Conclusions: This study shows for the first time that there is increased association of LR1P and ERK1/2 with myocardial lipid rafts in IDCm patients. Future studies are needed to elucidate whether LR1P relocation to lipid rafts reinforces downstream ERK activation and leads to the characteristic alterations found in diseased hearts.

2796 | BENCH
CCAT/enhancer-binding proteins mediate interferon gamma-induced upregulation of NADPH oxidase in human aortic smooth muscle cells

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Aim: In atherosclerosis, oxidative stress-induced vascular Smooth Muscle Cells (SMC) dysfunction is partially mediated by upregulated NADPH oxidases (Nox); the mechanisms of enzyme regulation are not entirely defined. CCAT/enhancer-Binding Proteins (C/EBP) regulate the expression of inflammatory and immune genes, the differentiation of immigrating and resident cells, eventually influencing atherosclerotic plaque development. We aimed at elucidating the role of C/EBP in the regulation of Nox in SMC exposed to proinflammatory conditions.

Methods and results: Human aortic SMC were exposed to interferon gamma (IFNg) for 24 h. Luciferin-enhanced chemiluminescence, real-time PCR, Western blot, promoter-lucerase reporter analysis, and chromatim immunoprecipitation assays were employed to investigate Nox regulation. The expression and function of four C/EBP isoforms were controlled by pharmacological and molecular interventions. IFNg dose-dependently induced Nox activity/expression, nuclear translocation of C/EBPβ, and C/EBPβ protein expression levels. C/EBPβ, C/EBPβ or C/EBPδ upregulated the IFNg-induced upregulation of Nox activity and gene/protein expression. Pharmacological inhibition of p38MAPK and ERK1/2 diminished significantly the IFNg-induced C/EBP nuclear translocation and Nox activity/expression. In silico analysis indicated the existence of typical C/EBP within Nox Nts, Nox4 and Nox6 promoters. Transient overexpression of C/EBPβ or C/EBPδ upregulated the luciferase level directed by the promoters of all SM-expressed Nox isoforms. Chromatin immunoprecipitation demonstrated the physical interaction of C/EBPβ, C/EBPδ, or C/EBP β proteins with the Nox-1 promoter. Moreover, transactivation assays demonstrated the existence of a crosstalk among C/EBPα, AT1 and STAT1/transcription factors.

Conclusions: C/EBP transcription factors are important regulators of Nox enzymes by both direct and indirect pathways in IFNg-exposed SMC. Activation of C/EBP may induce excessive Nox-derived reactive oxygen species formation, further contributing to phenotypic alterations of SMCs in atherosclerosis.


CATHETER ABLATION OF ATRIAL FIBRILLATION: LOOKING FOR THE BEST SOLUTION

2805 | BENCH
Progression of atrial fibrillation after a failed initial ablation procedure in patients with paroxysmal atrial fibrillation: a randomized comparison of antiarrhythmic drug therapy vs re-ablation

E. Pokushalov1, A. Romano1, M. De Melis2, S. Artyomenko1, V. Baranova1, D. Lus1, S. Bairamova1, A. Karasov1, S. Mittal2, J.S. Steinberg3, 1State Research Institute of Circulation Pathology, Novosibirsk, Russian Federation; 2Medtronic BRC, Maastricht, Netherlands; 1Columbia University, New York, United States of America

Introduction: Antiarrhythmic Drugs (AAD) are generally used as first-line therapy to treat patients with Atrial Fibrillation (AF), but effectiveness remains inconsistent. Catheter ablation has become an alternative therapy for patients with Paroxysmal AF. Catheter ablation has become a preferred therapy for patients with Paroxysmal AF. The mechanisms of enzyme regulation are not entirely defined. CCAAT/enhancer-Binding Proteins (C/EBP) regulate the expression of inflammatory and immune genes, the differentiation of immigrating and resident cells, eventually influencing atherosclerotic plaque development. We aimed at elucidating the role of C/EBP in the regulation of Nox in SMC exposed to proinflammatory conditions.

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Conclusions: C/EBP transcription factors are important regulators of Nox enzymes by both direct and indirect pathways in IFNg-exposed SMC. Activation of C/EBP may induce excessive Nox-derived reactive oxygen species formation, further contributing to phenotypic alterations of SMCs in atherosclerosis.


2807 | BENCH
Does power matters during pulmonary veins isolation with open irrigated catheter: results from a randomized study

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Introduction: Durable pulmonary veins (PVs) isolation is key for the long term success of catheter ablation of atrial fibrillation (AF). We compared two different energy settings to achieve PVs isolation and we evaluated the PVs reconnection at follow up.

Methods: 104 patients (pts) undergoing paroxysmal AF ablation were prospectively randomized to PVs isolation with a power of 30 Watts (Group 1, n=52) versus PVs isolation with a power 40 Watts (Group 2, n=52). All pts underwent PV antrum isolation with an open irrigated catheter. In the period between 3 to 6 months post ablation, irrespective of recurrences, pts underwent a left atrial catherization to exclude the presence of PVs reconnection. In case of reconnection, pts underwent re-isolation of the pts with 40 Watts and a third procedure was considered to confirm permanent isolation. Pts were given event recorders and followed up at 3, 6, 9, 12, and every 3 months thereafter for a minimum of 3 years.

Results: Baseline characteristic had no significant difference between groups. At the repeat study, PVs reconnection was seen in 61% (32 pts) of Group 1 and 29% (15 pts) of Group 2 respectively (p<0.001). At 14±2 months follow up, overall freedom from atrial arrhythmias was 63% (66 pts). All 38 pts experiencing recurrences underwent a third procedure. At the redo procedure only 1 PV was reconnected and in 37 pts no PV triggers were documented and ablated.
Conclusions: This prospective randomized study shows that when utilizing a power of 40 Watts a lower PVs reconnection is shown at follow-up. In nearly 30% of paroxysmal AF pts, despite permanent PVs isolation at repeat procedure, arrhythmia recurrence due to non PV triggers was shown.

2808 | BEDSIDE
Ganglionated plexi ablation vs linear ablation in patients undergoing pulmonary vein isolation for persistent/longstanding persistent atrial fibrillation: a randomized comparison
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Introduction: The optimal ablation technique for persistent and longstanding per-

Background: Patients with atrial fibrillation (AF) require to achieve complete linear block at the mitral isthmus (MI). The purpose of this study is to elucidate the morphologic characteristics of the MI which may need ablation inside the CS.

Method and results: Ninety-eight consecutive patients (mean age 64±11, 74 male [76%], 51 persistent AF [52%]) who underwent the first linear ablation at the MI during catheter ablation for AF/AT were enrolled in the study. All patients underwent 64-slice MDCT scanning prior to the procedure and its anatomical features of the MI were analyzed.

Complete block along the mitral isthmus was achieved in 85 (87%) patients, of which 45 (50%) patients required radiofrequency ablation inside the CS (Group CS), and RF application was not required in the other 40 (47%) patients (Group Non-CS). There were no significant differences in the MI length, isthmus depth, CS diameter, CS cross-sectional area, and the distance between the CS and the MI. However, group CS patients were more likely to have interposed circumflex artery between the CS and the MI (40% vs. 18% p=0.02).

Conclusion: Interposition of the circumflex artery between the MI and the CS is associated with a higher probability of requiring ablation inside the CS to achieve complete mitral isthmus block.

HEART FAILURE: THE BIOMARKER BOOM
2819 | BENCH
Involvement of BAG3 and HSPB7 loci in various etiologies of systolic heart failure: results of a European collaboration assembling more than 2,000 patients
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Background and purpose: Genetic background of multifactorial systolic heart failure (systHF) is still poorly understood. However, through a recent genome wide association study we identified two loci significantly associated with sporadic Dilated Cardiomyopathy (DCM): BAG3 and HSPB7 loci. We further studied these two loci and hypothesized that the loci could also be involved in systHF due to coronary artery disease (CAD) and (2) that the loci could be involved in the severity of systHF and not only in the susceptibility to develop HF.

Methods: We genotyped polymorphisms (SNPs) previously associated with DCM (rs2234962 for BAG3 locus, rs945417 for HSPB7 locus) in a European population of 1160 patients with systHF due to CAD (ischemic-HF) and 1322 controls. The severity of systHF (assessed by left ventricle ejection fraction or LVEF, LV end diastolic diameter or LVEDD, age and NYHA dyspnea at inclusion) was also compared according to the SNPs in the cohort of ischemic-HF patients as well as in a European cohort of 1141 patients with DCM.

Results: We observed that SNPs related to DCM-HF were significantly associated with more severe systHF (P=0.002). After a second procedure in 78 patients of the PVI+LL group and 55 patients of the PVI+GP group, the long-term overall success rate was 52% and 68%, respectively (p=0.005).

Conclusions: The prevalence of STL while performing AF ablation was 11% of the cases while performing the procedure with warfarin discontinuation. The incidence of post-ablation STL was 2.1% in overall population. When sorting the results by AF type we found that it was 0% (0/37) in paroxysmal patients, 0% in persistent AF patients and 7% (3/43) in long-standing persistent AF patients with cardioversion.

Here, we present the results of the TURBO-HF study, a European, multi-centre, prospective, randomized, parallel group study aimed at investigating whether PVI+LL is superior to PVI+GP in terms of ablation success and type I adverse events. The study included 264 consecutive patients with persistent or longstanding persistent atrial fibrillation (AF) with open irrigated radiofrequency energy (RF) ablation (within 24 hours) dMRI. All patients had to maintain ACT above 300 ± 30 seconds. Pre and post-procedural dMRI was obtained in all cases. Sinus rhythm was restored in 21% of patients with cardioversion in 35 pts (24%) of the cases. The incidence of post-ablation STL was 2.1% in overall population. When sorting the results by AF type we found that it was 0% (0/37) in paroxysmal patients, 0% in persistent AF patients and 2% (1/43) in long-standing persistent AF patients with cardioversion.

Conclusion: Complete block along the mitral isthmus was achieved in 85 (87%) patients, of which 45 (50%) patients required radiofrequency ablation inside the CS (Group CS), and RF application was not required in the other 40 (47%) patients (Group Non-CS). There were no significant differences in the MI length, isthmus depth, CS diameter, CS cross-sectional area, and the distance between the CS and the MI. However, group CS patients were more likely to have interposed circumflex artery between the CS and the MI (40% vs. 18% p=0.02).

Conclusion: Interposition of the circumflex artery between the MI and the CS is associated with a higher probability of requiring ablation inside the CS to achieve complete mitral isthmus block.

2820 | BEDSIDE
Metabolomics in heart failure as a novel diagnostic tool
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Purpose: Diagnosis and risk stratification of heart failure (HF) is often challenging and predominantly relies on clinical symptoms, imaging techniques and biomarkers such as N-terminal (NT)-pro-B-type-natriuretic-peptide (BNP). The clinical utility of these biomarkers is limited by their lack of specificity for HF and inadequate sensitivity for the detection of early disease stages. We sought to identify and validate novel metabolite biomarkers for HF subdivision: Dilated (DCM) and ischemic cardiomyopathy (ICM) as well as HF with preserved ejection fraction (HFpEF).

Methods: Metabolite profiling of plasma samples was performed by both un-