less desirable because of expense and suboptimal image quality. We investigated the ability to achieve adequate heart rate for the evaluation of chest pain in the deconditioned obese patient by static walking in place.

We stressed 11 (8 female, 3 male) obese (average weight 415 lb [body mass index 65]) patients by walking in place to achieve adequate heart rate. Each walked in place while pulse, blood pressure, and ECG were monitored. The speed of static walking was increased as needed and at maximal exercise, techniuim-99m sestimibi was injected and walking in place continued for an additional 1-2 minutes.

The target heart rate (85% of the age predicted heart rate) was achieved in 6 of 11 patients (55%), 80% of age predicted in 9 of 11 (82%), and 75% of age predicted in 100% of the patients. The systolic blood pressure increased by an average of 42mmHg and all test were ended due to fatigue after an average of 7 minutes and 18 seconds of walking in place.

Static walking in place is an option for achieving adequate heart rate in some obese patients for the evaluation of chest pain.

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**EXERCISE-INDUCED AND SILENT ISCHEMIA: DIFFERENT EFFECTS OF MONOTHERAPY**

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The study was performed to compare the effects of lacidipine, bisoprolol and trimetazidine on ischemia during exercise-testing and 24-hour ECG monitoring. Sixty patients with stable coronary artery disease, positive exercise tests and at least two transient ischemic episodes during 24-hour Holter monitoring were randomized to receive lacidipine (n = 30), bisoprolol (n = 20; 60 mg) for 8 weeks subsequent to a 2-week placebo phase. All drugs increased exercise tolerance in terms of its duration (29% with lacidipine, 20% with bisoprolol and 24% with trimetazidine), time to onset of 1 mm ST-depression (23% with lacidipine, 18% with bisoprolol and 19% with trimetazidine) and reduced maximal ST-segment depression (30% with lacidipine, 20% with bisoprolol and 25% with trimetazidine). (p<0.001 vs placebo). The between group difference was significant only in case of lacidipine vs bisoprolol (p<0.05). Data obtained with 24-hour Holter monitoring revealed that the mean number of ischemic episodes/24-hours in all treatment groups decreased (56% with bisoprolol, 29% with lacidipine and 27% with trimetazidine). The between group difference was significant in case of bisoprolol vs lacidipine and trimetazidine. 1. Lacidipine and trimetazidine were the best in suppressing the excertional ischemia. 2. Bisoprolol was the best in suppressing ischemia during daily activity. Average heart rate was slightly increased with lacidipine (NS), unchanged with trimetazidine and decreased with bisoprolol. 3. Lacidipine and bisoprolol reduced the early morning peak and lowered the afternoon peak of transient ischemic episodes. Trimetazidine led only to a reduction of the late afternoon peak of transient ischemic episodes. All drugs left the circadian distribution of ischemic episodes unchanged.

Key Words: Exercise-testing, 24-hour ECG Monitriing, Ischemia

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**GLUCOSE INTERACTION EFFECTS ASSOCIATED WITH ISCHEMIC HEART DISEASE EVENTS IN TREATED HYPTERTENSIVE PATIENTS**

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This study assessed the effect of serum glucose on the association of baseline serum cholesterol with subsequent ischemic heart disease events. Baseline serum cholesterol and glucose levels were available for 11766 hypertension patients who participated in a systematic treatment program for >6 months. After excluding 1431 with baseline history of cardiovascular disease, 10335 were available for the study. The 7659 with normal glucose defined as <110 mg/dl were compared to those with either serum glucose >=110 (n=2539) or with history of diabetes at entry (n=137). Serum cholesterol was categorized as <180, 180-199, 200-219, 220-239, 240-259 and >=260 mg/dl. Outcome events were hospitalizations or deaths from ischemic heart disease (IHD) (ICD-9 codes 410-414), plus revascularizations and angioplasty. Age-sex-adjusted event rates for the cholesterol categories were calculated for both glucose strata. Hazard ratios adjusted for age, sex, smoking, systolic blood pressure, left ventricular hypertrophy, body-mass index, ethnicity and treatent status at entry were calculated with Cox models. During 5.9 years average follow-up, there were 342 IHD events. The abnormal glucose group had higher age-sex-adjusted rates in each cholesterol category. Only the highest cholesterol category (>=260) was significantly associated with IHD among the normal glucose stratum. In contrast, each cholesterol category >=180 with <180 as reference in the abnormal glucose stratum was significantly associated with IHD, with hazard ratios consistently greater than 2. Although high levels of serum cholesterol and glucose are well established as independent risk factors for atherosclerosis and ischemic heart disease, these datasuggest an interaction effect should be considered. Among hypertensive patients, even cholesterol levels >=180 may be associated with greater risk of IHD in the presence of abnormal serum glucose, while among patients with normal serum glucose the risk associated with cholesterol might be attenuated.

Key Words: stress testing, obesity, coronary artery disease

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**ENDOTHELIAL NITRIC OXIDE SYNTHASE (GLU298→ASP VARIANT) AND CORONARY ARTERY DISEASE IN AN ITALIAN POPULATION**

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Functionally important variants of endothelial Nitric Oxide Synthase (eNOS) could influence individual susceptibility to atherosclerosis. Recent reports have suggested that the Glu298→Asp variant of eNOS is associated with coronary spasm and acute myocardial infarction. This finding is potentially important but requires further confirmation in other populations. In this study, we investigated the relationship between the Glu298→Asp polymorphism and atherosclerotic coronary artery disease
(CAD) in an Italian population; moreover, we evaluated if this variant may affect endothelial function, which is not yet known.

We studied 57 consecutive patients aged <60 with angiographically proven CAD (>50% stenosis affecting at least 1 vessel) and 65 normal controls. We performed PCR/restriction fragment length polymorphism analysis to detect the missense Glu298→Asp variant in exon 7 of the eNOS gene. For the evaluation of the endothelial function, in 11 healthy, non smokers and genotyped young subjects (28.7±2.4 years), the percentage change of the brachial artery diameter (FMD) after forearm cuff occlusion and glyceryl trinitrate (GTN) was assessed.

The frequencies of the eNOS Glu/Glu, Glu/Asp and Asp/Asp genotypes in the CAD group were significantly different from those of controls (49.1%, 36.8% and 14.0% vs 38.5%, 55.4% and 6.1%, respectively, Chi Square =8.108, p=0.017). In comparison to Glu298 homozygotes, homozygosity for Asp298 was associated with an odds ratio of 1.8 (95% CI, 0.48 to 6.66). Moreover, homozygous carriers of the eNOS Asp298 displayed a significantly lower FMD compared to heterozygotes and individuals without the Asp298 allele (Asp/Asp: 7.35%±5.08% vs Glu/Glu: 18.1%±4.85%. Mean±SD, p=0.04). On the contrary, the endothelium-independent vasodilation did not change significantly in neither group.

In conclusion, the eNOSGlu298→Asp polymorphism is associated with the occurrence of CAD in an Italian population probably by altering the activity of the vascular NO system at endothelial level.

Key Words: Genetic Risk Factors, Nitric Oxide, Endothelial Function

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EVIDENCES FOR DNA DAMAGE IN PATIENTS WITH CORONARY ARTERY DISEASE

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Several studies suggest that cancer, hypertension and atherosclerosis may share common biological mechanisms. Although an increase in the mutation rate may be involved in the pathogenesis of some cardiovascular disease, its presence in patients (pts) with coronary artery disease (CAD) has not yet studied.

Aim of this study was to investigate the presence of chromosomal damage in peripheral blood lymphocytes in pts with CAD by using micronucleus (MN) test, a reliable biomarker in genetic and cancer risk assessment.

In the present study were included 53 pts with angiographically documented CAD (Group I) were included; 10 pts with valvular heart disease in absence of atherosclerotic lesions of the coronary arteries (Group II); furthermore 16 healthy subjects, age and sex-matched (Group III) were included as controls. For each subject, two separate cultures of lymphocytes were grown in vitro, and at each of these 24 h were incubated with γ-irradiation (300 rad) and then mitomycin C (10 μg/ml) was added to block the cytokinesis of the lymphocytes. 1000 binucleated cells were scored for the evaluation of MN frequency. Means (±SEM) of MN frequency were 11.9±1.7, 5.9±1.2 and 3.6±0.7 in group I, II, and III respectively. The MN frequency of group I was significantly higher than that of the group III (p=0.02).

Moreover, MN frequency increases with affected vessel number (6.3±0.7, 13.9±1.6, 14.9±5.3 for one-, two-, and three- vessel disease, respectively). ANOVA analysis showed that the MN frequency was significantly higher in two-vessel compared with one-vessel disease (p=0.0077).

Multiple regression analysis also showed that the Duke score, which indicates the severity of CAD, and systolic blood pressure appeared to be the two determinant factors in determining MN frequency (R=0.310, p=0.01; R=0.267, p=0.03, respectively). These results suggest that CAD in humans is a condition characterized by an increase of DNA damage, which positively correlates with the increased systolic blood pressure and the severity of the atherosclerotic disease.

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CARDIAC REHABILITATION PROGRAMS MAY BE MORE BENEFICIAL IN HYPERTENSIVE INDIVIDUALS

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Cardiac rehabilitation programs have become increasingly popular in subjects after acute coronary syndromes and revascularization procedures. The effect of such programs on cardiovascular risk has not been quantitatively assessed. The aims of our study were to examine the effect of cardiac rehabilitation program on cardiovascular risk and to identify subjects, in whom such programs would be more beneficial.

We compared the Framingham Cardiovascular Risk score in 62 subjects at the entrance to and upon the completion of a 3-month comprehensive cardiac rehabilitation program, which included supervised progressive exercise, counseling and behavioral intervention concerning control of risk factors.

The mean age of the participants was 63.7±11.8 years, 77% of the subjects were men. There was a significant reduction in modifiable risk factors score at the completion of the program (table). This resulted in a significant reduction of the total cardiovascular risk score (mean score 7.2 vs 6.3 points, P=0.002) Hypertensive subjects (systolic BP≥140 mm Hg) had a significantly larger reduction of systolic BP as compared to subjects with normal and high-normal BP (17.6±16 vs. 0.10 mm Hg, P<0.001), resulting in a trend towards a greater reduction of the total risk score (mean reduction of 1.7 vs. 0.6 points, P=0.085).

The observed decrease in cardiovascular risk score achieved by a cardiac rehabilitation program is equivalent to that of reducing the patients’ age by 5 years. The benefit of the program may be even greater in hypertensive individuals.

Score Category Baseline Final Visit P

| Total Cholesterol | -0.6±1.9 | -0.9±1.7 | 0.176 |
| HDL Cholesterol | 0.9±1.6 | 0.6±1.5 | 0.049 |
| Systolic BP | 0.7±1.3 | 0.4±1.3 | 0.007 |
| Smoking | 0.1±0.4 | 0.1±0.4 | 1.000 |
| Total Modifiable | 1.1±2.6 | 0.1±2.7 | 0.002 |

Key Words: Cardiovascular Risk, Cardiac Rehabilitation, Risk Assessment

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THE INSERTION/DELETION POLYMORPHISM OF THE ANGIOTENSIN-CONVERTING ENZYME GENE IS NOT CORRELATED TO THE STABLE OR UNSTABLE PRESENTATION OF PATIENTS WITH CORONARY ARTERY DISEASE

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The insertion/deletion (I/D) polymorphism of the angiotensin-converting enzyme (ACE) gene has been proposed as an independent risk factor for myocardial infarction (MI) and coronary artery disease (CAD). Although results are controversial, the D allele seems to bear a stronger relationship with MI than with the degree of CAD. In fact, the I/D polymorphism was found to be somehow related to the conversion of stable coronary syndromes into MI, independently of the presence and the severity of coronary lesions.