P3321 | BEDSIDE
Reduction of ICD indications after optimization of heart failure treatment in patients with severe left ventricular systolic dysfunction

Background: Patients with LVEF<35% and NYHA class II or III heart failure under heart failure medical treatment have an indication for an ICD in primary prevention. Data regarding the magnitude of improvement of LVEF after intensive optimization of heart failure medical treatment are scarce.

Purpose: To assess the clinical, echocardiographic and biological impact of intensive optimization of heart failure medical treatment in patients with severe left ventricular systolic dysfunction.

Methods: This is an observational prospective study in which patients visited in a heart failure unit with LVEF<35%, without an ICD, with heart failure and non-optimal heart failure medical treatment are included. Up-titration of beta blockers, ACE inhibitors/ARB and aldosterone antagonist are gradually performed in the day hospital of the heart failure unit up to 100% of the target dose or the maximum tolerated dose. At 6 month after completion of drug up-titration the echocardiography is repeated and clinical follow-up assessed again.

Results: 35 patients have been already included. 34/85 are still being-up titrated. 3/85 died during follow-up. The 6 month follow-up has been accomplished in 48/85 patients, age 65±14 years, 9 (19%) female, 20 (42%) with ischemic heart disease. Patients on 100% of target dose of beta blockers, ACE inhibitors/ARB and aldosterone antagonists increased from 6%, 23% and 17% to 81%, 77% and 72%, respectively, with up-titration. NYHA-class diminished at 6 month: 2.1±0.6 vs 1.6±0.3. Hospital admissions for heart failure and Minnesota Quality of Life Score were also reduced: 5.4±0.5 vs 4.0±0.1 admissions/patient, and 30±1 vs 22±13, p=0.044, respectively. LVEDV, LVEDV and functional mitral regurgitation grade were reduced: 63.1±7 vs 58.9±9mm; p=0.001, 159.5±66 vs 138±56 ml; p=0.003 and 1.7±1 vs 1.3±0.9, p=0.009, respectively. Mean LVEF increased from 25.6±3 to 38.12%, p<0.001. LVEF was >35% in 25/48 (52%) patients at 6 month after up-titration. Consequently, patients with an ICD indication were reduced: 44 (88%) vs 12 (25%) when comparing before and after 6 month of completion of optimization of heart failure medical therapy. Moreover, pro-BNP levels were also reduced: 267±227 to 1774±1804 pg/ml before and after 6 month of up-titration completion.

Conclusions: Intensive optimization of heart failure medical therapy in patients with severe systolic left ventricular impairment improves symptoms and quality of life and reduces hospital admissions. Furthermore LVEF increases in the majority of patients and ICD indications are accordingly reduced.

P3327 | BENCH
M-atrial natriuretic peptide and nitroglycerin in a model of acute hypertensive heart failure: a comparison of two cGMP activating therapeutics
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Purpose: Systemic hypertension is a common characteristic in acute heart failure (HF). This commonly phenotypically is commonly associated with renal dysfunction and there is an unmet need for renal enhancing therapies. In a canine model of HF and acute vasoconstrictive hypertension we characterized and compared the cardiorenal actions of M-atrial natriuretic peptide (M-ANP), a novel particulate guanylyl cyclase activator (pGC), and nitroglycerin, a soluble guanylyl cyclase (sGC) activator.

Methods: HF was induced by rapid right ventricular pacing (180 bpm) for 10 days. On day 11 hypertension was induced by continuous angiotensin II infusion. We characterized the cardiorenal and humoral actions prior to, during, and for 300 minutes following intravenous M-ANP (n=7), nitroglycerin (n=7), and vehicle (n=7) infusion.

Results: Mean arterial pressure (MAP) was reduced by M-ANP (139±4 to 118±3mmHg; p<0.05) and nitroglycerin (137±3 to 116±4mmHg; p<0.05), similar finding was also observed in the decrease of mean wedge pressure (PCWP) by M-ANP (12±2 to 6±1mmHg; p<0.05) and nitroglycerin (12±2 to 6±1mmHg; p<0.05). M-ANP enhanced renal function with significant increases (p<0.05) in glomerular filtration rate (48±4 to 53±5ml/min), renal blood flow (132±1 to 236±23ml/min), and natriuresis (11±4 to 68±9±3 mEq/min) and also inhibited aldosterone activation (32±3 to 2±3ng/dL; p<0.05), whereas nitroglycerin had no significant (p>0.05) effects on these renal parameters or aldosterone activation.

Conclusions: Our results advance the differential cardiorenal actions of pGC (M-ANP) and sGC (nitroglycerin) mediated cGMP activation. These distinct renal and aldosterone modulating actions make M-ANP an attractive therapeutic for HF with concomitant hypertension, where renal protection is a key therapeutic goal.

P3328 | SPOTLIGHT 2013
Effects of cholecalciferol supplementation in patients with low vitamin D levels and chronic heart failure - a randomized double blind controlled trial
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Purpose: To investigate the effects of cholecalciferol administration to chronic heart failure (CHF) patients with low vitamin D (VD) levels on physical performance, echocardiographic and hormonal parameters.

Methods: From March to December 2012, in a randomized, double blind, placebo-controlled trial, 33 patients (age 78±7 - M 15) with stable CHF, VD<30ng/ml and GFR≥30/ml/min (age 45), received 300000 U oral cholecalciferol plus 50000 Umonth for six months (17) or placebo (16). The primary end point was distance at 6 minute walking test (6MWT) at three and six months. Additional secondary endpoints were hormonal (PTH, Renin, BNP, FGF23) and echocardiographic (chamber size, systolic/diastolic function) changes.

Results: After six months VD levels significantly rose in both groups even if treated group reached higher levels (38±7.2 vs 14.3±7.2). In treated group PTH drop significantly at third month (from 76.8±50.5 to 52.0±20.3 p<0.05), but
not at sixth, and 6MWT improved at three months (from 210±104 m to 225±94 m ±0.033) but not at sixth. Echocardiographic and hormonal parameters were unchanged in both groups. Among treated patients improvement of 6MWT was positively related to baseline PTH (p<0.07) and negatively to GFR (p=0.003); this was not seen in placebo group.

**Conclusion:** In CHF our scheme of VD supplementation produced transient improvement of 6MWT and PTH but not of echocardiographic and hormonal parameters. Due to relation of 6MWT changes and basal PTH in treated patients, it might be possible that a more restrictive patient selection (hyperPTH) and higher VD doses, driven by PTH levels, would produce better and longer results.

### P3329 | BEDSIDE

**Elderly patient with heart failure and preserved ejection fraction: effects of ivabradine**

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Approximately half of patients with a diagnosis of heart failure have a normal left ventricular ejection fraction. This patients are usually older, female and with comorbidities such as hypertension, diabetes and renal failure. Unfortunately, no pharmacologic therapy has been shown to be effective in improving outcomes in patients with Heart Failure with a preserved ventricular Ejection Fraction (HFpEF). On this background, it is assumed that a reduction in Heart Rate (HR) could be advantageous. The use of ivabradine is never been tested in elderly patients with HFpEF.

**Purpose:** To evaluate safety and efficacy of ivabradine in improving diastolic function as well as symptoms of elderly patients (aged 75-85 ym) with HFpEF. We enrolled 106 patients (62 females, mean age 79±4, ym) NYHA class II (28 pts) and III (78 pts), in sinus rhythm with ventricle ejection fraction> 50%. Patients were treated with ivabradine up to 7.5 mg BID. Patients undergone echocardiographic examination at baseline, and at 1, 3 and 6 months. Four patients were lost at follow-up and were excluded from analysis. The dose of 7.5 mg BID was achieved by 66% of pts. The HR decreased significantly after 1 month with a plateau at 3 months and echocardiographic parameters improved likewise.

Twenty pts in NYHA class II step down of a class. Fifty-six pts in III class step to II and 6 in I class. There were 2 case of symptomatic bradycardia that required down-titration.

**Conclusions:** In elderly patients with HFpEF, ivabradine has proved feasible and effective in improving symptoms and echocardiographic diastolic function, together with a significant reduction in HR.

### P3330 | BEDSIDE

**The effect of long-term angiotensin receptor blocker administration on improvement in diastolic function in hypertensive patients with diastolic dysfunction**

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Aichi P3330 | BEDSIDE

**Background:** It is not well known whether angiotensin receptor blocker (ARB), which can reduce ventricular hypertrophy and myocardial fibrosis, is superior to the other anti-hypertensive agents in terms of improving diastolic function.

**Methods:** This prospective randomized controlled study is consists of 80 patients with newly diagnosed hypertension with diastolic dysfunction (diastolic relaxation velocity as determined by tissue doppler imaging (e') was less than 8 cm/second). Patients were randomly assigned to receive Valsartan (V-Group; n=31) or Amlopidine (A-group; n=29). Patients in both groups also received concomitant anti-hypertensive agents that did not inhibit the renin-angiotensin system to reach target blood pressure of 135/80 mm Hg. The changes in e' during follow-up period (6 months, 1 year and 2 years) were investigated.

**Results:** There were no significant differences in baseline clinical characteristics between the two groups. Decreases in systolic and diastolic blood pressure at each follow-up visit were also similar between the 2 groups. Both agents significantly improved e' at each time point compared to baseline. The changes in e' from baseline at 2 years were significantly larger in V-group compared to A-group. While there were no significant differences between the two groups at 6 months and 1 year.

**Conclusions:** Both anti-hypertensive agents significantly improved diastolic function. Long-term administration of ARB might be more effective than Ca-channel blocker to improve diastolic function.

### P3331 | BEDSIDE

**Trimezdazide MR in very elderly hypertensive patients with diastolic heart failure**

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**Purpose:** To explore the efficiency of trimetazidine MR (T) in the treatment of chronic heart failure (CHF) with preserved ejection fraction (EF) in very elderly hypertensive patients.

**Materials and methods:** 115 hypertensive pts aged 81.9±0.5 with CHF NYHA II were examined by transthoracic Doppler echocardiography, duplex scanning of carots and aorta, creatinine clearance (CC) calculated after Cockcroft-Gault before and after 6 months of therapy in two modes: enalapril and metoprolol (EM) and enalapril/metoprolol plus T (EMT).

**Results and discussion:** Both EM and EMT treatment resulted in positive dynamics of clinical symptoms, blood pressure decrease. LH regression, statistically more pronounced in EMT compared EM, was accompanied by improvement of left ventricular function. EF increased from 54.4±0.5% to 81.5% in EM and from 56.6±0.7% by 12.1% in EMT to EM-AF - from 0.74±0.01 by 12.1% and from 0.74±0.01 by 16%, respectively (all p<0.05). Positive effect of T as a part of combined therapy was confirmed by greater positive dynamics of LVH, EF, E/A, IVRT/RR (p<0.05 between EM and EMT).

Better dynamics of clinical symptoms and quality of life improvement was also related to no cardiac influences of T. Regression of vascular hypertrophy assessed by carotid intima-media thickness (IMT) reducing did not differ in two groups: IMT decreased from 0.99±0.01 to 0.97±0.01 cm in EM (p<0.05) and from 0.97±0.02 to 0.94±0.01 cm in EMT (p<0.05) with no statistically significant differences between two treatment groups. The ultrasound study of local aorta elasticity demonstrated the more marked decrease of index of aorta rigidity (SI) EM (by 0.20%, p<0.01) compared EM (by 16.8%, p<0.001) group with statistically significant differences between EM and EMT treatment.

EM treatment led to acceleration of initially low CC in CHF 55±4±2.5 to 61±3±3.0 ml/min in EM and from 55.3±3.3 to 68.3±3.4 ml/min in enalat in EM-AF describing effect resulted in regression of LVH with concomitant improvement both systolic and diastolic function, reduction of IMT with the increase of local aorta distensibility, the rise of CC Metabolic effects of trimetazidine MR are essential for greater improvement of systolic and diastolic heart function, aorta elasticity as well as glomerular filtration.