

## Summaries of Articles

### *Clinical Investigations*

#### **Fasting Hyperinsulinemia Among Nondiabetics: Independent Association with Coronary Disease**

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Controversy is not resolved whether plasma insulin levels serve as a risk indicator for coronary risk in the general population. The purpose of this cross-sectional study was to evaluate the role of insulin concentrations with respect to prevalent coronary heart disease (CHD) in the Turkish population sample. In 761 men and women (>30 years of age) residing in two large regions of the Turkish Adult Risk Factor Survey in 2001 plasma insulin levels, in addition to other risk parameters, were assessed. Diagnosis of CHD was based on clinical findings and Minnesota coding of resting ECGs. The chemiluminescent immunometric method was used to determine insulin values.

Fasting log insulin concentrations in 688 nondiabetic persons averaged 9 in men and 8.8 mIU/L in women ( $p>0.05$ ); they increased modestly with age. Best determinants of fasting insulin on multivariate analysis were waist circumference (and body mass index). In addition, triglycerides, blood pressure and, inversely, HDL-cholesterol values displayed strong correlations with insulin. In a logistic regression model controlling for age and obesity, the odds ratio (OR) for CHD in the quartile with hyperinsulinemia ( $\geq 10$  mIU/L) as opposed to the lowest quartile was 2-fold in both genders ( $p<0.05$ ). Adjustment for dyslipidemia, blood pressure, glucose intolerance, physical activity and smoking status did not attenuate the OR, nor did adding C-reactive protein into the model (which was correlated with fasting insulin only in women). Thus, hyperinsulinemia may not only add useful information on CHD likelihood to that provided by the other risk factors, it may also contribute to the coronary risk independent of the latter factors.

Key words: Hyperinsulinemia, coronary heart disease, C-reactive protein, Turkish Adult Risk Factor survey

#### **Effect of Growth Hormone Replacement Therapy on Lipid Profile, Blood Pressure and Body**

#### **Composition in Patients with Hypopituitarism: Six-Month Results**

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Growth hormone deficiency can increase cardiovascular mortality and morbidity, negatively affecting some risk factors, like lipid profile known to predispose to coronary artery disease. The aim of this study was to investigate the effects of growth hormone replacement therapy (GHRT) on impaired lipid profile, blood pressure and body composition.

Method: Twenty patients (13 females, mean age:  $51 \pm 6$  years; 7 males, mean age:  $46 \pm 13$  years) who were followed-up at the Endocrinology clinic due to hypopituitarism with no cardiac involvement (normal ECG, echo, and holter monitoring) were included in the study. The diagnosis was based on the insulin tolerance test. The patients, who were on the replacement therapy also for other pituitary hormone deficiencies, were planned to receive GHRT for 2 years in doses recommended by the Growth Hormone Society Workshop. Data from 20 patients, who received GHRT for 6 months were assessed in this study. At baseline, third and sixth months after GHRT, total cholesterol, triglycerides, HDL- and LDL- cholesterol and fasting blood glucose levels were measured; systolic and diastolic blood pressures, body mass index (BMI), waist-hip-ratio (WHR) were also evaluated.

Results: Before treatment, cardiological findings were normal in all patients. While BMI of the patients did not change during the treatment, WHR decreased significantly ( $p<0.05$ ). Blood pressures at baseline, were normal and remained so after the treatment. Total and LDL-cholesterol levels dropped significantly ( $p<0.05$ ). There was a significant increase in HDL levels ( $p<0.05$ ). Although triglycerides and fasting glucose levels showed an increasing tendency, the difference from baseline did not reach a significant level.

Conclusion: With a 6-month GHRT, an improvement in cardiovascular risk factors has been observed; an improvement in lipid profile and a decrease in abdominal obesity. However, it is questionable whether these favorable effects will continue in the

long-term. Therefore, it is obvious that there is a need for long-term prospective studies with GHRT.

Key words: Growth hormone replacement therapy, coronary artery disease, coronary risk factors

### **Aortic Stiffness and its Relation with the Left Ventricular Diastolic Function in Patients with Hypertension and Diabetes Mellitus**

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**Aim:** This study aims to evaluate the elastic properties of the aorta and its relation with the left ventricular diastolic function in patients with hypertension (HT) and/or diabetes mellitus (DM) by using routine echocardiographic methods and Schieken's method.

**Methods:** Study groups were composed of 21 normal subject, 21 patients with HT, 21 with DM, and 15 with HT+DM. The aortic strain, beta index, distensibility and Schieken index were evaluated as aortic elasticity parameters. Aortic elasticity parameters of normal and patient groups were compared. The correlations of Schieken index with three other parameters were evaluated by simple linear regression analysis. Multivariate analysis was performed for determinants of the left ventricular diastolic function.

**Findings:** There were significant differences between normal and patient groups (HT, DM, HT+DM) for aortic strain ( $21.62 \pm 6.26$  vs.  $8.93 \pm 3.16$ ,  $11.48 \pm 3.78$  and  $7.17 \pm 2.74$  %,  $p < 0.001$ ; respectively), beta index ( $2.26 \pm 0.84$  vs.  $7.28 \pm 3.46$ ,  $4.06 \pm 2.16$  and  $10.65 \pm 4.95$ ,  $p < 0.001$ ; respectively), and distensibility ( $13.44 \pm 4.81$  vs.  $2.59 \pm 1.06$ ,  $7.03 \pm 3.92$  and  $1.89 \pm 0.72$   $10^{-3} \text{ cm}^2 \text{ dyn}^{-1}$ ,  $p < 0.001$ ; respectively). HT and HT+DM groups had significant differences of Schieken index compared to normal group ( $38 \pm 5.8$  and  $39.4 \pm 4.37$  vs.  $27 \pm 5.24$  kHz/sec,  $p < 0.001$ ). However Schieken index of DM group ( $31.3 \pm 7.4$  kHz/sec) was similar to normal group. Schieken index showed significant correlations with aortic strain, beta index, and distensibility ( $r = -0.40$ ,  $0.41$  and  $-0.51$ ,  $p < 0.001$ ; respectively). In multivariate analysis, the strongest predictor of isovolumetric relaxation time was aortic strain.

**Conclusion:** There was an increase in aortic stiffness in patients with HT and/or DM. The increase in aortic stiffness may be the main cause of left ventricular diastolic dysfunction observed in patients with HT

and/or DM. Schieken index was suitable to be used in evaluating aortic stiffness.

Key words: Aortic stiffness, hypertension, diabetes mellitus, left ventricular diastolic function

### **Relationship of Myocardial Performance Index During Low Dose Dobutamine with the Myocardial Improvement After Revascularization and Its Value in Prediction of Myocardial Viability in Patients with Acute Myocardial Infarction**

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**Aim:** This study was planned to evaluate the relationship of the change in the myocardial performance index (MPI) obtained by low dose dobutamine stress echocardiography (DSE) with the myocardial improvement after revascularization and its value in identifying the significant viable myocardial tissue in patients with acute myocardial infarction (AMI).

**Methods:** Forty patients (mean age  $57 \pm 9$  years, 6 female) with Q-AMI, who had no prior myocardial infarction, were enrolled. The wall motion score index (WMSI) and MPI were obtained echocardiographically in basal and low dose DSE in all patients and in the second month after revascularization in 24 revascularized patients. The WMSI was assessed qualitatively by scoring normal to dyskinesia (1-4 points) according to 16-segments model.

**Results:** The MPI and WMSI obtained by low dose DSE were similar to those after revascularization ( $0.5 \pm 0.14$  and  $1.24 \pm 0.24$  vs.  $0.52 \pm 0.15$  and  $1.28 \pm 0.22$ ,  $p < 0.001$  and  $< 0.001$ ; respectively). The change rate ( $\% \Delta \text{MPI} = 17 \pm 13$  %) in MPI with low dose DSE correlated with that ( $\% \Delta \text{DHSI} = 12 \pm 7$  %) in WMSI after revascularization ( $r = 0.68$ ,  $p < 0.001$ ). Although the negative predictive value of  $\% \Delta \text{MPI} \geq \% 25$  in prediction of the significant viable myocardial tissue was high (96%), its positive predictive value was low (62%).

**Conclusions:** The change rate in MPI with low dose DSE correlates with myocardial healing after revascularization. This rate has a high negative predictive value in prediction of the significant viable myocardial tissue, but its positive predictive value is

low. Thus, MPI can be used as an alternative method of WMSI in some cases in when specificity decreases.

Key words: Acute myocardial infarction, dobutamine stress echocardiography, myocardial viability, and myocardial performance index

### **Role of Homocysteine in Atherosclerotic Coronary Artery Disease; Its Association With Lesion Stenotic Severity, Vitamin B<sub>12</sub> and Folic Acid**

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Recent studies have shown that elevation in homocysteine (Hcy) levels is an independent risk factor other than classical risk factors for atherosclerotic coronary artery disease (CAD). In our study, we aimed to investigate the role of Hcy in CAD, its association with vitamin B<sub>12</sub> (B<sub>12</sub>), folic acid (FA) and severity of stenotic lesion.

This study was made in the Cardiology Department of Uludağ University Medical Faculty between June 1998 and August 1999 among persons in whom a coronary angiography was performed. The coronary angiographies were evaluated quantitatively by two experienced cardiologists who were unaware of the laboratory findings. In order to show lesion severity of CAD, coronary artery lesions were assessed according to the Gensini scoring system. Blood samples were drawn from patients for serum Hcy, B<sub>12</sub> and FA levels. Role of hcy in atherosclerotic coronary artery disease; and its association with B<sub>12</sub>, FA and lesion stenotic severity were examined statistically. Coronary angiography was completely normal in 45 of 209 patients. In 164 patients, coronary lesions were detected. In the group with CAD; mean age, male/female ratio, incidence of smoking and diabetes, levels of B<sub>12</sub>, FA, Hcy and total cholesterol were higher than the group without CAD and the differences between the groups were statistically significant (p<0.05). In the study group when the binary logistic regression test was used for determination of coronary risk factors, elevated levels of hcy were found as an independent risk factor other than classical risk factors and were found to increase risk of having CAD 1.6 times (p<0.001). In group analysis it was found that elevated Hcy levels had a positive correlation with Gensini score and a negative correlation with levels of B<sub>12</sub> and

FA which were both significant statistically (p<0.05), (p<0.05).

We concluded that elevated levels of Hcy was an independent risk factor for CAD other than the classical risk factors. In addition the extent and severity of CAD increases with elevated in levels of Hcy.

Key words: Homocysteine, vitamin B<sub>12</sub>, folic acid, lesion stenotic severity.

### **Rationale for Lowering the Upper Normal Limit of Total Cholesterol Levels to 180 mg/dl Among Turks**

*A. Onat*

Since the coronary risk profile of Turkish adults was found to differ significantly from Western populations and international guidelines on prevention are considered to have shortcomings for Turks, a new approach was sought. With the purpose of comprising into a prevention program those individuals at high risk who have thus far not been included in primary and secondary coronary prevention, the thesis is proposed (based on the database of the Turkish Adult Risk Factor Study) that the upper limit of normal total cholesterol (TC) levels be reduced to 180 mg/dl. Of the estimated 5 million adults harboring levels of TC 180-200 mg/dl, about 800,000 are considered to be at high coronary risk.

Subjects at high risk were defined by a TC/HDL-cholesterol ratio >5 in men aged (50 or women aged (60 years. Even in primary prevention in this group, the benefit of drug therapy should not be withheld, in addition to lifestyle changes, with the aim of improving the dyslipidemia involving plasma triglycerides and HDL-cholesterol. The hypothesis was supported not only by mathematical and metabolic evidences, but also by the British recommendations and the Framingham risk function as well as the findings of the Turkish Adult Risk Factor Study. If these criteria are incorporated into the forthcoming guidelines of the Turkish Society of Cardiology and are implemented, a significant proportion of the estimated 45-50,000 new coronary events each year occurring in persons with TC levels of 180-200 mg/dl may be prevented.

### Reviews

### **Congestive Heart Failure and Ventricular Arrhythmias**

*E. Diker*

Congestive heart failure (CHF) is a rather frequent disease especially in the older population. This disease has a very grave prognosis and death usually comes suddenly. Despite the ratio of sudden death approaches 80% in groups with relatively well functional capacity sudden death rate drops to 5 % in end-stage patient groups. Nevertheless, the cause of sudden death shifts from ventricular tachycardia/fibrillation to bradyarrhythmias when illness becomes grave. Many comprehensible reasons, such as myocardial fibrosis, stretch, increased sympathetic drive, electrolyte imbalance, may easily cause ventricular arrhythmia in failing hearts. Holter monitoring, signal averaged electrocardiogram, programmed ventricular stimulation procedures are used to find out the population under risk. Randomised trials have been designed to seek the most advantageous drug in terms of reducing the arrhythmic and total mortality. Unfortunately, even amiodarone failed to show any impressive benefit to reduce deaths in population at risk. Implantable cardioverter defibrillator devices (ICD) seem to be very promising to reverse the evil course.

Key words: Congestive heart failure, ventricular arrhythmias, sudden cardiac death

### When Should Fibrates Be Used?

*H. Yüksel*

Epidemiologic studies have shown that not only raised low density lipoprotein cholesterol but also dyslipidaemic syndromes characterized by elevated plasma triglyceride and low high density lipoprotein cholesterol are powerful risk factors for coronary heart disease (CHD). Combined hyperlipidemia and atherogenic lipoprotein phenotype are the most common dyslipidaemia types seen in patients with CHD. An alternative approach is to increase high density lipoprotein cholesterol (HDL-c) level and to decrease plasma triglyceride (TG) level in addition to decreasing level of low density lipoprotein cholesterol (LDL-c) to reduce the risk of CHD.

It is known that fibrates are useful for the treatment of low HDL-c with or without hypertriglyceridaemia. The recommendation for the use of fibrates in certain types dyslipidaemia has gained additional support from Helsinki Heart Study. Fibrates are a broad spectrum lipid lowering drug. They increase the HDL-c level while decreasing plasma TG level and LDL-c

considerably. Furthermore, they change the composition of LDL-c. Highly atherogenic small, dense LDL particules are converted to less atherogenic large LDL particules. The effects of fibrates are mediated by nuclear hormone receptor termed peroxisome proliferator activated reseptor (PPAR). Fibrates bind to PPAR and initiate a sequence of events that lead to hypolipidaemic effect.

It has been supported by the recent data from multicenter large clinical studies that fibrates can be used safely and they can decrease CHD mortality and morbidity considerably by raising HDL-c and lowering TG. In this review, we focused on the mechanism of action of fibrates on the lipid metabolism and clinical studies investigating their effects on CHD mortality/morbidity and clinical indications.

Key words: Fibrate, hipertriglyceridemia, combined dislipidemia, metabolic syndrome

### Case Report

#### **A Case with Brugada Sydrome Misdiagnosed as Acute Myocardial Infarction: A case report**

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A forty-year old man admitted to the emergency department due to left shoulder pain. His electrocardiogram (ECG) revealed 3-5 mm ST segment elevation on leads V<sub>1-3</sub> and right bundle branch block (RBBB) pattern. The diagnosis of acute anteroseptal myocardial infarction was made and streptokinase had given. The next day, nomore ST segment elevation on leads V<sub>1-3</sub> and RBBB was present on ECG and all cardiac enzymes were in normal limits. All ECGs were reviewed and seen that the diagnosis of myocardial infarction was excluded. Because of typical ECG findings, Brugada syndrome (BS) was suspected. For diagnosis, provacation test with propafenone, a Class IC antiarrhythmic agent, was performed. Test was markedly positive for BS. ECG of his four relatives revealed the same RBBB pattern. His coronary angiogram and cardiac MRI were normal. This case is reported because of its rarity and successfully provoked ST segment elevation with propafenone.

Key words: Brugada syndrome, myocardial infarction, propafenone