characterized by DCM and heart failure with conduction system disease and/or ventricular arrhythmia necessitating ICD implantation and heart transplantation, although four were asymptomatic. In three families, clinical evaluation and cardiac imaging were performed. Among the LMNA mutation carriers, six received HTx, fourteen ICD and five were treated with pacemaker. In addition, we present the results of ultrastructural study on Thr510fsX42 mutation, as well two expression studies (Ser431Stop and Tyr481Stop) by transient cell transfections.

**Conclusions:** In the two referral centre populations, the screening revealed five (7.6%) mutations among 68 patients HTx recipients or patients referred for HTx and four (9.1%) mutations within 44 consecutive DCM patients referred for familial evaluation. DCM patients with LMNA mutations have poor prognosis, however clinically considerable variability is present among family members.

**P1922**

Fulminant myocarditis associated with Influenza A H1N1pdm2009 in Japan

A. Ukirmura1, Y. Karazaki2, T. Izumi3

1. Department of General Internal Medicine, Osaka Medical College, Takatsuki, Japan; 2. Third Department of Internal Medicine, Osaka Medical College, Takatsuki-City, Japan; 3. Kikai University, School of Medicine, Department of Cardio-Angiology, Saga-hama, Japan

**Background:** An influenza pandemic occurred in 2009. We performed a national survey of H1N1pdm2009 myocarditis patients in the 2009/2010 season in Japan, and report the clinical feature of 15 H1N1pdm2009 myocarditis patients.

**Methods:** We performed a retrospective national questionnaire survey about H1N1pdm2009 myocarditis in the 2009/2010 and 2010/2011 seasons in Japan and collected data from 360 hospitals. The diagnosis of myocarditis was performed using the guidelines for Diagnosis and Treatment of Myocarditis (JCS2009).

**Results:** Twenty-nine patients with influenza A H1N1pdm2009 myocarditis were reported with 25 from the 2009/2010 season, and 4 patients from the 2010/2011 season. Seventeen patients (12 men, 5 women mean age, 34±20 years) were diagnosed with fulminant H1N1pdm2009 myocarditis with fatal arrhythmias, and/or varying degrees of cardiogenic shock. Fifteen fulminant myocarditis patients were seen in the 2009/2010 season, and only two in the 2010/2011 season. Myocarditis was proven by endomyocardial biopsy and/or autopsy. In the patients with most patients showed mild myocarditis. In the 17 fulminant myocarditis patients, the most frequent baseline disease was respiratory disorder in 4 patients (24%), but 9 patients (53%) had no baseline disease. Two fulminant myocarditis patients were complicated by pneumonia. A ventilator was used in 15 patients. Mechanical circulatory support with intra-aortic balloon pumping (IABP) and/or percutaneous cardiopulmonary support (PCPS) was emergently inserted in 14 patients. Of these, 9 patients were rescued with mechanical circulatory support, and 5 patients died. Three fulmi-
nant myocarditis patients treated without IABP/PCPS died. Sixteen (96%) fulmi-
nant myocarditis patients were treated with anti-nehuaminidase inhibitors.

Discussion: H1N1 pdm09 fulminant myocarditis seemed to be more com-
mon in the 2008/2009 season, compared with seasonal influenza seasons. Ap-
propriate treatment with neuraminidase inhibitors and mechanical circulatory sup-
port (IABP and/or PCPS) was required to rescue patients with fulminant H1N1 pdm09 myocarditis.

Conclusion: The number of fulminant myocarditis patients associated with H1N1 pdm09 decreased in the post-pandemic (2010/2011) season, compared with the pandemic (2009/2010) season in Japan.

P1923 Cardioprotective effects of seapolynol (polyphenol purified from eckonia cava) against adriamycin-induced cardiomyopathy in an animal rat model

H. Jeon1, D. H. Lee1, H. C. Shin1, H. J. Youn1, K. T. Kim1, U. Jeong2, ST. Mary’s Hospital, The Catholic University of Korea, Uijeongbu, Korea Republic of; 2BOTA MEDI RESEARCH, Seattle, United States of America; 3Seoul ST. Mary’s Hospital, The Catholic University of Korea, seoul, Korea, Republic of

Background: The purpose of this study was to elucidate the cardioprotective ef-
fects of seapolynol (polyphenol purified from Eckonia cava) against adriamycin-
induced cardiomyopathy in an animal rat model. Seapolynol, approved as a new di-
aphyte (NDI) from US Food and Drug Administration (FDA) in 2008 (FDA-1995-5-0039-01976), is known to protect cells by its potent and wide spec-
trum of antioxidant functions.

Methods: Of total forty-two rats, we divided 21 rats into Group 1 (low-dose seapolynol plus adriamycin, n=7), Group 2 (high-dose seapolynol plus adri-
mycin, n=7), and Group 3 (single adriamycin, no seapolynol, n=7) for efficacy of seapolynol. We administrated seapolynol (32/64 mg/kg, daily; oral) one week before adriamycin (2.5mg/kg, weekly, intraperitoneal) was injected for 6 weeks. For safety of seapolynol, the other 21 rats were divided into Group 4 (low-dose seapolynol only, n=7), Group 5 (high-dose seapolynol only, n=7), and Group 6 (neither seapolynol nor adriamycin, n=7). We performed transthoracic echocar-
diography (15MHz linear array,GE VIVID 7) before (baseline) and after (4-
week) injection of adriamycin and analyzed cardiac function.

Results: Adriamycin-induced cardiomyopathy was identified by Group 3 and there was no adverse interaction in Group 4, 5 and 6. In Group 1, relative wall thick-
ness (RWT: 0.6±0.0mm baseline vs. 0.4±0.1mm 6-week, p=0.001), fractional shortening (FS: 63.6±3.1% baseline vs. 52.9±6.3% 6-week, p=0.007), and left ventricular ejection fraction (LVEF: 88.7±5.8% baseline vs. 78.6±5.8% 6-week, p=0.005) significantly decreased and the left ventricular end diastolic/systolic dimension (LVEDD: 5.8±0.7mm baseline vs. 7.1±0.7mm 6-week, p=0.002, LVEDV: 2.1±0.2mm baseline vs. 3.4±0.6mm 6-week, p=0.003, respec-
tively) significantly increased. However, there were no interval changes in Group 2, LVEDV and the change of LVEF (±) upon 6-week adriamycin injection were significantly higher in Group 1 compared with Group 2 (LVEDV: 7.7±1.0±mm vs. 6.3±0.4mm, p=0.016, LVEF: -11.1±6.9% vs. -2.0±8.5%, p=0.048, respec-
tively). For safety and cardiprotection against adriamycin-induced cardiomyopathy in a dose-
dependent manner.

Conclusion: Our rat-model study results showed that Seapolynol was safe and cardiprotecive against adriamycin-induced cardiomyopathy in a dose-
dependent manner.

P1925 Primary AL-amyloidosis in the structure of a cohort of patients with chronic heart failure of the Russian population

A. Goodkova1, E. Sernenni1, A. Polyakova1, E. Meloranska2, I. Kuznetsova1, M. Rubakov3, E. Shlyakhto1, A. Almanskaya4, M. Slabova5, K. Schelkunov6, I. P. Pavlov Medical Federal Heart, Blood & Endocrinology Center, I. P. Pavlov Medical Federal University, Saint Petersburg, Russian Federation; 2State Medical University of St. Petersburg, I.P. Pavlov, St. Petersburg, Russian Federation

Purpose: To establish the share of AL-amyloidosis in the structure of chronic heart failure and to examine clinical features with systemic AL-amyloidosis, mainly affecting the heart.

Material and methods: The study included 182 patients with severe congestive heart failure with preserved ejection fraction associated development of hyper-
trrophic, restrictive or dilated phenotype. The patients’ ages ranged from 37 to 84 years. Instrumental study of cardiovascular system included echocardiography (M-modal, two-dimensional and Doppler modes). Assessment of diastolic func-
tion during echocardiography was performed with a pulsed (PW) and tissue (TDI) Doppler. The diagnosis of AL-amyloidosis was suspected clinically and confirmed by immunomorphological examination of biopsy specimens, bone marrow and buccal mucosa (using histological stains hematoxylin and eosin, Congo red, Van Gieson by pikrofuksin and polarizing microscopy - immunohistochemical reac-
tion with A. Amyloid cardiolipin and Congo red reagents).

Results: Systemic AL-amyloidosis, mainly affecting the cardiovascular system was diagnosed in 20 patients (11%). Plasma cell dyscrasia was proved by im-
balance λ and κ (1:7). The most severe course was found in 2 patients aged 37 and 40 years. Life expectancy after the onset of symptoms to death was 5.5 and 8 months respectively. The relatively benign course was observed in 2 patients aged 70 to 84 years. Life expectancy after the onset of symptoms to death was 36 months or more. In cases of AL-amyloidosis with predominant renal survival was 56 months or more. Remodeling of the heart consistent with RCM, HCM and DCM (3, 3 and 3, respectively). Overdiagnosis of coronary heart disease and hy-
pertension was found in 11 patients (%). In 16 cases, leading to the clinic was progressive congestive right ventricular heart failure with preserved ejection frac-	ion fraction. Recurrent venous and arterial thrombosis were the leading symptom in one patient. Weight loss, intoxication, fever were the leading in the three losing. Within 5 years of follow - death was diagnosed in 17 patients (6 cases there was a sudden death (36) and 11 patients (65%) of death from cardiac causes.

Conclusion: AL-amyloidosis with lesions of the cardiovascular system is about 11% of the cohort of patients with CHF of Russian population. Cardiac involve-
ment in AL-amyloidosis can occur under the guise of various vascular - vascular dis-
orders: restrictive, dilated, hypertrophic cardiomyopathy, and ischemic heart disease. A high incidence of sudden death in patients with AL-amyloidosis

Results: Nine patients (12.8%) met the criteria for cardiotoxicity. Averaged cumu-
lative doxorubicin dose was 177±59 mg/m². Univariate logistic regression identi-
fied ΔLVF, S/F5, Δ isolacticamin release time, ΔS', ΔE/A, ΔTNT as pre-
dicators for cardiotoxicity (all p < 0.05). Age, sex, cardiac risk factors, Δ blood pressure, Δ heart rate, ΔLV end-diastolic volume, ΔLV end-
systolic volume, Δ left atrial volume, Δ pulmonary artery systolic pressure, Δ myocardial performance index, ΔE/E' and ΔNTPoBNP, were not associated with future cardiotoxicity. On multiple logistic regression analysis, including all the univariate predictors, ΔTNT emerged as the only independent predictor of later cardiotoxicity (Odds ratio = 1.22, p = 0.009).

Conclusion: The change of ΔTNT level after 6 weeks of treatment with doxoru-
bicin was able to predict future doxorubicin-induced cardiotoxicity, unlike Tissue Doppler imaging and conventional echocardiographic parameters.
Serum levels of placental growth factor is associated with left ventricular hypertrophy in men


1 National Hospital Organization Kyoto Medical Center, Kyoto, Japan; 2University of Shizuoka, Shizuoka, Japan

Background: Placental growth factor (PlGF) is a homologue of vascular endothelial growth factor (VEGF) which is essential for compensated left ventricular (LV) hypertrophy. PI GF plays an important role in pathological, but not physiological, angiogenesis. However, the role of PIGF in the development of left ventricular hypertrophy (LVH) in human is unknown.

Methods and Results: We carried out a cross-sectional study involving 168 consecutive male outpatients whose NYHA classes were stable for at least 3 months. All participants provided written informed consents. We divided these patients into two groups: those with (LVH, left ventricular mass index (LVM) >116 g/m2, n=27, 63±15 (mean±SD)) y) and those without LVH (LVM <114, 5±14 g/m2). There were no significant differences in age, the body mass index (BMI), blood pressures, lipid and metabolic profiles, and medical treatment between the two groups. Serum levels of VEGF were similar between the two groups. However, serum levels of NT-pro B-type natriuretic peptide (NT-proBNP) (30.5±64 pg/mL vs 39.5±24 pg/mL, P=0.0011), PlGF (11.9±6.7 vs 7.0±2.9 pg/mL, P=0.027) and BMI (27.8±6.0 vs 25.8±3.9 kg/m2, P=0.016) were independently associated with LVH. In simple regression analyses, the PI GF level was significantly correlated with LVH volume (rs=0.30, P=0.005), systolic volumes (rs=0.33, P=0.003) and cardiac output (rs=0.26, P=0.011). The PI GF level was also significantly decreased in LVH+ compared to LVH- group. In simple regression analysis, we showed that serum levels of PI GF were independently associated with LVH (P=0.027). PI GF, PI GF and BMI were independently associated with LVH (P=0.005, P=0.011 and P=0.016), respectively.

Conclusion: The PI GF level is associated with LVH and left ventricular hypertrophy. PI GF, a biomarker for LVH, is a predictor of LVH.

Characterization of two new Adenosine-2a receptors isoforms in cardiac tissue of minipigs pacing-induced HF

M. Cabai, L. Panchetti, F. Vigliore, C. Casselli, T. Precisonne, G. Cismaru, M. Pauriah, P. Louis, O. Selton, A. Terrier De La Chaise, H. Blangy. University Hospital of Nancy - Hospital Brabois, Vandoeuvre les Nancy, France

Purpose: Adenosine, a potent endogenous physiological mediator, mediates a wide variety of physiological effects through its interaction with cell-surface receptors (A1, A2a, A2b and A3). Adenosine anti-inflammatory effects are predominantly mediated by A2aR. In human 8 A2aR SUTR variants were found while both isoforms are not reported in Sus Scrofa. Aim of this study was to evaluate the possible presence of AR2a isoforms in Sus Scrofa genome.

Methods: Heart failure (HF) was induced by pacing tachycardia (200 bpm) in the right ventricle of minipigs (n=4). Cardiac tissue was collected for each minipig from left ventricular (LV) wall corresponding to the septal (pacing site, PS; n=4) and to the lateral (opposite site, OS; n=8) regions of left ventricular (LV) wall. AR2a specific primers, derived from Sus scrofa AT 772412 sequence, was used to perform Real-Time PCR in PS and OS. The DNA, obtained from different Real-Time PCR, was sequenced using the Sanger method. Histological standard analysis was also carried out in OS and PS.

Results: By RT-PCR experiments we observed, in melting curve, a peak corresponding to AR2a in OS and two peaks in PS. After gel electrophoresis the two peaks were isolated and sequenced. A long isoform (GenBank:JQ229674.1 Fig 1) 1-213bp and a short AR2a isoform (1-94 bp) were obtained. The short isoform showed an alignment with adenosine A2aR (AY772412 as well as with JQ229674.1) and appears to include an alternative promoter region codifying a different AR2a isoform which protein is M A V P W G C * (insilico software). Histology showed no significant endocardial fibrosis nor inflammatory infiltrates in PS. A greater number of endocardial and intramyocardial Purkinje cells was observed in PS compared to OS.

Conclusion: The presence of two different isoforms in the area of pacing can suggest a differential state-specific expression of A2aR in cardiac tissue.

Biventricular dysfunction following administration of anthracycline based chemotherapy in breast cancer: a prospective multi-center study using advanced cardiac imaging and biochemical markers

S. Grover1, C. Depasquale1, D. Leong2, K. Cheong3, D. Kotasek4, R. Joshi5, L. Joeg6, M. Joseph7, B. Koczwar7, J. Selvanayagam1, Flinders Medical Centre, Department of Cardiology, Adelaide, Australia; 2Department of Medicine, University of Adelaide, Adelaide, Australia; 3Adelaide Cancer Centre, Adelaide, Australia; 4Leyli McEvins Hospital, Adelaide, Australia; 5Flinders Medical Centre, Department of Oncology, Adelaide, Australia

Background: Previous studies have shown that subtle left ventricle [LV] dysfunction can be detected early following anthracycline chemotherapy but none have prospectively correlated this with myocardial oedema or necrosis. Furthermore, although right ventricle [RV] systolic dysfunction is an adverse prognostic marker in cardiomyopathies, the RV effects of chemotherapy are not well defined.

Methods: 36 breast cancer patients [pts] undergoing anthracycline based therapy underwent serial CMR imaging (for LV/RV volumes, myocardial oedema and necrosis), advanced echocardiography (for LV global longitudinal strain [GLS], diastolic function and tricuspid annular plane systolic excursion [TAPSE]), pro brain natriuretic peptide [pro-BNP], high-sensitivity [hs] Troponin T [hs-TnT] and hs C reactive protein [hs-CRP] measurements. Tests were conducted at baseline, 1 month [mth], and 3 mths.

Results: In the study pts, significant changes in CMR volumes and systolic function were observed in both the ventricles (see table). 23% of pts had reduction of CMR LV RVEF below the lower limit of normal range at 3 mths. GLS and TAPSE decreased from -21.2±3% at baseline to -19.0±2%; p<0.001 and 23.5±3.5 to 21.1±3.7; p<0.001 at 3 mths respectively. Diastolic function did not change with time. No variation was observed in pro-BNP, however hs-TnT and hs-CRP increased from 3.8±1.7 to 9.7±9.8; p<0.001 and 2.8±3.1 to 6.7±5.9; p<0.001 at 3 mths respectively. 52% of pts had an abnormal T2 signal (SI increase to >3 standard deviation of normal) at 3 mths. 4 pts (11%) developed a new MI, 1 patient developed new epicardial interstitial myocyte oedema at 3 mths.

Conclusion: Both CMR and advanced echo techniques detect LV and RV functional changes within 3 mths of anthracycline based chemotherapy. These changes are likely mediated by myocardial inflammation. These findings may be a basis for development of early predictors of cardiac damage facilitating earlier intervention/preventive strategies.

Gender-related prognosis of syncope associated with underlying heart disease


Purpose of study: To evaluate the influence of gender on the results of electrophysiological study (EPS) performed for syncope associated with heart diseases (HD) and to predict prognosis. The management and the prognosis of some HD's may depend on the gender of the patient. EPS is recommended in patients with syncope, HD, left ventricular ejection fraction (LVEF) <30% while the implantation of a defibrillator (ICD) is recommended when LVEF <30% without evaluation of the cause of syncope.

Methods: 523 patients, 89 women, 434 men were admitted for syncope. They had an HD, either ischemic HD (n=380) or a left ventricular impairment of other origin (n=133). Electrocardiography, Holter monitoring and head-up tilt test were systematic. EPS was complete including the evaluation of AV conduction and sinoatrial conduction, programmed atrial and ventricular stimulation (PVS). Patients were followed from 1 to 10 years.

Results: Women had the same age (67±14.5 years) and the same LVEF (41±15%) as the men (64.5±11 years, 40±13%). Ischemic HD was less frequent in women (68.5%) than in men (78%) (p<0.001). Monomorphic sustained ventricular tachycardia (VT) -270 bpm was induced less frequently in women than in men (10 vs 25.5%; p<0.001). The frequency of non specific VT (ventricular flutter or fibrillation) was similar in women and men (16 vs 18%). The frequency...
of negative programmed ventricular stimulation was higher in women than in men (72 vs 56%) (p<0.005). Syncope was related to hyperventilatory more frequently in women than in men (15 vs 7%) (p<0.01). Other causes of syncope were similar in both sexes: at supraventricular tachycardia (13 vs 14.5%) (NS), AV con-duction disturbances (9 vs 8%) (NS), coronary ischaemia (9 vs 8%) (NS). Noninvasive and invasive studies remained more frequently negative in women (31%) than in men (16%) (p<0.007). Implantable defibrillator (ICD) was implanted less frequently in women than in men (7 vs 15%) (p<0.03). After a mean follow-up of 5.4 years, the frequency of sudden death (7 vs 57%) (p<0.01), heart failure-related death (15 vs 13%), transplantion (1 vs 3%), (p<0.28) was similar in women and men. 

Conclusions: Women with heart disease and syncope had less inducible monomorphic VT than men, had more hyperventilatory and unexplained syncope than men. However, despite a similar LVEF and rarer inducible life-threatening arrhythmias, their prognosis was similar probably due to a lower frequency of ICD implantation.

**P1932** Differences between males and females in intrinsic myocardial properties of the left ventricle established by “automated function imaging”

J. Claessens,1 P. Claessens,2 C. Claessens3, M. Claessens1, 5, A.Z. Monica Antwerpen, Antwerp, Belgium;2 General Hospital St. Jozef, Malle, Belgium;3 General Hospital St. Jozef, Turnhout, Belgium;4 General Hospital Klin, Brusschaat, Belgium;5 Klippert Hart Schilde, Schilde, Belgium.

Purpose: Ischemic heart disease is mostly a male problem. Genetic, hormonal and environmental factors are undoubtedly decisive but intrinsic myocardial qual-ities could also be important. Strain measurement give a correct idea about the contractile reserve of the myocardium. Automated function imaging(AFI) is a novel algorithm based on speckle-tracking imaging that can be used for assessment of segmental and global longitudinal strain of the left ventricle(GLPSSagg).

Methods: The study population consisted of 1040 subjects, equally divided in 26 groups of 40 patients. 480 females(I) divided in 8 age groups healthy sub-jects(H): 1:19 years; 2:20-29years; 3:30-39years; 4:40-49years; 5:50-59y; 6:60-69y; 7:70-89years; 8:90 years. All subjects underwent AFI for determination of GLPSSagg and for assessment of average strain of the 5 myocardial segments with the lowest standard deviation(GLPSSavg).

Results: In all age groups the GLPSSavg is significant(p<0.001) lower in coronary patients. Some findings significantly (p<0.001) different between males and females for AvgLSS. In all age groups left atrium and left ventri-cle diameters are smaller in females and are increased in coronary patients. GLPSagg: IH1: 20.45±20.03; IH2: 23.9; IH3: 19.99; IH4: 20.41±16.18; IH5: 19.99±16.17; IH6: 19.99±16.17; IH7: 19.99±16.17; IH8: 19.99±16.17; IH9: 19.99±16.17; IH10: 19.99±16.17. RA Ejection Fraction (RAEF) was calculated using Modified Simpson’s method: \[ \text{RAEF} = \frac{A_{\text{RA}} \times A_{\text{RA}}} {2 \times A_{\text{RA}} \times H_{\text{RA}} \times H_{\text{RA}}} \] where LSSavg: IH1:-16.15; IH2:-17.33; IH3:-21.4; IH4: -16.83; IH5:-16.88/14.48; IH6:-18.85/14.28; IH7:-18.91/14.28; IH8:-18.16/14.28; IH9:-18.16/14.28; IH10:-18.16/14.28. Correlation of pulmonary venous flow better evaluated the level of PCWP since both Ap-Am duration and systolic fraction significantly correlated with PCWP (r=0.57 for Ap-Am duration and r=0.5 for systolic fraction) respectively. In addition, decrease in Ap-Am duration were also correlated to improvement in PCWP values. 

Analysis of pulmonary venous flow better evaluated the level of PCWP in patients hospitalized in intensive care unit for severe decompensation of advanced chronic systolic heart failure.

Methods: 27 consecutive patients (66±11 years old) with advanced decompen-sated heart failure were prospectively enrolled after admission in intensive care unit and followed during 48 hours. They underwent both haemodynamic evalu-ation by Swan Ganz catheter and echocardiography for simultaneous measure-ment of LVFP assessed by pulmonary capillary wedge pressure (PCWP). Using echocardiography, the following parameters were analyzed: mitral E/e ratio (E: early diastolic mitral annulus mitral velocity was the average of the lateral and septal values); reverse LA-Ejection fraction (RAEF) was calculated using Modified Simpson’s method: \[ \text{RAEF} = \frac{A_{\text{RA}} \times A_{\text{RA}}} {2 \times A_{\text{RA}} \times H_{\text{RA}} \times H_{\text{RA}}} \] 

Results: At admission, mean LV ejection fraction was 32±7% and PCWP was 19±6 mmHg. Mitral E/e ratio was 14±7 and was not significantly correlated with PCWP (r=0.30; p<NS). Using ROC curve analysis, E/e ratio poorly predicted increased PCWP (>18 mmHg) with an AUC of 0.48. In addition, changes in PCWP values under therapy were not correlated with E/e changes. Analysis of pulmonary venous flow better evaluated the level of PCWP since both Ap-Am duration and systolic fraction significantly correlated with PCWP (r=0.57 and r=0.5 for systolic fraction respectively; p<0.05). Using ROC curve analysis, Ap-Am duration and systolic fraction identified PCWP >18 mmHg with an AUC of 0.73 and 0.78, respectively. In addition, decrease in Ap-Am duration were also correlated to im-provement in PCWP values.

Conclusion: In patients with advanced and decompensated systolic heart fail-ure, E/e ratio is not reliable both for the initial evaluation of PCWP and evolution under therapy. In contrast, pulmonary venous parameters provide a better assessment of PCWP in this high risk population.

**P1933** Effects of long term right ventricular apical pacing on the right atrium


Purpose: To investigate anatomical and functional changes in the right atrium and its relationship if any to left ventricular function.

Method: 96 patients with LVWI pacemakers implanted between 2002 and 2004 were included. Pacing was at the RV apex in all cases. Transthoracic echocardiographic measurements were obtained at baseline and annually.

RA-Ejection fraction (RAEF) was calculated using Modified Simpson’s method: \[ \text{RAEF} = \frac{A_{\text{RA}} \times A_{\text{RA}}} {2 \times A_{\text{RA}} \times H_{\text{RA}} \times H_{\text{RA}}} \] 

Results: Mean and standard deviations were analysis using independent T tests. Relationships between RA function and new onset TR as well as changes in LV parameters were investigated using Pearson’s and Spearman’s correlations.

Results: 96 patients were enrolled. Only 75 patients were follow-up for a mean of 5.5 years. 25 patients’ data were available for analysis till 7 years. Their mean age was 68.7±12.17 years old. 67.89% had complete heart block, 15.78% had sick sinus syndrome and 7.86% had AV nodal disease and decompensation time at baseline and at 5 years was 31.45% at 5 years (p<0.008). Mean RA area, RA end-diastolic volume and RA end-systolic volume increased from 16.79±20.58 cm³ (p = 0.047), 50.78±69.30 ml (p = 0.043) and 31.28±50.20 ml (p = 0.036) respectively at baseline and 5 years.

Conclusion: Single chamber pacing at the RV apex led to significant RA dilata-tion and dysfunction which may explain the worsening TR, new onset atrial ar-rhythmias and deterioration of LV function.

**P1934** Adaptive servo ventilation versus nocturnal oxygen therapy in patients with sleep disordered breathing and impaired cardiac function


Introduction: The high incidence of sleep disordered breathing (SDB) in patients with congestive heart failure (CHF) is well known. We compared adaptive pressure support servo-ventilation therapy (ASV) with nocturnal oxygen therapy (N- HOT) in patients with CHF.

Methods: Thirty four patients (26 men; 68±11.3 years old; mean left ventric-ular ejection fraction(VLVEF): 31.5±9.5%) with sleep disordered breathing(SDB): apneic-hypopnea index (AHI) >15 with impaired cardiac function (VLVEF <50%) who were admitted due to congestive heart failure were analyzed retrospectively. All patients received polysomnographic evaluations during steady state of heart failure. After discharge from the hospital, patients received ASV or N-HOT ther-apy (non-randomized). Cardiac events (cardiac death, and hospitalization due to congestive heart failure) were analyzed.

Results: Mean follow up period was 609±616 day. Mean AHI of all patients was 16±4.6. Kaplan-Meier survival analysis showed that there was a significant dif-ference between ASV and N-HOT in cardiac death and hospitalization due to congestive heart failure event (P<0.004). There were no significant differences between ASV and N-HOT in patients’ baseline characteristics.
Significance of periodic leg movements during sleep in patients with chronic heart failure and sleep-disordered breathing


Background: Periodic leg movements during sleep (PLMs) are a disorder characterized by regularly recurring movements of the legs during sleep. Recent reports demonstrated that PLMs were highly prevalent and independently associated with increased mortality in chronic heart failure (CHF) patients. The purpose of this study is to investigate the prevalence and significance of PLMs in Japanese CHF patients with sleep-disordered breathing (SDB).

Methods: We enrolled 60 consecutive CHF patients with SDB (apnea-hypopnea index [AHI] ≥15/h) who diagnosed by attended polysomnography (PSG). After a few days, all patients received positive airway pressure (PAP) titration during PSG for treatment of SDB. The PLMs index (PLMI) was quantified as the frequency of PLMs per hour of sleep.

Results: PLMI was negatively correlated with AHI (r = -0.27, p = 0.035). Seventeen patients (28%) had PLMI > 5. They were similar in age, gender, body mass index, Epworth Sleepiness Score, creatinine, left ventricular ejection fraction, B-type natriuretic peptide and AHI compared to those of the patients without PLMs (PLMI < 5). During PAP titration, PLMI significantly increased in patients without PLMs (from 0.9 ± 2.6 to 6.5 ± 14.7/h, p = 0.016), whereas PLMI in patients with PLMI > 5 maintained at high level (from 48.4 ± 69.1 to 36.8 ± 43.0/h, p = ns). Some patients with severe SDB have an increase in severity of PLMS after PAP therapy.

Conclusions: These results show that the prevalence of PLMs is high in CHF patients with moderate to severe SDB. PSG should be recommended to CHF patients to evaluate not only SDB but also PLMs.

Which subtypes of cardio renal syndrome is associated with worse clinical outcomes?

S.H. Sung1, P.F. Hsu1, H.M. Cheng1, J.S. Yeh2, W.L. Liu3, S.Y. Chuang3, 1Taipei Veterans General Hospital, Taipei, Taiwan; 2Tapei Medical University, Taipei, Taiwan; 3National Health Research Institutes, Taichung, Taiwan.

Background: The cardio renal syndrome (CRS) indicated intimately interplays between dysfunctional heart and kidney, among which primary disorder of one organ often results in secondary damage to the other. Although there have been classifications of five, proposed to discriminate the complexity of this cluster of conditions, whether their clinical impacts on cardiovascular morbidities and mortalities are different or not remain to be elucidated.

Methods: A nationwide population-based study using the Taiwan National Health Insurance database was conducted from 1 million sampling cohort data set. A total of 2838 patients who presented with both heart failure (HF) and chronic kidney disease (CKD) during 1997 to 2009 were identified. The control group consisted of 28380 subjects by matching age and sex.

Results: Among 2838 subjects with CRS, 1230 patients presented with HF ahead of CKD (group 1), 1585 presented with initial CKD (group 2), and 284 subjects had concurrent HF and CKD within 1 month (group 3). The group 3 was younger, more likely to be women, and had less diabetes. During a median follow-up duration of 2.84 years, patients with CRS had higher adverse events for coronary heart disease (CHD) (97.7 vs. 8.5/1000 person-year), stroke (45.8 vs. 13.8), and death (55.1 vs. 9.1) comparing to the control group. Among 2838 subjects with CRS, group 3 had the lowest event rate for stroke, CHD, and death comparing to the other groups (Figure 1). Such the survival advantage remained true in multivariate analyses when age and comorbidities were accounted for.

Conclusions: The CRS indeed carried high risks for cardiovascular morbidity and mortality. However, a leading chronicity of HF or CKD rather than an acute insult to both organs is associated with worsen clinical outcomes.

Adaptive-servo ventilation may be a new additional therapy to improve symptoms and cardiac function for patients with chronic heart failure regardless of accompanying sleep disordered breathing

S.I. Momomura1, Y. Seino1, Y. Kihara2, H. Adachi3, Y. Yasumura1, H. Yokoyama1 on behalf of The SAVIOR investigators, 1Jichi Medical University, Sakai Medical Center, Sakai, Japan; 2Osaka National Hospital, Cardiovascular Division, Osaka, Japan; 3National Cerebral and Cardiovascular Center Hospital, Department of Cardiovascular Medicine, Suita, Osaka, Japan.

Introduction: Adaptive servo ventilator (ASV) was developed as a device to abolish sleep disordered breathing (SDB) in heart failure patients. Recently, ASV is getting widely used for heart failure patients not only with SDB but also without SDB in Japan, because it may improve hemodynamics through its favorable effect on preload and afterload. However, there have been very few evidences on ASV therapy for heart failure patients without SDB. This study “SAVior-R” was carried out to establish real-world evidences on this therapy.

Methods: We performed a retrospective cohort study of 115 chronic heart failure patients who were firstly treated with ASV in 16 institutes from January to December 2009. Data on symptoms, echocardiography, chest X-ray, plasma BNP and sleep study were obtained from medical records for baseline and on ASV for one year.

Results: After ASV therapy, the ratio of NYHA class III patients decreased significantly from 43.2% to 23.5% (p < 0.0002), LVEF increased significantly from 34.9 ± 16.0 to 38.9 ± 15.7% (p < 0.0002). The improvement in LVEF was more remarkable in the low LVEF group as compared with the preserved-LVEF group. BNP and CTR were also improved, although these changes did not reach statistical significance. These effects of ASV were consistent irrespective of the degree of SDB.

Conclusion: ASV therapy would improve symptoms and cardiac function in chronic heart failure patients regardless of accompanying SDB. A randomized controlled trial to confirm the effects of ASV not through the attenuation of SDB is needed.

A single night use of adaptive servo ventilation improves renal function in heart failure patients with sleep disordered breathing

S. Suzuki1, A. Yoshishia1, K. Sugimoto2, T. Yamaki2, H. Kunii2, K. Nakazato3, H. Suzuki3, S. Saiwah3, Y. Takeishi4, 1Department of Cardiology and Hematology, Advanced Cardiovascular Therapeutics, Fukushima Medical University, Fukushima, Japan; 2Department of Cardiology and Hematology, Fukushima Medical University, Fukushima, Japan.

Background: Sleep disordered breathing (SDB) deteriorates the prognosis of patients with chronic heart failure (CHF). Adaptive servo ventilation (ASV) is a new therapeutic modality to treat SDB including Cheyne-Stokes respiration associated with central sleep apnea (CSA). SDB is thought to cause renal dysfunction because of intermittent hypoxia and sympathetic nervous activation. Renal function plays a critical role in the progression of CHF and is a strong predictor of clinical outcomes. Cystatin C is a more sensitive biomarker of renal function than creatinine. The purpose of present study was to examine whether ASV is effective for cardiac overload and renal dysfunction in CHF with SDB.

Methods and Results: Fifty patients with CHF and SDB (mean age 59.9 ± 9.9, male 45, mean left ventricular ejection fraction 34.0 ± 12.4%) were examined. We performed polysomnography for five consecutive days (baseline and on ASV) and measured levels of serum N terminal pro B-type natriuretic peptide (NT-proBNP), cystatin C, creatinine, and estimated glomerular filtration rate by the MDRD formula (eGFR). ASV significantly improved apnea hypopnea index (3.1 ± 1.6 to 9.1 ± 13.3/h, p < 0.01), central apnea index (16.4 ± 13.7 to 11.1 ± 5/h, p < 0.01), obstructive apnea index (3.2 ± 5.9 to 1.2 ± 2.0/h, p < 0.05), arousal index (25.8 ± 10.6 to 15.7 ± 7.4/h, p < 0.01), mean SPO2 (94.5 ± 2.6 to 96.5 ± 1.6%, p < 0.01), and lowest SPO2 (79.2 ± 9.7 to 88.9 ± 5.6%, p < 0.01) compared to
Adaptive servo ventilation improves cardiac function and reduces re-hospitalization in chronic heart failure patients with Cheyne-Stokes respiration after cardiac resynchronization therapy


Department of Cardiology and Hematology, Fukushima Medical University, Fukushima, Japan

Backgrounds: Cardiac resynchronization therapy (CRT) has been accepted as a useful therapeutic modality for heart failure (HF). Sleep disordered breathing (SDB), especially Cheyne-Stokes respiration (CSR), is often observed in HF patients and is associated with poor prognosis. CRT is thought to improve CSR. Although adaptive servo ventilation (ASV) is effective for CRT, it is unclear whether ASV improves cardiac function and prognosis of HF with CSR after CRT.

Methods and Results: In this study, 51 HF patients with moderate to severe SDB who were scheduled to implant CRT were enrolled. Although, mean apnea hypopnea index (AHI) decreased 6 month after CRT (31.1±19.5/hr to 22.1±17/hr), all 51 patients still had moderate-severe SDB (AHI >15/hr). 10 patients treated with ASV (ASV group) and 41 patients treated with conventional medications alone (Non-ASV group) were divided before and 6 months after ASV. Patients were followed to register cardiac events (average follow up period 11, re-hospitalization 12) occurred in this follow up period. Importantly, event free rate was significantly higher in ASV group than in Non-ASV group (77.8% vs. 36.7%, logrank P=0.01).

Conclusions: ASV improved cardio-renal function and long-term prognosis in HF patients with CKD and SDB.

Methods: Forty eight HF patients with CKD (defined as eGFR of ≤ 60 ml/min/1.73m²) and moderate-severe SDB (defined as apnea hypopnea index > 15/hr) were enrolled. Study subjects (mean LVEF 37.0%, mean eGFR 52.8 ml/min/1.73m², mean apnea hypopnea index 38.2 times/hr) were divided into two groups: 18 patients treated with conventional medications for HF and ASV (ASV group) and 30 patients treated with conventional medications alone (Non-ASV group). BNP, eGFR, and LVEF were measured before and 6 months after treatments. Patients were followed to register cardiac events (average follow up period 656 days).

Results: BNP, eGFR, and LVEF significantly improved in ASV group (BNP, 469.7±240.4 to 198.2±156.4 pg/ml; eGFR, 55.1±10.7 to 57.8±15.6 ml/min/1.73m²; LVEF, 36.6±16.9 to 45.1 ±15.2%, P<0.05, respectively), but any of these parameters did not change in Non-ASV group. Twenty-three events (death 11, re-hospitalization 12) occurred in this follow up period. Importantly, event free rate was significantly higher in ASV group than in Non-ASV group (77.8% vs. 36.7%, logrank P=0.01).

Conclusions: ASV improved cardio-renal function and long-term prognosis in HF patients with CKD and SDB.

Background: Guidelines of the Diagnosis and Management of Heart Failure (HF) recommend investigating exacerbating conditions, such as thyroid dysfunction, but without specifying impact of different TSH levels. Limited prospective data exist regarding the association between subclinical thyroid dysfunction and HF events.

Methods: We performed a pooled analysis of individual participant data using all available prospective cohorts with thyroid function tests and subsequent follow-up of HF events. Individual data on 25,390 participants with 216,247 person-years of follow-up were supplied from 6 prospective cohorts in the USA and Europe. Euthyroidism was defined as TSH 0.45-4.49 mIU/L, subclinical hypothyroidism as TSH 4.5-19.9 mIU/L and subclinical hyperthyroidism as TSH <0.45 mIU/L, both with normal free thyroxine levels. HF events were defined as acute HF events, hospitalization or death related to HF events.

Results: Among 25,390 participants, 2068 had subclinical hypothyroidism (8.1%) and 648 subclinical hyperthyroidism (2.6%). In age- and gender-adjusted analyses, risks of HF events were increased with both higher and lower TSH levels (P for quadratic pattern <0.01: hazard ratio (HR) was 1.01 (95% confidence interval [CI] 0.81-1.26) for TSH 4.5-6.9 mIU/L, 1.65 (CI 0.84-3.23) for TSH 7.0-9.9 mIU/L, 1.86 (CI 1.27-2.72) for TSH 10.0-19.9 mIU/L (P for trend <0.01), and was 1.31 (CI 0.88-1.95) for TSH 0.10-0.44 mIU/L and 1.94 (CI 1.01-3.72) for TSH <0.10 mIU/L (P for trend=0.047). Risks remained similar after adjustment for cardiovascular risk factors.

Conclusions: Risks of HF events were increased with both higher and lower TSH levels. Our findings might help to interpret TSH levels in the prevention and investigation of HF events.
Diagnosis of hypothiroidism is associated to an increased risk of acute decompensated heart failure occurrence, but not of mortality among heart failure outpatients

N. Pezzali, E. Vizzardi, C. Lombardi, L. Bettari, M. Metra, L. Dei Cas. Sec. of Cardiovasc. Diseases, Department of Experimental and Applied Med., University and Hospital, Brescia, Italy

Purpose: Red cell distribution width (RDW), a marker of anisocytosis, is a recently assessed predictor of adverse outcomes in heart failure (HF). The mechanisms underlying this observation have not been fully elucidated yet. We analysed possible correlations between clinical variables, RDW and changes in RDW among patients with chronic HF, to evaluate factors possibly associated with anisocytosis in HF.

Methods: Among our database of outpatients with chronic HF caused by left ventricular systolic dysfunction, we selected consecutive patients who had two consecutive visits with measurements of the laboratory exams, Doppler echocardiography and cardiopulmonary exercise testing at a 6 to 12 months interval. Follow-up data after the second visit were obtained by medical records and by telephone calls to the patient, her/his relatives or physician. We analysed possible correlations between clinical variables, RDW baseline values and RDW changes during the follow-up (HOT, i.e. follow-up - baseline RDW) assessing Pearson correlation coefficient (r).

Results: Three-hundred-fourteen consecutive patients (age 67±12 years, LVEF 34.8±9.9%) were included into the study. The interval between the two visits was of 202±48 days. The correlations between baseline RDW and other baseline clinical characteristics were the following: age r=0.2302 (p<0.0001), BUN r=0.3950 (p<0.0001), LVEF r=-0.3466 (p<0.0001), HR r=-0.1521 (p=0.0079), Hb r=-0.3266 (p<0.0001), creatinine r=0.2942 (p<0.001), cholesterol r=-0.1113 (p=0.0592), peak oxygen consumption r=-0.2395 (p=0.0442). DeltaRDW had no correlations with baseline clinical variables. Regarding RDW baseline values, significant variables at univariate analysis were assessed by multivariable regression analysis. Only baseline Hb (r=-0.2565, p=0.0384) and creatinine (r=0.9607, p=0.0117) were independently related with RDW baseline values at multivariate analysis.

Conclusions: Both baseline RDW values and RDW changes have a prognostic significance among patients with chronic heart failure, as already demonstrated. RDW baseline values are related with other clinical characteristics, while RDW changes are possibly related with change in clinical conditions and hence prognosis, independent from other clinical variables.

High incidence of transitory arterial hypotension in patients with chronic heart failure

D. Serova, V. Serov, A. Shitov, M. Menzarov. Ulyanovsk State University, Ulyanovsk, Russian Federation

Purpose: The aim of this study was to determine the incidence of arterial hypotension in patients with chronic heart failure (CHF) according to the results of Ambulatory Blood Pressure Monitoring (ABPM).

Methods: 152 patients with CHF (90 males and 62 females, mean age was 57.2±11.2 years) were studied. 19 patients had functional class I of CHF, 72 - Class II, 60 - Class III, 1 patient - Class IV according to NYHA classification. Causes of CHF were: arterial hypertension in 24 patients, coronary artery disease (CAD) - 5 patients, CAD and arterial hypertension - 120, other diseases of cardiovascular system - in 3 patients. Patients were treated according to Russian National Guidelines for Diagnosis and Management of Chronic Heart Failure, 2009. The ABPM was performed in hospitalized patients according to criteria P.E. Owens and E.T. O'Brien (1996). The time index of hypotension, also was taken into account.

Results: We recorded systolic arterial hypotension in 149±30.4 mmHg, diastolic blood pressure (DBP) – 91.0±15.9 mmHg. Office systolic arterial hypotension was diagnosed in 4 (2.6%), diastolic arterial hypotension in 3 (2.0%), systolic-diastolic hypotension in 5 (3.3%) patients. So, systolic and/or diastolic hypotension was identified in 12 (7.9%) patients. During ABPM average systolic blood pressure was 133.4±18.9 mmHg, average DBP – 78.4±12.2 mmHg. Episodes of systolic arterial hypotension during the 24-hour were revealed in 4 (2.6%), diastolic arterial hypotension – in 47 (30.9%), systolic-diastolic hypotension - in 64 (42.1%) patients. Systolic and/or diastolic hypotension during ABPM was revealed in 115 (75.7%) patients more often in the daytime: 63 (41.4%) patients in daytime versus 3 (2.0%) in nighttime (χ²=69.67, p<0.001). Also 49 patients had arterial hypotension both in daytime and nighttime.

Conclusions: Using ABPM improve the diagnosis of arterial hypotension in patients with chronic heart failure. Episodes of arterial hypotension are diagnosed in 75% of patients with CHF more often in the daytime. Further researches are necessary to define the connection between arterial hypotension and increased mortality in patients with CHF.
The association between sleep-disordered breathing and life-threatening ventricular arrhythmias in patients with chronic heart failure

S. Yamada1, H. Suzuki1, M. Sabo1, S. Iwaya2, M. Kamioka2, Y. Kaniyama1, S. Suzuki1, A. Yoshida2, S. Sabo1, Y. Takahashi1
1Fukushima Medical University, Fukushima, Japan; 2Fukushima Medical University, Department of Cardiology and Hematology, Advanced Cardiac Therapeutics, Fukushima, Japan

Introduction: It has been shown that sleep-disordered breathing (SDB) is associated with adverse prognosis in patients with chronic heart failure (CHF). However, little is known about the relationship between SDB and life-threatening arrhythmias. Thus, we investigated this issue in patients with CHF.

Methods: The study subjects consisted of 50 CHF patients (33 males, mean age 59 years, ischemic etiology 42%, mean left ventricular ejection fraction 42%). These patients underwent 24-hr Holter ECG and polysomnography. T-wave alternans (TWA) was calculated by the modified moving average method, and the circadian variation in positive TWA (>5 µV) was determined during the 6-hour intervals (0-6, 6-12, 12-18, and 18-24 hour). In addition, we investigated the power spectral analysis and the time domain analysis of heart rate variability (HRV), and the appearance of ventricular tachycardia (VT, >5 beats) by 24-hour Holter ECG. All subjects were divided into two groups based on whether apnea-hypopnea index was above or below 20 events/h (Group A: n=25; Group B: n=26) by polysomnography. These parameters were compared between two groups.

Results: The ratio of positive TWA in Group A was significantly higher than in Group B in all of 6-hour intervals (0-6 hr: 23% vs. 8%, p<0.05; 6-12 hr: 50% vs. 25%, p<0.05; 12-18 hr: 50% vs. 25%, p<0.05; and 18-24 hr: 36% vs. 4%, p<0.05). These results suggest that SDB may impair ventricular repolarization and modulate autonomic nervous system across 24-hour period, resulting in the appearance of life-threatening ventricular tachyarrhythmias in CHF patients.
Left atrial enlargement in sickle cell disease patients: remodelling associated with haematological parameters or index of left ventricular filling pressures

N. Hammoudi\textsuperscript{1}, M. Charbonnier\textsuperscript{2}, M. Djebbar\textsuperscript{3}, D. Aranglade\textsuperscript{3}, K. Stankovic\textsuperscript{4}, R. Isnard\textsuperscript{1}, P.L. Michel\textsuperscript{1}, F. Lionnet\textsuperscript{4}, J.-P. -Hospital Pitié-Salpêtrière, University Pierre & Marie Curie Paris VI, Dept of Cardiology, Paris, France; \textsuperscript{2}AP-HP - Hospital Saint Antoine, Paris, France; \textsuperscript{3}AP-HP - Hospital Pitié-Salpêtrière, Department of Cardiology, Paris, France; \textsuperscript{4}AP-HP - Hospital Tenon, Paris, France

Purpose
Diastolic left ventricular (LV) dysfunction is a common finding in sickle cell disease. Furthermore, left atrial (LA) size usually reflects left ventricular filling pressures. The aim of our study was to determine if LA size is an expression of left ventricular filling pressures or reflects remodelling associated with anaemia and/or haemolysis in sickle cell disease.

Methods: We evaluated 127 patients with sickle cell disease in stable condition (mean age 28±6.85 years, 63 women) and 38 age and sex-matched healthy controls. LA size was measured with Simpson’s method in apical 4-chamber view. LV filling pressures were assessed using ratio between pulsed Doppler peak E velocity and peak Ea velocity obtained with tissue Doppler imaging of the lateral annulus (E/Ea ratio). Clinical and biologic data were collected from clinical records.

Results: Compared with the normal group, patients with sickle cell disease had a LA volume and E/Ea ratio significantly increased (48.4±11.2 m\(^3\)/m\(^2\) and 5.9±1.7, 30.5±7.6 m\(^3\)/m\(^2\) and 4.5±1.1, respectively, p<0.0001). In multivariate analysis, LA enlargement in patients is only influenced by age and haematological parameters (haemoglobin and reticulocyte levels).

No correlation was found between LA volume and E/Ea ratio (figure).

Conclusion: Subjects with sickle cell disease have LA enlargement. However, in this population, LA dilatation is not an index of left ventricular filling pressures.

Plasma NGAL predicts mortality but not post discharge worsening renal function in patients with chronic heart failure

V.M. Van Deursen\textsuperscript{1}, K. Damman\textsuperscript{1}, A.A. Voors\textsuperscript{1}, M.H.L. Van Der Wal\textsuperscript{1}, T. Jaarsma\textsuperscript{2}, D.J. Van Veldhuisen\textsuperscript{1}, H.L. Hillege\textsuperscript{3} on behalf of COACH. \textsuperscript{1}University Medical Center Groningen, Department of Cardiology, Groningen, Netherlands; \textsuperscript{2}Linkoping University, Faculty of Health Sciences, Department of Social & Welfare Studies, Norrkoping, Sweden; \textsuperscript{3}University Medical Center Groningen, Department of Epidemiology, Groningen, Netherlands

Background: In patients with heart failure (HF), urinary Neutrophil Gelatinase Associated Lipocalin (NGAL), a marker of renal tubular damage, is elevated and associated with worse outcome, independent of glomerular filtration rate (GFR), whereas the prognostic value of plasma NGAL in HF is not well established.

Methods: A total of 39 patients with established OSA (apnoea-hypopnoea index, AHI = 10/h) with (NYHA ≥ II, LV-EF < 40%; n=26, 16 male, 67±9.4 years) and without (EF ≥ 50%, FprBNP < 400; n=13, 6 male, 72±5.8 years) HF underwent simultaneous right- and left-heart catheterization within 12h of cardiorespiratory polygraphy recording. AHI as well as obstructive apnoea index (aAHI) were comparable in both groups (AHI=34.3±26.5 h vs. 32.3±18.0, p=n.s.; aAHI=8.5±7.8 h vs. 10.0±10.8, p=n.s.). We were able to verify increased CL, VL, time to peak ventilation (TTPV) and circulatory delay (CD) in patients with HF (CL: 37.8±10.6 vs. 46.0±10.6, p=0.004; VL: 21.3±7.1 vs. 25.4±3.8, p=0.044; TTPV: 8.3±2.5 s vs. 10.6±3.0 s, p=0.021; CD: 22.6±3.7 s vs. 28.5±7.5 s, p=0.005). Apnoea length (AL) was higher in HF patients (16.5±3.9 s vs. 20.5±4.9 s, p=0.013). Positive and robust correlations between parameters of OSA and degree of congestion were found in OSA patients with HF exclusively: CL, VL, and TTPV increased with elevation of PCWP (CL: r=0.53; p=0.006; VL; r=0.55; p=0.004; TTPV: r=0.47; p=0.015).

Conclusion: Plasma NGAL predicts mortality in patients with heart failure, independent of eGFR and even in patients without chronic kidney disease. However, plasma NGAL does not predict worsening renal function post discharge.

Apixaban after acute coronary syndrome in patients with heart failure: insights from the APPRAISE-2 trial

J. Cornell\textsuperscript{1}, S. James\textsuperscript{2}, R.D. Lopes\textsuperscript{3}, P. Mohan\textsuperscript{4}, M. Neely\textsuperscript{5}, J. Amerena\textsuperscript{6}, Y. Hua\textsuperscript{7}, J.H. Alexander\textsuperscript{3}, R.A. Harrington\textsuperscript{8}, L. Wallentin\textsuperscript{9} on behalf of APPRAISE-2 Study Group. \textsuperscript{1}Medical Center Alkmaar, Alkmaar, Netherlands; \textsuperscript{2}Uppsala University, UCR-Uppsala Clinical Research Center; Uppsala, Sweden; \textsuperscript{3}Duke Clinical Research Institute, Duke University Medical Center, Durham, United States of America; \textsuperscript{4}Bristol-Myers Squibb, Princeton, United States of America; \textsuperscript{5}Barwon Health, Geelong, Australia; \textsuperscript{6}Feking University First Hospital, Beijing, China; People’s Republic of China

Background: In patients with ACS who did not lead to a meaningful reduction in ischemic events.

Methods: We assessed the association between history of HF or acute HF and outcomes as well as the efficacy and safety of apixaban vs placebo.

Figure 1. Mortality among groups of NGAL and CKD

Conclusions: Plasma NGAL predicts mortality in patients with heart failure, independent of eGFR and even in patients without chronic kidney disease. However, plasma NGAL does not predict worsening renal function post discharge.

Figure 1. PCWP-VL

Conclusions: Respiratory parameters of OSA (CL, VL, TTPV) correlate with the degree of congestion in patients with OSA and HF, but not in non-HF patients with OSA. These results point to a reciprocal relationship of HF and OSA severity.

Figure 1. Interaction of heart failure and obstructive sleep apnoea: cycle lengths of obstructive sleep apnoea are dependent on left ventricular filling pressures

O. Oldenburg, C. Elken, T. Bitter, B. Koerber, K. Buttler, D. Horstkotte. Department of Cardiology, Heart and Diabetes Centre North Rhine-Westphalia, Ruhr University Bochum, Bad Oeynhausen, Germany

Purpose: Obstructive sleep apnoea (OSA) may lead to or worsen heart failure (HF), however it is controversial if HF itself may influence OSA parameters such as: AHI (Beverley’s index), severity (apnoeic/hypopnoeic episodes (AHI), number of apnoeic/hypopnoeic episodes (AHI), number of events per hour of sleep (AHI)), AHI parameters (aHI, assessed with apnoea hypopnoea index (aAHI), confidence interval (CI) 0.88 - 1.89, P = 0.194). Plasma NGAL levels were univariately associated with the incidence of the combined endpoint of HF hospitalization or all-cause mortality (P < 0.001), but not in multivariate analysis (Hazard ratio (HR) 1.22 per doubling NGAL, 95% CI 0.98 - 1.52, P = 0.071). Higher plasma NGAL levels were independently associated with 3 year mortality rates (HR: 1.98, 95% CI 1.44 - 2.73, P < 0.001), even in patients without chronic kidney disease (CKD: eGFR < 60 mL/min/1.73m\(^2\); HR: 1.86, 95% CI 1.07 - 3.02, P = 0.027).
Evaluation of psychological pain, a measure of Long-term effects of tri-level adaptive servoventilation (ASV) therapy on respiratory and cardiac parameters in chronic heart failure (CHF).

**Purpose:** Combined central and mixed apnoeic events are challenging to treat. In selected CHF patients, trilevel ASV-treatment using the Somnolator CR™ device is able to sustain decrease central and mixed sleep apnoea, may improve HF symptoms and increase cardiopulmonary exercise capacity.

**Methods and Results:** In 45 patients with NYHA ≥ II, elevated NT-proBNP levels and echocardiographic and/or cardiopulmonary exercise testing signs of HF, moderate to severe SDB (apnoea-hypopnoea-index, AIH ≥ 15/h with central and mixed apnoeic events was diagnosed by polysomnography (PSG). All PSG results were explained individually and ASV treatment (Somnolator CR™, Weimann) was offered to every patient. In 15 patients, efficacy of ASV treatment and HF status was evaluated after 3.6±1.2 months. Respiratory events were suppressed effectively (AIH baseline 42.8±17.5/h vs. 12.9±11.8/h during initial therapy initiation vs. 8.9±5.8/h at follow-up; p<0.05 for each comparison). Central apnoea-index (cAI) decreased from 10.4±12.0/h at baseline to 1.3±3.0/h at ASV initiation vs. 0.3±0.6/h at follow-up; p<0.05 for each comparison (figure) while oxygen saturation improved significantly while pCO2 decreased from 36.4±3.1 to 37.9±3.8 mmHg (p<0.05), indicating a possible positive effect on respiratory control stability.

**Conclusions:** In selected HF patients, trilevel ASV treatment using the Somnolator CR™ device is able to sustain decrease central and mixed sleep apnoea, may improve HF symptoms and increase cardiopulmonary exercise capacity.

### Comorbidities in heart failure

<table>
<thead>
<tr>
<th>Event</th>
<th>No Prior HF + No HF at Index</th>
<th>No Prior HF + HF at Index</th>
<th>No Prior HF + No HF at Index</th>
<th>No Prior HF + HF at Index</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CV death, MI or ischemic stroke</td>
<td>10.75</td>
<td>12.77</td>
<td>18.19</td>
<td>20.06</td>
<td>Reference group</td>
</tr>
<tr>
<td>CV death</td>
<td>1.9 (90.1, 1.57)</td>
<td>2.1 (45.2, 2.29)</td>
<td>2.04 (1.65, 2.52)</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td>3.2 (1.17)</td>
<td>6.5</td>
<td>9.04</td>
<td>11.86</td>
<td></td>
</tr>
<tr>
<td>Safety: Bleeding</td>
<td>0.28 (1.15, 3.46)</td>
<td>0.28 (1.15, 3.46)</td>
<td>0.28 (1.15, 3.46)</td>
<td>0.28 (1.15, 3.46)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TIM major bleeding</td>
<td>0.85 (90.9, 1.24)</td>
<td>1.05 (90.9, 1.24)</td>
<td>1.05 (90.9, 1.24)</td>
<td>1.05 (90.9, 1.24)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*HF compared the hazard of HF groups.*
biofilm in patients (18/20 vs. 15/22) was associated with a higher concentration of anaerobes, aerobes and total bacteria in stool (6.4±0.3 vs. 4.6±0.2, p<0.015; 8.3±0.2 vs. 6.5±0.7, p<0.02 and 8.3±0.2 vs. 6.5±0.7, p<0.02 respectively). The same applied to the increased occurrence rate of strictly anaerobic Firmicutes prausnitzii in patients’ biofilms (18/20 vs. 12/22) which was reflected by more anaerobes, aerobes and total bacteria in stool of these patients (8.3±0.2 vs. 6.4±0.7, p<0.015; 8.3±0.2 vs. 6.5±0.7, p<0.015; 8.3±0.2 vs. 6.5±0.7, p<0.02, respectively).

Conclusion: Concentration of stool bacteria reflects the increased occurrence rate of strictly anaerobic bacteria within the mucosal biofilm of the sigmoid indicating better conditions for these specific anaerobes directly at the surface of the mucus membrane in CHF. This may contribute to gastrointestinal symptoms in patients with CHF.

**P1957** Brain natriuretic peptide (BNP): A general mortality predictor in HIV-infected patients? - Results from the 5 year follow-up of the HIV-HEART trial

N. Reinsch1, H.W. Kloetgen2, R. Jablonka3, J. Storm3, A. Warnke2, G. Gelbrich1, R. Eitel1, T. Neumann1, D. Schadendorf1, S. Esser1 on behalf of all the members of the German Competence Network Heart Failure and the German Competence Network for HIV/AIDS. 1West German Heart Center Essen Clinic for Cardiology, Essen, Germany; 2Department of Dermatology and Venerology, University of Essen, Essen, Germany; 3Center for Clinical Trials (KKS), University of Leipzig, Leipzig, Germany

Background: HIV-infected patients exhibit an increased rate of cardiac diseases, due to an elevated rate of cardiac risk factors and side effects of antiretroviral therapy. The aim of the present study was to analyze the impact of B-type natriuretic peptide (BNP) as a prognostic parameter for death in HIV-infected individuals.

Methods: This prospective multi-centre observational cohort study elucidates cardiovascular disease prevalence by standardized non-invasive cardiovascular screening program and laboratory tests including BNP in 790 HIV-infected patients from four specialised outpatient clinics in Germany between 2004 and 2011. Within the 5-year follow-up period 50 (6.3%) of the individuals died. Characteristics of survivors and deceased patients were compared and evaluated for their predictive value.

Results: At baseline, 83.3% of the 790 patients were male, 88.5% Caucasians, 3.5% Asians, 5.7% were CDC-categorised C and 48% immunological stage 3. The mean age was 44.3 years and the mean measured CD4 cell counts were 507 cells/μl. 687 (87.0%) patients underwent antiretroviral treatment, of whom 55% had a normal viral load, 51% were CDC-categorised C and 48% immunological stage 3.

Purpose: Diabetes mellitus (DM) is an independent predictor of heart failure (HF). The optimal approach to this problem involves identifying patients at risk early in the course of the condition. Previous studies have shown a high prevalence of diastolic dysfunction in diabetic subjects. We set out to study the wider burden of structural and functional problems that could lead to heart failure.

Methods and Results: The STOP-HF cohort consists of subjects over 40 with at least one cardiovascular risk factor. Each had a Brain Natriuretic Peptide level and Doppler-Echocardiography performed. Stage B heart failure was defined as structural heart disease (consisting of ejection fraction <50%, left atrial volume index>34 ml/m2 and/or left ventricular mass index>149g/m2 [M], >122g/m2 [F]) in the absence of symptoms of heart failure. Of 1025 total patients, 234 (22.8%) were documented as having DM. Prevalence of stage B HF was 19.8% in the total population, 23.5% in those with DM and 18.8% in those without (p=0.001). Age distribution was similar across the two groups. Considering only those patients with BMI≥30kg/m2, 82 (27%) of the total of 303 had DM: 32% of these had stage B HF. Prevalence of stage B was 44% in those with DM and BMI≥30kg/m2 compared to 28% in non-diabetics (p=0.013).

Conclusions: Though asymptomatic, a significant proportion of the diabetic population had stage B HF, particularly those with BMI≥30 kg/m2. At a time of limited resources, this identifies a cohort of patients requiring more intensive risk factor control to prevent progression to symptomatic heart failure.

**P1958** Differences in general health status and functional capacity in patients with chronic heart failure and chronic obstructive pulmonary disease after one-year of hospital discharge

N. Arenja, M. Potocki, R. Ziller, T. Mommann, C. Heinrichs, C. Slebzig, M. Freese, C. Mueller. University Hospital Basel, Department of Internal Medicine, Basel, Switzerland

Background: The aim of this prospective observation study was to assess self reported health status and functional capacity in patients with chronic heart failure (CHF) and chronic obstructive pulmonary disease (COPD) one-year after hospitalisation for acute dyspnea.

Methods: 684 consecutive patients presenting to the emergency department with acute dyspnea were included in the study. The final diagnosis was adjudicated by two independent cardiologists. General health status and functional capacity was determined at presentation and one-year after hospital discharge, by EuroQol-5

**P1959** The hidden truth: stage B heart failure among diabetics and the obese

G. Murtagh, J. O’Connell, I. Dawkins, T. King, J. Griffin, E. Tallon, R. O’Hanlon, A. Patel, M. Ledwidge, K.M. Mc Donald. St Vincent’s University Hospital, Heart Failure Unit, Dublin, Ireland

Purpose: Diabetes mellitus (DM) is an independent predictor of heart failure (HF). The optimal approach to this problem involves identifying patients at risk early in the course of the condition. Previous studies have shown a high prevalence of diastolic dysfunction in diabetic subjects. We set out to study the wider burden of structural and functional problems that could lead to heart failure.

Methods: Among 100 patients, 51 of them (51%) were shown to have worse BDS (BDS <23), compared to those with good BDS (BDS ≥23) (71 vs 33.5%, p<0.001). Serum PTH levels were correlated with New York Heart Association (NYHA) functional class (p<0.001), BNP levels (p<0.001), Tricuspid Annular Plane Systolic Excursion (TAPSE) (p<0.001). Left ventricle ejection fraction (p<0.001), creatinine clearance (p<0.001), presence of pretilab edema (p<0.001), HF related rehospitalization (p<0.001), and C-reactive protein levels (p<0.002).

Parathyroid hormone, LVEF, NYHA functional class, C-reactive protein, pretilab edema, HF related rehospitalization, TAPSE, BNP Disease duration, Sodium, Left atrium size, creatinine clearance, left ventricle systolic diameter, and female gender were associated with worse BSDs in univariate analysis. In multivariable logistic regression model, PTH level (Odds ratio=1.035, p<0.001), LVEF (Odds ratio=1.085, p<0.004), NYHA Functional Class III/IV (Odds ratio=28.022, p=0.005), C-reactive protein (Odds ratio=1.088, p=0.020), and presence of pretilab edema (Odds ratio=12.341, p<0.001) were found to be independent predictors of worse BSDs after adjustment of potential confounders.

Conclusions: Patients with moderate to severe depression had higher serum levels of PTH and CRP, poor functional status and lower left ventricle EF, all of which are predictors of advanced HF. The association of depression with predictors of advanced HF may explain the contribution of depression to hospitalization and mortality in HF.
dimensions (EQ-5D), VAS (0 = worst and 100 = best possible health) and 12-item Duke Activity Status Index (DASI) questionnaire.

Results: A total of 184 patients (27%) died within 360 days. At one-year follow-up out of the 500 patients alive, the questionnaires were completed and returned by 179. Within these, 94 patients with CHF and 39 with COPD were included in the analyses. No statistically significant difference was found in neither of the two disease groups regarding EQ-5D dimensions. Additionally Figure 1 shows the sum of the proportion of reported level 2 and level 3 problems for each of the 5 EQ-5D dimensions. The median (interquartile range) of EQ-VAS score was 60 (50–76) for patients with CHF and 60 (39–70) for COPD (p=0.1). Average DASI-estimated functional capacity was 8.3 (7.6–9.2) metabolic equivalents (METs) in CHF and 8.9 (7.35–9.4) METs in COPD patients, without significant difference (p=0.07).

Conclusions: Our analysis demonstrates high prevalence of poor general health status and functional capacity in patient with CHF and COPD even after One-year hospital discharge. Therefore future research is needed in outpatients, - management and advanced care planning is justified.