P4201 I BENCH

Bigilican is beneficial in angiotensin II induced heart failure by prevention, and regulates inflammation and LV function and mortality by preventing transdifferentiation of myofibroblasts.

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Bigilican is a small leucine rich proteoglycan and is important for the structural integrity of the extracellular matrix, but also serves as a danger signal and triggers sterile inflammation. Whether bigilican is beneficial or delirious in angiotensin induced heart failure, a model were remodeling as well as inflammation plays a crucial role, is unknown. The present study investigated whether gene deletion of bigilican influences cardiac inflammatory stress response, adverse remodeling and mortality leading to cardiac dysfunction and mortality after 3 weeks of angiotensin induced heart failure in vivo.

Methods and results: Bigilican knockout mice (BGN−/−) and their controls (WT) were subjected to receive angiotensin II (ANGII) or saline for 3 weeks via osmotic minipump and 21 days later LV function was analyzed invasively. ANGII induced significant cardiac inflammation (increased CD3+ (3.5 fold) and CD11b+ (+5 fold) cells) as well as cardiac dysfunction in WT-BGN animals. Interestingly, deletion of BGN impaired cardiac function (significantly impaired stroke work, cardiac output and diastolic function) when BGN−/− ANGII were compared to WT-ANGII.

Conclusion: The immune protein MD-2 is a novel independent predictor for long term mortality in dilated cardiomyopathy and non-inferior to nt-pro BNP.

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Background: Myeloid Differentiation protein 2 (MD-2) is strongly involved in the cardiovascular response to acute mental stress. The current study examined the cardiovascular response to acute mental stress in patients with chronic heart failure.

Methods and results: We included 174 patients between 2005 and 2011 with chronic heart failure in our study. MD-2 plasma levels were measured in 107 patients with dilated cardiomyopathy and 67 patients with ischemic heart disease.

Conclusion: The observed blunted autonomic and vascular reactivity to acute mental stress were independent associates of all cause mortality.

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Objective: Psychological factors have been related to poor outcome in patients with heart failure. Pathophysiological mechanisms explaining this link may include the cardiovascular response to acute mental stress. The current study examined whether heart rate and blood pressure response to acute mental stress predicted mortality in patients with chronic heart failure.

Methods: Patients with HF (N=100, 26% female, mean age 65±12 years) underwent a public speech task, during which heart rate (HR) and blood pressure (BP) were recorded. Their all cause mortality status was assessed 4.8 years later.

Results: HR reactivity was recorded in high (12±2 bpm), medium (6±1 bpm) and low (<2 (3)mmHg) responsiveness based on the 25th and 75th percentile. Heart rate and blood pressure reactivity to mental stress were not significantly related to future mortality risk.

Conclusion: The immune protein MD-2 is a novel independent predictor for long term mortality in dilated cardiomyopathy and non-inferior to nt-pro BNP.
reactivity. These findings call for replication by larger studies that also should examine whether mental stress reactivity is a mediator in the relation between psychological risk factors and adverse cardiac outcomes.

HEART FAILURE: PATHOPHYSIOLOGY AND PROGNOSIS

P4210 | BEDSIDE
Multi-slice computed tomography in dilated cardiomyopathy: comparison with myocardial biopsy, diagnostic and prognostic value


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Purpose: To study diagnostic and prognostic value of Multislice Computed Tomography (MSCT) in patients with dilated cardiomyopathy in comparison with myocardial biopsy

Methods: 89 patients (65 men, 42.2±17 years) with dilated cardiomyopathy (mean left ventricular diastolic diameter 6.7±0.9 cm, LVEF 28±0.10%, n=72) had 302-row MSCT, in 21 patients morphological study (endomycocardial/interatrial biopsy or explanted heart examination) was also performed. Anti-cardiac antibodies were also measured as well as virus detection, EchoCG, scintigraphy (n=23), MRI (n=10), coronary angiography (n=36) were performed. Results: Areas of low contrast enhancement were found in 8 patients (9.1%, 1 point), myocardial late enhancement in 40 (45.5%), subendocardial, 16 (2 points), subepicardial, 17 (3 points), transmural, 16 (4 points). In addition, fat in the right ventricle (n=3, 3.4%) and both ventricles (n=2, 2.3%), noncompact myocardium of the left ventricle (n=16, 18.2%), myocardial late enhancement in aorta (n=1, 1.1%), coronary artery stenosis more than 50% (n=10, 11.4%), vascular anomalies (n=3, 3.4%), including massive pelvic arterovenous malformation as a cause of hypertensive diastolic cardiomyopathy were found. The sensitivity and specificity of the subepicardial/transmural enhancement for myocarditis diagnostics were 55% and 100% with biopsy and 44.9% and 84.6% with combined study, respectively. Myocarditis was diagnosed based on combined study in all patients with coronary atherosclerosis (MSCT), late subendocardial/ transmural enhancement was found in 4 cases (40%); coronary angiography has not confirmed significant stenoses in 3 patients but after three weeks of pacing activation, at 180 beats/min, when LV ejection fraction was <35% and end-diastolic pressure was <18 mmHg. At the same intervals, we also evaluated the differences in the cellular cholesterol efflux efficiency mediated by HDL.

Conclusion: After three weeks of pacing there were no significant changes in total cholesterol and triglycerides compared to baseline (57.7±16.0 vs 54.2±13.0 mg/dl and 31.7±7.6 vs 31.4±14.8 mg/dl respectively). Conversely, HDL and ApoA1 levels were dramatically decreased (24.5±8.0 vs 12.4±5.7 mg/dl, p<0.001 and 20.9±9.3 vs 11.8±5.5 mg/dl, p<0.005 respectively). Among the inflammatory markers ceruloplasmin levels were significantly increased (24.7±20.8 vs 83.9±54.6 mg/dl, p<0.005). After pacing-on efflux mediated by SRBI and by gradient concentration (passive diffusion) are reduced compared to the basal levels (38% vs 0.065 and -28%, p<0.05, respectively). No statistical change was observed analyzing the efflux mediated by ABCA1 and ABCG1.

Conclusions: In this experimental model the HDL induced a progressive reduction in HDL and ApoA1 plasma levels together with a reduced cellular cholesterol efflux mediated by passive diffusion and SRBI ligand. This phenomenon could promote or facilitate the process leading to the full-blown dilated cardiomyopathy via mechanisms that surely deserve further studies.

P4211 | BEDSIDE
BNP usefulness in elderly dyspneic patients. The Bed Study

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Aims: Hospital discharge registries are frequently used for identification of individuals with heart failure in large cohort studies. However, validity of discharge codes is heterogeneous across earlier studies and current data on European populations are sparse. We examined the validity of the ICD-10 discharge code I50 for heart failure in participants of the population-based EPIC-Norfolk study.

Methods and results: Hospital records of a random subset of participants with a hospital discharge code I50 between 1997-2009 identified through a national hospital record linkage system were scrutinized for diagnostic criteria of heart failure according to recommendations of the European Society of Cardiology. Of 396 cases with records available for review 77.8% were classified as definite, 10.4% as probable, 7.6% as possible and 43.3% as no heart failure, i.e. 95.8% of cases had definitive, probable or possible diagnosis of heart failure. Of the 17 participants with no heart failure, 10 had evidence of LV-dysfunction or structural heart disease. The validity of I50 was similar in subgroups by age, gender, BMI and the time period of hospitalization.

Conclusion: Obtaining ICD-10 discharge code I50 through hospital record linkage offers a feasible and accurate method of identifying heart failure in contemporary cohort studies in the UK.