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heart failure may affect TNF-α and TNF receptor system, activating a cytokine network which may modulate the progression of congestive heart failure.

**SKELETAL MUSCLE INFLAMMATORY CHANGES CORRELATE WITH FUNCTIONAL CLASS AND CIRCULATING CYTOKINE LEVELS IN PATIENTS WITH CONGESTIVE HEART FAILURE**

Michael Yeh, Masaha Goldstein, Bang-Ying Zhu, Marco Gerstuzn, Marco Testa, Joman Berman, Stephen Factor, Theony LeJemtel, Albert Einstein College of Medicine, Bronx New York, New York University Medical Center, New York New York, Ospedale Casa Solleno della Cofetture, San Giovanni Rotondo Italy

Circulating cytokine levels are elevated in symptomatic patients with congestive heart failure (CHF).

Whether peripheral abnormalities which are present in the skeletal muscles (SM) and vasculature of symptomatic patients contribute to cytokine production in CHF is unknown. Accordingly, vastus lateralis SM biopsies were obtained in 14 patients with functional class (FC) I to IV CHF (peak ejection fraction (EF) <40%) and in 8 age-matched normal subjects who served as controls. Mean patient and control age was 59 years and 22 ±2 years, respectively.

The etiology of CHF was coronary artery disease (n=5) or hypertension (n=9). All patients were treated with angiotensin converting enzyme inhibitors, digoxin and loop diuretics. Parafin sections of SM biopsies were obtained in 14 patients with functional class (FC) I to IV CHF (peak ejection fraction (EF) <40%) and in 8 age-matched normal subjects who served as controls.

**Table 1**

<table>
<thead>
<tr>
<th>Function</th>
<th>Controls (n=6)</th>
<th>FC II (n=6) peak Vo2 15.23</th>
<th>FC II-V (n=5) peak Vo2 8-14</th>
<th>TNF-α ng/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls (n=6)</td>
<td>1.0</td>
<td>0.2</td>
<td>1.1</td>
<td></td>
</tr>
<tr>
<td>FC II (n=6) peak Vo2 15-23</td>
<td>2.1</td>
<td>0.8</td>
<td>2.7</td>
<td></td>
</tr>
<tr>
<td>FC II-V (n=5) peak Vo2 8-14</td>
<td>2.6</td>
<td>2.8</td>
<td>4.2</td>
<td></td>
</tr>
</tbody>
</table>

*p<0.05 vs controls; tP < 0.05 vs FC II-V

**Clinical Cardiology:**

**Exercise Factors by Gender, Age, and Functional Status**

Tuesday Afternoon

Exhibit Hall

Abstracts 2908 – 2916

**Does the Change in Quantitatively Assessed Coronary Artery Disease After Lipid-Lowering Therapy Relate to the Change in Functional Status of the Patient?**

Wim R. Appelvaguer, Gerald J. Lilien, Albert R. Brusinck, Wouter J. Jukema, Tjerk Wert van der. University Hospital Nijmegen, NL, University Hospital Nijmegen, NL, University Hospital Nijmegen, NL, University Hospital Nijmegen, NL, The Netherlands (ICN), Utrect NL

In general the effects of lipid-lowering therapy are evaluated by clinical events or anatomical parameters. Assessment of functional parameters is an alternative approach, that may provide relevant additional information. Therefore we assessed regional myocardial blood flow and exercise parameters and related the changes in those measurements to the results of the quantitative coronary arteriography (QCA). Methods: Patients were randomized to pravastatin (prav.) 40 mg o.d. or placebo (plac.) according to the REGRESS protocol (Regression Growth Evaluation Study). Before and after 2 years of therapy the following measurements were performed: 1) Mean diameter stenosis (MS) and minimal lumen diameter (MLD) assessed by QCA, 2) assessment of the regional myocardial blood flow by digital subtraction angiography after i.v. papaverine with video-densitometric calculation of the hyperemic mean transit time (HMTT). 3) Exercise time (EXT) and maximal ST-segment depression (MST), assessed during a standardized bicycle test. Results: 109 Patients as part of this subsidy were included. Complete follow-up after 2 years was available in 25 patients in the medical management (M), 10 in the PTCA and 14 in the CABG (C) stratum, respectively. Effect analysis of prav. versus plac. was based on 36 patients (M and P stratum, PTCA vessels excluded). The change in MST was related to the change in HMTT (r = 0.32, p < 0.003). In the CABG group, the change in HMTT was not correlated with change in exercise parameters or change in HMTT. The change in HMTT was correlated with the change in EXT (r = 0.58, p = 0.002). Conclusion: Change in MST is moderately related to maximal ST-segment depression during the exercise test. Myocardial perfusion better correlates with the functional status of the patient, presumably because HMTT also reflects changes at the microcirculatory level.

**Platelets in Athletes are Supersensitive to Nitric Oxide**

Yuko Ishitahi, Shinia Saika, Tomoyuki Watanabe, Takashi Ashikaga, Taekeuzaki Kukula, Hoshitaki Mamiyana, Yuji Hashimoto, Fujio Numano. Tokyo Medical and Dental Univ., Tokyo, Japan

Animal studies have revealed that regular exercise may enhance coronary vasodilation in response to physiological stimuli such as NO. However, little is known about the effect of regular exercise on the sensitivity of target cells to NO have not been extensively studied. We conducted in vitro studies on the responsiveness of the platelets to NO in athletes. Fifteen male athletes (Group A, aged 29-36 years, training daily for a triathlon-race meeting, and 15 age- and gender-matched sedentary subjects (Group B) entered this study. Fasting blood samples were obtained and washed platelets were prepared for determination cyclic GMP (cGMP) accumulation in response to 1 nM to 10μM SIN-1 (NO donor). Cyclic GMP accumulation in the platelets was measured by guaniure prelabelling method and was expressed as percentage of conversion from radiolabeled GTP. Physical fitness of the athletes was confirmed by the blunted heart rate and blood pressure response to submaximal treadmill exercise. Cyclic GMP accumulation in the platelets of athletes was significantly enhanced at basal levels (in percentage of conversion, A: 0.19±0.02, B: 0.12±0.009, mean±SEM, P<0.01) and in response to SIN-1 in the concentration range of 1-1000 nM (in fold of basal values, at 1 nM, A: 1.8±0.05, B: 1.1±0.05, mean±SEM, P<0.01). However, there were no differences at 1 μM or more. In summary, cGMP levels in the platelets of athletes were significantly higher at basal levels possibly due to enhanced NO synthesis associated with chronic exercise. In addition, platelets may be supersensitive to physiologically-relevant low concentrations of NO in athletes. These observations in platelet GMP metabolism in athletes may partially explain the protective effects of regular exercise against thrombotic cardiovascular diseases.

**Myocardial Injury in Athletes Participating in the Hawaii Ironman Triathlon**

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Can protracted aerobic exercise cause myocardial injury? CK-MB and myoglobin, biochemical markers of muscle injury, lack the specificity to detect cardiac specific muscle damage. Cardiac troponin I (cTnI) and troponin T (cTnT) are highly specific and sensitive for detecting cardiac myocyte necrosis. To assess whether exercise can induce cardiac specific myocyte injury, blood samples were collected from 23 athletes (11 males, mean age 38±10 yrs, none with risk factors for CAD) 24 hours prior and immediately after the Hawaii Ironman Triathlon (2.4 mi swim, 112 mi bike, 26.2 mi run). cTnT (Enzyme, Boehringer Mannheim) was measured by immunoenassays. The cTnT assay has a 0.05 ng/ml cross-reactivity with skeletal TnT. No subject had detectable cTnT or cTnI in the pre-race samples. However, following the race 2 subjects (8%) had marked increases in both cTnT (0.15 and 0.35 ng/ml) and cTnI (2.03 and 4.4 ng/ml). 4 subjects (17%) had mild increases in cTnT (0.04-0.50 ng/ml) but no detectable cTnI. Quantitative echocardiographic wall motion analysis was performed on 16 myocardial segments in 11 of the subjects before and immediately after the triathlon. All pre-race echo scores were completely normal. Average increase in the mean echo score, indicating worsening ventricular function, was 0.6 in those with a marked increase in cTnT and cTnI, 2.3 in those with a moderate increase and 1.4 in those with no increase. Therefore, ultra-echo scores alone may cause myocardial damage manifested as a rise in cTnT and cTnI and wall motion abnormalities detected by echocardiography. Individuals, should be aware of the possibility of myocardial injury associated with prolonged periods of exercise.

**Improved physical fitness is associated with enhanced basal formation of nitric oxide and increased flow-mediated vasodilation in healthy young subjects.**

Lennart Jungertors, Bjorn West, Tomas Hallbom, Glenn Vemborn, Ralf Pikkarinen, Åke Wennergren. Göteborg University, Göteborg Sweden

Acute physical exercise is associated with an enhanced formation of nitric oxide (NO), which lasts during and shortly after the exercise session. In the present study the effects of regular (chronic) training on resting (i.e. between exercise sessions) NO formation and increased flow-mediated vasodilation in healthy young subjects were investigated. Sixteen healthy subjects (5 males, aged 21-34 years, followed an exercise program for four weeks. Before entering the exercise program and at the end of the training period, the maximal aerobic capacity (stepwise bicycle exercise test) and brachial artery endothelium-dependent dilution (high-resolution ultrasound at rest and after arterial occlusion) were determined.

**Lipid-Lowering Therapy Relates To the Change In Functional Status of the Patient?**

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