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

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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 aerobic capacity (VO2) ranging from 6 to 23 ml/kg/min) and in 6 age-matched normal subjects who served as controls. Mean patient age and ejection fraction were 55.7 years and 52.4%, respectively. The etiology of CHF was coronary artery disease (5) or hypertension (8). All patients were treated with angiotensin converting enzyme inhibitors, digoxin and loop diuretics. Paraffin sections were evaluated by hematoxylin and eosin staining and immunostained using a histocyte marker (KP-1), T cell marker (CD3) and B cell marker (L26). Tumor necrosis factor alpha (TNF-alpha) levels were determined 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.

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Clinical Cardiology:

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

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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 (prav.) 40 mg o.d. or placebo (plac.) according to the REGRESS protocol (Regression Growth Evaluation Statin Study). Before and after 2 years of therapy the following measurements were performed: 1. Mean segment diameter stenosis (MSS) and minimal luminal diameter stenosis (MLD) assessed by QCA. 2. Assessment of the regional myocardial blood flow by digital subtraction angiography after i.v. papaverine and 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: 193 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 group and 4 in the CABG (C) groups, respectively. Effect analysis of prav. versus plac. was based on 36 patients (M and P, PTCA, PTCA vessels excluded). The change in MSS was related to the change in HMTT (t = -3.92, p < 0.005, not to EXT or MST). The change in MSS was not correlated with changes in exercise parameters or change in HMTT. The change in HMTT was correlated with the change in EXT (r = -0.57, p = 0.02). Conclusion: Change in MOD is moderately related to maximal ST-segment depression during the exercise test. Myocardial pertusion better correlates with the functional status of the patient, presumably because HMTT also reflects changes at the microvascular level.

Platelets in Athletes are Supersensitive to Nitric Oxide

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Animal studies have revealed that regular exercise may enhance coronary vasodilatation in response to pharmacological NO synthase (NOS) agonists and to physical effort. However, the effect of regular exercise on the sensitivity of control 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 23-36 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 nM to 10uM SIN-1 (NO donor). Cyclic GMP accumulation in the platelets was measured by guanine precollaboration and expressed as percentage conversion from radioactive GTP. Physical fitness of the athletes was confirmed by the blunted heart rate and blood pressure responses to the submaximal treadmill exercise. Cyclic GMP accumulation in the platelets of athletes was significantly enhanced at basal levels (in percentage conversion, A: 0.19±0.02, B: 0.25±0.15, p<0.009) and in response to SIN-1 in the concentration range of 1-200 nM (in basal levels of platelets, at 1 nM, A: 1.56±0.02, B: 1.1±0.01, p<0.02; at 10 nM, A: 4.0±0.2, B: 3.0±0.2, p<0.01). However, there were no differences at 1 ¡¿M 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 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 prolonged aerobic exercise cause myocardial injury? CK-MB and myoglobin, biochemical markers of muscle injury, lack the specificity to detect cardiac specific muscle damage. Cardiac troponins (cTnT and cTnI) and troponin T (cTnT) are highly sensitive and specific for detecting cardiac myocyte necrosis. To assess whether exercise can induce cardiac specific myocyte injury, blood samples were collected from 23 athletes (male, 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) and cTnI (The Binding Site) were measured by immunoassays. The cTnT assay has <0.05% cross-reactivity with skeletal 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 cTnT (0.15-0.33 ng/ml) and cTnI (2.03 and 4.49 ng/ml). 4 subjects (17%) had mild increases in cTnT (0.04-0.05 ng/ml) but no detectable cTnI. Quantitative electrocardiographic 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 6.6 in those with a marked increase in cTnT and cTnI, 2.3 in those with a moderate increase and 0.6 in those with a mild increase in cTnT and cTnI. In summary, systemic release of troponins may cause myocardial damage manifested as a rise in cTnT and cTnI and wall motion abnormalities detected by echocardiography. Individuals could 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.

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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 endothelial function were assessed. 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 dilation (high-resolution ultrasound at rest and after arterial occlusion) were determined.