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**Supplement I Circulation**

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Clinical Cardiology:

Exercise Factors by Gender, Age, and Functional Status

Tuesday Afternoon

Exhibit Hall

Abstracts 2980–2916

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. Aengenvooren, Gerard J. Liem, Albert V. Bruschke, Wouter J. Jukema, Tjerk Werd van der. 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 additional information. Therefore we assessed regional myocardial blood flow and exercise parameters and related them to changes in these measurements to the results of the quantitatively 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 (MSTD) and minimal luminal diameter (MLD) assessed by QCA; 2) assessment of the regional myocardial blood flow by digital subtraction angiography after i.e. 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: 293 Patients as part of this study were included. Complete follow-up after 2 years was available in 25 patients in the medical management (M), 10 in the PTCA, 13 and in the CABG (C) stratum, respectively. Effect analysis of prav. versus plac. was based on 36 patients (M and P strata, PTCA vessels excluded). The change in MSTD was related to the change in MST (r = 0.32, p < 0.003), to EXT or to HMTT. The change in MSTD was not related with change in exercise parameters or change in HMTT. The change in HMTT was correlated with the change in EXT (r = 0.85, p < 0.002). Conclusion: Change in MOD is moderately related to maximal ST-segment depression during the exercise test. Lipid lowering therapy better correlates with the functional status of the patient, presumably because HMTT also reflects changes at the microvascular level.

Platelet in Athletes are Supersensitive to Nitric Oxide

Yuko Kishi, Shinya Saito, Tomoyuki Watanabe, Takashi Ashikaga, Taonekazu Fukuda, Toshiaki Manymaru, Fusho Hashimoto, Fujio Numazato. Tokyo Medical and Dental University, Tokyo, Japan.

Animal studies have revealed that regular exercise may enhance coronary vasodilatation in response to acetylcholine. However, no studies have been performed to determine whether chronic exercise on the sensitivity of target cells to NO have not been extensively studied. We conducted in vivo studies on the responsiveness of the platelets to NO in athlete. Fifteen male athletes (Group A, aged 20-36 years), training daily for a triathlon race, and 15 age- and gender-matched sedentary subjects (Group B) entered this study. Platelets samples were obtained and washed platelets were prepared for determination cyclic GMP (cGMP) accumulation in response to 1 mM to 10uM SIN-1 (NO donor). Cyclic GMP accumulation in the platelets was measured by guanine prelabelling method and was expressed as percentage of conversion from radioactively labelled GTP. Physical fitness of the athletes was confirmed by the blunted heart rate and blood pressure responses 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±0.01, B: 0.12±0.009, mean±SEM, P<0.01) and in response to SIN-1 in the concentration range of 1-100 mM (in fold of basal values, at 1 mM, A: 1.82±0.53, B: 1.11±0.03, mean±SEM, P<0.01, at 100 mM, A: 4.4±0.23, B: 3.0±0.25, P<0.01). However, there were no differences at 1 mM 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 findings 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 Hawaiian Ironman Triathlon

Nander Nitsi, Mary O'Toole, Pamela S. Douglas, Geoffrey S. Gimbburg. Cincinnati 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 muscular injury, fail the specificity to detect cardiac specific myocardial muscle damage. Cardiac troponin I (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 (11 males, mean age 38±10 yrs, none with risk factors for CAD) 24 hours prior and immediately after the Hawaiian Ironman Triathlon (2.4-mi swim, 112-mi bike, 26.2-m run). cTnI (Enzyme, Biothong), and cTnT (staphylococcal protein A) were measured by Immunoassays. The cTnI assay has <0.005% cross-reactivity with skeletal muscle myoglobin. 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 and 0.33 ng/ml) and cTnI (2.09 and 4.44 ng/mL). 4 subjects (17%) had mild increases in cTnT (0.04-0.05 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 0.8 in those with a marked increase in cTnT and cTnI, 2.5 in those with a moderate increase in cTnT, 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 would be the awareness 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.


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 synthesis 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.