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

WITH CONGESTIVE HEART FAILURE

SKELETAL MUSCLE INFLAMMATORY CHANGES CORRELATE WITH the progression of congestive heart failure. Patients With Chronic Congestive Heart Failure

The etiology of CHF was coronary artery disease (n=9) or hypertension (n=5). All patients were served as controls. Mean patient age and ejection fraction were 55.7 years and 22.4% respectively.

Levels of soluble intercellular adhesion molecule-1 (sICAM-1) and soluble vascular cell adhesion molecule (sVCAM-1) in 83 patients with CHF (left ventricular ejection fraction (LVEF)<45%, mild CHF; NYHA classes I and II) were measured by immunoassay (Quantikine HS, R&D Systems). No B cells were detected. Reproducibility of SM biopsy findings was established in 3 patients who underwent 2 serial biopsies.

In conclusion, increased numbers of perivascular and interstitial T cells in SM accompany the rise in circulating cytokine levels as the symptoms progress in patients with CHF.

Prognostic Value of Soluble Cytokine Receptor and Adhesion Molecule in Patients With Chronic Congestive Heart Failure

To evaluate the role of immune system activation in the pathophysiology of chronic congestive heart failure (CHF), we determined the plasma soluble cytokine receptors such as soluble tumor necrosis factor receptor-I (sTNFRI), and sTNFRII, and soluble adhesion molecules such as soluble intercellular adhesion molecule-1 (sICAM-1), and soluble vascular cellular adhesion molecule (sVCAM-1) in 83 patients with CHF (all ventricular ejection fraction (EF)<45%, mild CHF; NYHA II, n=40, severe CHF; NYHA III-IV, n=43) by means of enzyme-linked immunosorbent assay. Furthermore, they were monitored for a follow-up period of more than 1 year. The plasma levels of sTNFRII increased with the severity of CHF (mild CHF: 102.5±74 ng/ml vs. severe CHF: 1264.2±679 pg/ml, p<0.0001) and the plasma level of sTNFRII also increased with the severity of CHF (mild CHF: 3320±250 pg/ml vs. severe CHF: 4834±452 pg/ml, p=0.0002). The plasma levels of sICAM-1 and sVCAM-1 were also increased in relation to the severity of CHF (mild CHF: 234.11 ng/ml vs. severe CHF: 318.23 ng/ml, p=0.001, mild CHF: 796.23 ng/ml vs. severe CHF: 1193.75 ng/ml, p=0.0001, respectively). Correlation analysis showed that the plasma levels of sICAM-1 and sVCAM-1 were significantly related to the plasma levels of soluable cytokine receptor and soluble adhesion molecule and the severity and mortality of patients with CHF, suggesting an important role of the immune system activation in the pathophysiology and progression of CHF.

Clinical Cardiology:

Exercise Factors by Gender, Age, and Functional Status

Tuesday Afternoon

Exhibit Hall

Abstracts 2909–2916

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

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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 these measurements to the results of the quantitative coronary angiography (QCA). Methods: Patients were randomized to pravastatin (40 mg/day or placebo (placebo). According to a randomized, controlled trial (REGRESS protocol. Determination of exercise performance and progression of coronary atherosclerosis assessed by QCA. (1) assess the regional myocardial blood flow by digital subtraction angiography after i.v. papaverine and video-densitometric calculation of the hyperemic mean transit time (HMTT). (2) exercise time (EXT) and maximal ST-segment depression (MST) assessed during a standardized bicycle test.

Results: 99 Patients as part of this substudy 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) (n=3). The change in HMTT was significantly related with the change in EXT (r=0.85, p=0.002). Conclusion: Change in EXT is related to the severity of MD during the exercise test. Lipid-lowering therapy 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

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Animal studies have revealed that regular exercise may enhance vascular vasodilation in response to physiological stimuli such as shear stress and eNOS-dependent NO production. Although the effect of regular exercise on the sensitivity of target cells to NO has 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 23-26 years), training daily for a triathlon race, 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 of cyclic GMP (cGMP) accumulation in response to 1 mM to 10 µM SIN-1 (NO donor). 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 1-100 µM (in basal levels of samples, A: 1.1±0.13, B: 1.11±0.03, 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 differences in platelet cGMP metabolism in athletes may partly 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 prolonged aerobic exercise cause myocardial injury? CK-MM and myoglobin, biochemical markers of muscular injury, lack the specificity to detect cardiac specific myocardial damage. Cardiac troponins I (cTnI) and troponin T (cTnT) are highly sensitive and specific for detecting cardiac myocyte necrosis. To assess whether exercise induced CKB 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 (Enzymune, Boehringer Mannheim) and cTnI (Behring Diagnostics) 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 (Enzymune, Boehringer Mannheim) and cTnI (Behring Diagnostics) were measured by immunobiosays. The cTnT assay has <0.05% cross-reactivity with skeletal muscle TnT. No subject had detectable cTnT or cTnI in the pre-race samples. However, following the race 2 subjects (9%) had marked increases in both cTnI (0.15-0.33 ng/mL) and cTnT (2.03 and 4.46 ng/mL). 4 subjects (17%) had mild increases in cTnI (0.04-0.05 ng/mL) but no detectable cTnT. 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 in both cTnT and cTnI, and 1.4 in those without any change. Therefore, ultra-endurance exercise 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 Jungner, Börje Wall, Tomas Wallenfels, Glenn Vemming, Ralf Mikkelsen, Åke Werner. Göteborg University, Göteborg Sweden

Acute physical exercise associated with enhanced basal formation of nitric oxide (NO), which lasts during and shortly after the exercise session. In the present study we evaluated the effects of regular (chronic) training on resting (i.e. between exercise sessions) nitric oxide and endothelial function were investigated. Sixteen healthy subjects (5 males), aged 21-24 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 dilation (high-resolution ultrasound at rest and after arterial occlusion) were determined.