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**

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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 contribute to cytokine production in CHF is unknown. Accordingly, vastus lateralis SM biopsies were obtained in 14 patients with functional class (FC) I-IV CHF (peak aerobic capacity [VO2] ranging from 8 to 23 ml/kg/min) and in 6 age-matched normal subjects who served as controls. Mean fibrotic area and collagen fraction were 55.7 ± 22% and 22% respectively. The etiology of CHF was coronary artery disease (n=9) or hypertension (n=5). All patients were treated with angiotensin converting enzyme inhibition, digoxin and loop diuretics. Paraffin sections were evaluated by hematoxylin and eosin staining and immunostained using a histocyte marker (KP-1), pan T cell marker (CD3) and pan B cell marker (L26). Tumor necrosis factor α (TNFα) levels were evaluated by immunohistochemistry (Quintusite IS RAD 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.

**Perivascular & Interstitial Histocyes (Scale 1-3)**

Controls (n=6) | 1.0 | 0.8 | 0.9

FC II (n=6) peak VO2 15-23 | 2.1 | 2.0 | 2.8

FC II-VI (n=8) peak VO2 8-14 | 2.6 | 2.4 | 2.8

*p<0.05 vs controls; †p<0.05 vs FC II

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

Takayoshi Tsuchimoto, Tomoki Hisanaga, Keiko Maeda, Yukiharu Maeda, Daisuke Fukai, Mataro Omihashi, Shiga Univ. Med. Science, Osho Japan

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 (sTNF-R1), and sTNF-R-II, and soluble adhesion molecules such as soluble intercellular adhesion molecule-I (sICAM-1), and soluble vascular cell adhesion molecule (sVCAM-1) in 83 patients with CHF [all ventilator 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 level of sTNF-R-I increased with the severity of CHF [mild CHF: 1028 ± 74 pg/ml vs. severe CHF: 1294 ± 207 pg/ml, p<0.0001] and the plasma level of sTNF-R-II also increased with the severity of CHF [mild CHF: 3230 ± 250 pg/ml vs. severe CHF: 4834 ± 452 pg/ml, p<0.002]. 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: 786 ± 39 ng/ml vs. severe CHF: 1120 ± 78 ng/ml, p<0.0001, respectively]. Cor proportional hazards analysis was performed to determine the independent significant predictors of EF, plasma levels of sTNF-R1, sTNF-R-II, sICAM-1, and sVCAM-1, high plasma levels of sTNF-R (p=0.013), sVCAM-1 (p=0.04), and EF(p=0.004) were shown to provide independent significant prognostic indicators in 83 CHF patients. These findings indicate the significant relation between the plasma levels of soluble 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 2098 – 2099**

**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. Aengevaeren, Gerard J. Uijen, Albert V. Bruschke, Wouter J. Jukema, Tjeerd Werf van Zwanenbergh, Wim R. Aengevaeren, Gerard J. Uijen, Albert V. Bruschke, Wouter J. Jukema, Tjeerd Werf van Zwanenbergh, University Hospital Nijmegen, NL, Interuniversitary Cardiology Institute The Netherlands (ICIN), Utrecht 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 to 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 (MSD) and minimal obstruction diameter (MOD) assessed by QCA. 2) Assessment of the regional myocardial blood flow by digital subtraction angiography after i.e. papaverine injection during the exercise test. The study was performed to determine the independent significant predictors of EF, plasma levels of of soluble 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.

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

Ninder Ntli, Mary O'Toole, Pamela S. Douglas, Geoffrey D. Gainsburg, Children's Hospital, Boston MA 1, Beth Israel Hospital, Boston MA 2, Harvard Medical School, Boston MA 3

Can prolonged aerobic exercise cause myocardial injury? CK-MB and myoglobin, biochemical markers of muscle injury, lack the specificity to detect cardiac epicardic muscle damage. Cardiac troponins (TnI and TnT) and troponin T (cTnT) are more 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 (mean age 38 ± 10 years, n=10, prior risk for CAD) 24 hours prior and immediately after the Hawaiian Ironman Triathlon (2.4m swim, 112 mi bike, 26.2 mi run). TnI (Enzymatic, Boehringer), TnT (cTnT,Campo), and cTnI (radioimmunoassay) were measured by immunoassays. The cTnT assay has a 0.005% cross-reactivity with skeletal TN. 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 and 0.33 ng/ml) and cTnT (2.09 and 25.4 ng/ml) and 1 subject (5%) had marked increases in cTnT and cTnI. 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 0.9 in those with a marked increase in cTnT and cTnI, 2.3 in those with a moderate increase (cTnT or cTnI) and 1.4 in those with no increase. 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 Jungenb-li, Bjorn Wall, Tomas Wallander, Glenn Vemberg, Rafl Mikkaninen, Ake Wennerg-am, Gothenburg University, Gothenburg Sweden

Acute physical exercise is associated with an enhanced formation of nitric oxide (NO), which lasts during and after the exercise session. In the present study the effects of regular (chronic) training on resting (i.e. between exercise sessions) and endothelium-dependent dilatation 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 dilatation (high-resolution ultrasound at rest and after arterial occlusion) were determined.