Background: Previous work has shown that patients with advanced HF have higher levels of mNOS2 gene expression compared to normal controls. We examined mNOS2 expression in patients with varying degrees of HF severity and examined the relationship between mNOS2 expression and subsequent reverse remodeling.

Methods: We performed endomyocardial biopsies on 45 ambulatory patients with chronic HF (NYHA II-III, LV ejection fraction (LVEF) <45%). To quantify the severity of HF, plasma NT-proBNP (Roche) was measured during the procedure. Intensity of mNOS2 gene expression was determined using quantitative TaqMan RT-PCR in ng/mg tissue. Reverse remodeling was estimated by change in LVEF, determined by serial echo >6 months apart.

Results: Myocardial NOS2 expression correlated inversely with plasma NT-proBNP levels (r = -0.40, p = 0.02, see Figure), but not with baseline LVEF (r = 0.09, p = 0.56). Furthermore, mNOS2 expression correlated directly with improvement in LVEF (r = 0.50, p = 0.03) in the subset of patients with echo follow-up (n=19).

Conclusions: Levels of mNOS2 expression are associated with more advanced HF and decreased likelihood of subsequent LV reverse remodeling in patients with chronic HF. These observations do not support the hypothesis that increased mNOS2 expression impairs LV function and leads to the progression of HF. Rather, increased mNOS2 expression identifies a subset of patients with advanced HF who still have the potential for subsequent reverse remodeling.

One-Minute Heart Rate Recovery After Cycloergometer-Exercise Test as a Predictor of Mortality in a Cohort of 1,420 Real-Life Exercise Test Candidates: Substantial Differences With the Treadmill Derived Parameter

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Background: Previous studies have shown a strong reverse association between one-minute heart rate recovery (1min-HRR) after exercising on a treadmill and all-cause mortality. We sought to determine whether the results could be replicated in a large population of "real world" exercise-ECG candidates, using a standard bicycle exercise test.

Methods and Results: 1,420 consecutive patients underwent ECG exercise test using our standard cycloergometer protocol between 1991 and 1997. We tested 3 pre-specified cutpoint-values of 1min-HRR, derived from previous studies using treadmill(Kaplan-Meier curves for one of these values are reported in Fig.1) to check whether they could discriminate a higher-risk group for all-cause mortality; furthermore we tested the possible association between 1min-HRR as a continuous variable and mortality, using logistic regression. Both statistical methods showed lack of statistically significant association between 1min-HRR and all-cause mortality.

Discussion: We could not validate the clear-cut results from some previous studies performed using treadmill exercise-test. Results of our study only can not exclude a mild inverse association between 1min-HRR measured after cycloergometer exercise-test and all-cause mortality. 1min-HRR measured after cycloergometer exercise-test should probably be discarded as a clinically useful prognostic marker.
changes in response to coronary ESC perfusion, including declines in CF, HR, LVP, dp/dtmax, and -dp/dtmax, with increased ESC perfusion rates. However, the magnitude of these parameters differed between the two mouse strains. At less than 10 cells/millon, the percent decline of these parameters in wild type hearts appeared significantly greater (p<0.05) than those of apoE(-/-) CF 15.2% in wild type vs. 10% in apoE(-/-); HR 19% vs. 7%, LVP 9% vs. 6%, dp/dtmax 11% vs. 8%, and -dp/dtmax 24% vs. 11%. Increasing the perfusion rates to 300 cells/ml/min led to further deterioration of the heart function but the apoE(-/-) hearts remained lower levels of the parameter declines. Histopathological analysis showed the presence of numerous ESC in microcirculation as well as in the extravascular tissue.

Conclusions: Perfusion with ESC through coronary arteries causes concentration-dependent changes in heart function. Compared to wild type controls, the hearts of apoE(-/-) mice which underwent atherosclerosis-related chronic ischemia appeared to be better tolerant to high EESC perfusion.

**1011-107** The Mitochondrial Metabolic Phenotype and Mouse Strain Influence Isoproterenol-Induced Cardiac Hypertrophy

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Introduction We previously described a novel model of isoproterenol-induced hypertrophy in which A/J mice exhibit greater cardiac hypertrophy than B6 mice. The objective of this study was to determine the relation between this variable hypertrophic response and the mitochondrial metabolic phenotype.

Methods 39 male mice (19 A/J, 20 B6) received randomly either ISO (100 mg/kg, sc) or vehicle by t-test. Results ISO-treated A/J mice displayed a greater increase in cardiac weight (vs. vehicle) than ISO-treated B6 (24% vs. 3%, respectively; p < 0.001). Enzyme activities were greater in vehicle-treated B6 than A/J mice (Table). ISO administration reduced active PDH activity (PDHα) in B6 mice by 47% (p < 0.001), with no significant change in A/J. The hypertrophic response and basal and stimulated enzyme activities were similar in B6 and B6 mice.

Conclusions 1) Compared to A/J, B6 mice demonstrate less ISO-induced cardiac hypertrophy, but greater activity of fatty acid and carbohydrate oxidative enzymes. 2) ISO-induced hypertrophy reduces myocardial oxidative enzymes in a strain-dependent manner. 3) These mitochondrial enzyme activities are not influenced by mitochondrial DNA.

Data are mean ± SEM. * p<0.01 B6 vs. A/J by ANOVA. † p<0.001 ISO vs. vehicle by t-test.

<table>
<thead>
<tr>
<th>Group</th>
<th>B6 vehicle</th>
<th>A/J vehicle</th>
<th>A/J ISO</th>
<th>B6 ISO</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citrate synthase (µmol/min/gww)</td>
<td>59 ± 4</td>
<td>171 ± 5</td>
<td>56 ± 3</td>
<td>163 ± 6</td>
</tr>
<tr>
<td>MCAD (µmol/min/gww)</td>
<td>10.4 ± 1.1</td>
<td>11.7 ± 0.9</td>
<td>8.9 ± 0.9</td>
<td>13.2 ± 0.9</td>
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<tr>
<td>CPT1 (µmol/min/gww)</td>
<td>1.7 ± 0.1</td>
<td>2.4 ± 0.2</td>
<td>1.5 ± 0.1</td>
<td>2.4 ± 0.2</td>
</tr>
<tr>
<td>PDH active (U/gww)</td>
<td>2.2 ± 0.4</td>
<td>4.8 ± 0.5</td>
<td>1.9 ± 0.3</td>
<td>2.5 ± 0.3</td>
</tr>
</tbody>
</table>

1011-111 Homocysteine Promotes Ventricular Remodeling by Induction of Apoptosis of Rabbit Cardiomyocytes and Priming the Mast Cells to Induce interleukin-6, With Significant Inhibition by Troglitazone

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Background: Homocysteine (Hcy) has been linked to the pathophysiology of atherosclerosis, on the other hand, it has been linked to ventricular remodeling and heart failure through pro-inflammatory causes. This may occur due to direct effects on the cardiomyocytes or indirectly by involving other cells like macrophages, fibroblasts and mast cells.

Methods: After isolating rabbit cardiomyocytes (CMs) using the standard perfusion method, we have given d,l Hcy (1x 10^-4 M) to the cells and at three hours we quantitated the apoptotic effects using Flow Cytometry. We used Annexin V (FITC -) Propidium iodide method for apoptosis detection. Apoptotic cells manifest as Annexin V - FITC positive and Propidium iodide negative, while necrotic cells manifest as Annexin V - FITC positive and PI positive. We have also given d,l Hcy to Human Leukemic Mast Cells (HMC-1) with 1 ng/ml of Interleukin 1 beta (IL1b) in a dose dependent manner (10, 50, 100 x 10^-6 M). We added the Pergoxiame Prolicerator Activated Receptors (PPAR) gamma agonist (Troglitzone-) to the cells as well (10 x 10^-6 M). We used ELISA technique to quantitate the amount of Interleukin 6 (IL 6) in the supernatants after 24 hours of incubation.

Results: We found that d,l Hcy induces apoptosis of CMs in the Hcy group (3.0% versus 1.0% control). On the other hand, we noticed a dose dependent increase in IL 6 concentration in the Hcy group. Hearts were isolated from Wistar rats and subjected to acute ischemia. The heart function was measured continuously in the presence and absence of the PKA-inhibitor H89 (5 mM). The results were as follows: Heart rate (HR) and heart weight (vs. vehicle) than ISO-treated B6 (24% vs. 3%, respectively; p<0.001). Enzyme activities were greater in vehicle-treated B6 than A/J mice (Table). ISO administration reduced active PDH activity (PDHα) in B6 mice by 47% (p<0.001), with no significant change in A/J. The hypertrophic response and basal and stimulated enzyme activities were similar in B6 and B6 mice.

Conclusions: 1) Compared to A/J, B6 mice demonstrate less ISO-induced cardiac hypertrophy, but greater activity of fatty acid and carbohydrate oxidative enzymes. 2) ISO-induced hypertrophy reduces myocardial oxidative enzymes in a strain-dependent manner. 3) These mitochondrial enzyme activities are not influenced by mitochondrial DNA.

Data are mean ± SEM. * p<0.01 B6 vs. A/J by ANOVA. † p<0.001 ISO vs. vehicle by t-test.

**1011-112** Use of Abciximab Prior to Primary Angioplasty in ST-Segment Elevation Myocardial Infarction Results in Early Recanalization of the Infarct-Related Artery: Results of the Multicenter Randomized ReoPro-BRIDGING Study

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Background. The ReoPro-BRIDGING Austrian multicenter randomized study investigated the effect of Abciximab (ReoPro) on infarct-related artery (IRA) patency and early reperfusion prior to primary coronary intervention (pPCI).

Methods. Thirty-eight patients with ST-segment elevation AMI were treated with ReoPro 0.25 mg/kg bolus followed by 10 μg/min infusion and randomized either to start ReoPro during the organization time (66±33 min) for pPCI (Group 1, n=18) or immediately after pPCI (Group 2, n=20). Serial measurements of creatine kinase (CK), CKMB, myoglobin, and 12-lead ECG were performed at baseline as well as 2, 4, 6, 8, 10, 12 and 24 h thereafter.

Results. A trend to a more rapid and higher release of cardiac enzymes was observed in patients of Group 1: rate of rise of CK 164±203 vs 127±170 U/l/min; CKmax: 922±954 vs 557±721 U/l; CKMB: 101±137 vs 63±80 ng/ml; troponin I: 10±14 vs 5±7 μg/l. Early recanalization of the IRA was achieved in 19/20 (95%) patients of Group 2: rate of rise of CK 122±183 vs 29±87 μg/l; CKmax: 798±626 vs 325±86 U/l; CKMB: 81±45 vs 8±3 ng/ml; troponin I: 10±11 vs 5±2 μg/l. In Group 1 and 6 patients (30%) in Group 2 (p=0.024) before pPCI. TIMI flow 0 was observed in 6 (33%) vs 11 patients (50%) of Group 1 vs 2 (p=0.3). Corrected TIMI frame count was significantly lower (57±33 vs 76±22 frames, p=0.034) and angiographic minimal lumen diameter was larger (0.7±0.7 vs 0.6±0.5 mm, p=0.020) in patients of Group 2.

Conclusions. Use of ReoPro in the organization phase for pPCI results in early and better recanalization of the infarct-related artery prior to pPCI with a consequent rapid release of cardiac enzymes.