

## Summaries of Articles

### Clinical Investigations

#### **The Effect of Homocysteine-Lowering Therapy on Vascular Endothelial Function and Myocardial Ischemic Burden in Coronary Patients with Hyperhomocysteinemia**

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This study was performed to determine whether homocysteine-lowering therapy (HLT) improves endothelium-dependent vasodilation and whether this results in a reduction in myocardial ischemic burden in patients with coronary artery disease. Sixteen male patients (plasma homocysteine levels  $>15 \mu\text{mol/L}$ ) on a waiting list for routine coronary angioplasty (PTCA) of a focal stenosis at least 70% in the left anterior descending artery were studied. Patients were randomized to receive HLT ( $n=9$ , 0.4 mg of folic acid, 2 mg of vitamin B6, and 6  $\mu\text{g}$  of vitamin B12) or placebo ( $n=7$ ) until the time of PTCA (mean  $4.8 \pm 0.9$  weeks). At baseline and after four weeks of HLT, brachial artery vasomotion was assessed noninvasively and exercise TI-201 scintigraphy was performed in each patient. Myocardial ischemic burden was defined as maximal perfusion defect and redistribution gradient of perfusion abnormality on the polar map display. All patients had a follow-up angiogram at the time of PTCA. Plasma homocysteine levels were significantly reduced by HLT compared with baseline ( $21.2 \pm 5$  vs.  $11.8 \pm 3.1 \mu\text{mol/L}$ ;  $p < 0.008$ ) whereas placebo had no effect ( $19.9 \pm 5$  vs.  $20.2 \pm 7 \mu\text{mol/L}$ ;  $p = \text{NS}$ ). HLT produced a marked improvement in endothelium dependent, flow-mediated dilation, from  $3.8 \pm 1.3\%$  to  $9.2 \pm 2.2$  ( $p < 0.0001$ ). There was no significant change in flow-mediated dilation with placebo ( $3.7 \pm 1.3\%$  vs.  $3.8 \pm 1.6\%$ ;  $p = \text{NS}$ ). Endothelium-independent, nitroglycerin-induced dilation was similar in the HLT ( $12.3 \pm 2.4\%$  vs.  $13.1 \pm 1.9\%$ ;  $p = \text{NS}$ ) and placebo ( $13.2 \pm 2.2\%$  vs.  $12.9 \pm 2.8\%$ ;  $p = \text{NS}$ ) groups compared with baseline. HLT resulted in significant reductions in maximal perfusion defect, from  $52 \pm 21\%$  to  $42 \pm 17\%$  ( $p = 0.004$ ) and in redistribution gradient, from  $24.8 \pm 13\%$  to  $16.7 \pm 8\%$  ( $p = 0.006$ ) whereas placebo did not. The severity of stenosis was not different between the initial and follow-up angiograms in HLT ( $81 \pm 9\%$  vs.  $82 \pm 11\%$ ;  $p = \text{NS}$ )

and placebo ( $79 \pm 8\%$  vs.  $80 \pm 9\%$ ;  $p = \text{NS}$ ) groups. In addition, the degree of reduction in plasma homocysteine level was negatively correlated with endothelium dependent vasodilation ( $r = -0.63$ ,  $p = 0.05$ ). Improvement in endothelium dependent vasodilation was also negatively correlated with maximal perfusion defect ( $r = -0.65$ ,  $p = 0.05$ ) and redistribution gradient ( $r = -0.67$ ,  $p = 0.04$ ).

In conclusion, lowering plasma homocysteine levels with HLT improves endothelium-dependent vasodilation and this may result in a reduction in exercise-induced myocardial ischemia in coronary patients with hyperhomocysteinemia.

Key words: Homocysteine, endothelial function, myocardial ischemia, exercise TI-201 scintigraphy

#### **Myocardial Ischemia in Patients with Slow Coronary Artery Flow Assessed by Coronary Sinus Blood Lactate Levels**

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Slow run-off dye in the coronary arteries during selective coronary angiography is known as slow coronary artery flow (SCAF). A few studies have been performed concerning its etiology and treatment since it was defined. It is accepted that abnormal increase of resistance at the microvascular level causes SCAF. In this study, the question whether coronary slow flow is associated with myocardial ischemia was analyzed by coronary sinus blood lactate screening under atrial pacing.

Ten patients with slow coronary flow (7 males, 3 females; mean age  $48 \pm 8$  yrs. were included in the study. TIMI frame count method was used to determine the coronary slow flow. All patients had exercise testing with using Bruce protocol after coronary angiography. We have performed atrial pacing to all patients and coronary sinus, and aortic blood samples was collected for the measurement of lactate levels during rest and peak heart rates. Lactate extraction was calculated using a formula:  $(\text{LAC ao} - \text{LAC cs}) / (\text{LAC ao})$ .

All exercise tests were negative by using standard criteria. Coronary sinus blood lactate level was  $9.52 \pm 1.89$  mg/dl at rest and  $9.33 \pm 1.68$  mg/dl at

maximum heart rate ( $p>0.05$ ). There was no difference between lactate extraction at rest and maximum heart rate ( $0.12\pm 0.04$  vs  $0.12\pm 0.04$ ;  $p>0.05$ ).

In conclusion, there was no metabolic evidence of myocardial ischemia obtained in patients slow coronary flow. However, there is need for further large, studies concerning the relationship between myocardial ischemia and coronary slow flow and also to long-term prognosis.

**Key words:** Myocardial ischemia, coronary angiography, slow coronary artery flow, coronary sinus lactate levels

### **Change of QT Dispersion in Patients with Coronary Artery Disease Undergoing Aneurysmectomy**

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The purpose of the study was to detect whether QT dispersion (QTD) was significantly different between patients with anterior myocardial infarction (MI) with and without left ventricular aneurysm and to evaluate the change of QTD after aneurysmectomy. For this purpose, 22 patients with anterior MI who underwent aneurysmectomy and coronary bypass surgery (Aneurysm Group: AG) and 15 patients with anterior MI but without aneurysm who had undergone coronary bypass surgery alone (Control Group: CG) were included in the study. QTD of patients were calculated from resting ECG recorded 1 day before and 1 month after the operation. Also heart-rate-corrected QT interval and QTD (QTcD) were calculated from Bazett's formula. **Results:** While preoperative QTcD were significantly higher in patients with left ventricular aneurysm (AG:  $89\pm 20$  vs. CG:  $76\pm 19$ ;  $p=0.04$ ), postoperative QTcD was significantly lower in both groups compared to preoperative QTcD (AG:  $89\pm 20$  vs.  $70\pm 25$ ;  $p=0.001$ ; CG:  $76\pm 19$  vs.  $61\pm 22$ ;  $p=0.02$ ). However, the decrease of QTcD provided by operation between the groups, was not significantly different in patients with aneurysmectomy from those in the CG ( $19\pm 28$  -  $14\pm 18$ ;  $p>0.05$ ).

Hence, QTD significantly increases in the presence of left ventricular aneurysm but aneurysmectomy does not provide additional reduction in QTD beyond that obtained from revascularization.

**Key words:** Aneurysm, QT dispersion

### **The Relationship Between Plasma Insulin Levels and Angiographical Severity of Coronary Artery Disease**

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The aim of this study was to investigate the relationship between plasma insulin levels and the angiographical severity of coronary artery disease in male patients with normal glucose tolerance and unstable angina. Two days before coronary angiography, a standard OGTT was performed on 126 patients with normal fasting blood glucose levels. Twenty-four patients were excluded because of impaired glucose tolerance. One-hundred-two patients with normal glucose tolerance underwent coronary angiography. To exclude possible confounding effects, angiographically normal two patients were excluded and the remaining 100 patients were included in the study. Significant coronary artery disease was determined in 68 patients (Group I). Angiographical results demonstrated that 32 patients had no significant coronary artery disease (Group II). The presence of significant coronary artery disease and total atherosclerosis score were used to determine the severity of coronary artery disease. While significant coronary artery disease was correlated with age, Lp(a), fasting plasma insulin level and tobacco consumption ( $r=0.34$ ,  $r=0.30$ ,  $r=0.28$ ,  $r=0.21$ , respectively), total atherosclerosis score was correlated with fasting plasma insulin level, Lp(a), age and glucose level in the first hour ( $r=0.26$ ,  $r=0.36$ ,  $r=0.90$ ,  $r=0.26$  respectively). In multivariate analysis, log fasting plasma insulin levels proved to be a significant independent determinant both of significant coronary artery disease and of total coronary atherosclerosis score in patients with normal glucose tolerance and unstable angina.

**Key words:** coronary artery disease, insulin, Lp (a)

### **Surgical Treatment of Type A Aortic Dissection: Early-Term Results**

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Despite medical and technological improvement, acute type A aortic dissection is still a serious

pathology, which causes death with any delay in early diagnosis. The aim of this study was to determine the early results of the surgical treatment of Stanford type A aortic dissection.

318 patients underwent surgical repair for intrathoracic aneurysm and/or dissection at Koşuyolu Heart and Research Hospital, between February 1985 and January 1999. Forty-eight (15.1%) of them were operated on for acute type A aortic dissection among whom 40 (83%) were male and 8 (17%) female with a mean age  $49.9 \pm 11.1$  years (range, 21 to 70). Only replacement of the ascending aorta (Group I) was performed at 24 (50%) patients and associated arch replacement (Group II) was performed at the other 24 (50%) patients. Aortic valve was preserved (Group A) in 35 (73%) patients and was replaced (Group B) in 13 (27%) patients. Surviving patients were followed up for  $2.67 \pm 1.95$  years (between 1 and 8).

Early mortality was 22.9% (11 patients) and late mortality 4.2% (2 patients), total mortality rate being 27.1%. Univariate analysis showed that preoperative hemodynamic instability, coronary artery disease, extracorporeal circulation, renal complications, major neurologic and cardiac complications were statistically significant risk factors for early mortality. Forward stepwise logistic regression analysis showed that age, previous cardiac operation, extracorporeal circulation, renal and cardiac complications increased early mortality. There was no difference between groups for survival. Renal dysfunction, neurologic complications and rhythm problems were common morbidities. In Group A, aortic insufficiency regressed significantly after surgery ( $p < 0.001$ ). Surviving 31 patients had functional capacity in NYHA class I, and 4 had functional capacity in NYHA class II.

Early surgical intervention for acute type A dissection decreases mortality rate because of the nature of the disease. It is important to determine predictors for early mortality. Sparing the aortic valve must be the first choice in all situations if possible. Flanged composite graft can be chosen when aortic root is included. TEE and CT must be performed annually for early diagnosis of late complications during follow-up.

**Key words:** Type A aortic dissection, flanged, arcus aorta, button technique

## Stentless Bioprosthesis in Surgical Treatment of Aortic Root: Mid-term Results

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Stentless bioprostheses with superior hemodynamics, laminar flow patterns, lack of need for anticoagulation and perhaps improved durability offer several advantages over traditional valves. The main purpose of this study was to determine early and mid-term results in surgical treatment of the aortic valve disease in elderly patients using stentless bioprosthesis. Between September 1997 and April 2000, 10 patients (8 males 2 females; mean age  $63 \pm 12.7$  years; range 33-74 years) received stentless bioprosthesis. Total root replacement was performed in nine patients and subcoronary implantation technique was done in one. The mean follow-up duration was  $14.8 \pm 9.4$  months (range, 2 to 31 months). There was one (10%) early mortality due to low cardiac output. Late mortality was not observed. Actuarial survival was  $90 \pm 9.5$  % at two years. We did not observe any valve-related morbidity. One patient was required permanent pacemaker due to complete heart block after the operation. Decreasing of the mean transbioprosthesis gradient and increasing of the effective orifice area were demonstrated. Stentless bioprosthesis can be used safely for the replacement of aortic valve pathology, especially in elderly patients because of optimal durability with almost not thromboembolic events and no requirement of anticoagulation.

**Key words:** stentless, bioprosthesis, aortic valve, aortic root.

## Higher Efficacy of 10 mg/Day of Simvastatin in Turkish Patients With Hyperlipidemia

*A. Onat, L. Tozğözoğlu, İ. Soydan, V. Sansoy, N. Koylan, R. W. Mahley, on behalf of the Simvastatin Sensitivity Study Group*

This open-label single-arm multicenter prospective study tested the hypothesis whether Turkish patients were more sensitive to the LDL-cholesterol (LDL-C) lowering effect of simvastatin than Western populations. A total of 86 subjects with a mean age  $54 \pm 9$  years (among whom 52 women) were enrolled who fulfilled the criteria of entry and exclusion. The effects of 6-week treatment period with 10 mg simvastatin a day in men and women on high baseline levels of LDL-C (177 and 214 mg/dl),

total cholesterol (TC, 256 and 296 mg/dl), as well as on those of triglycerides (TG, 184 and 177 mg/dl) and HDL-C (41 and 48 mg/dl, respectively) were studied.

An excellent overall mean decrease of 31.3% in LDL-C concentrations was attained with the stated low dose. Percent change values for TC, TG, and HDL-C were -23%, -4.5% and +5%, respectively, while TC/HDL-C ratio declined from 6.2 to 4.7. A significant reduction by 0.5 kg/m<sup>2</sup> was associated in the mean body mass index. The presence of coronary heart disease or smoking status did not affect the change in LDL-C. From the data of the 4S study, it could be deduced that a 31% reduction in LDL-C would be achieved in a Scandinavian population with a daily simvastatin dose of 17 mg, a result obtained among Turks with a dose 41% less.

Key words: Hyperlipidemia, lipoproteins, statins

### Case Reports

#### **Left Main Coronary Artery Disease Due to Primary Hypoalphalipoproteinemia in a 17-Year-Old Female**

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Low high density lipoprotein (HDL-C) levels are inversely related to risk for coronary artery disease (CAD). Some forms of hypoalphalipoproteinemias characterized by extremely low levels of serum HDL are associated with premature CAD.

We report a 17-year-old female with acute myocardial infarction associated with total occlusion of the left main coronary artery at coronary angiography. A successful angioplasty and stenting was performed and flow was restored. She died 4 months after myocardial infarction due to heart failure. No cause of CAD, besides atherosclerosis, was determined, in that case. She had extremely low levels of serum HDL-C and normal LDL-C, triglycerides (HDL-C: 2 mg/dL, LDL-C: 92 mg/dL, total cholesterol: 130 mg/dL, triglycerides: 180 mg/dL). The absence of low levels of HDL-C in her family members suggested that she might have primary hypoalphalipoproteinemia. Although we could not perform genetic analysis, we think she might have apo A<sub>I</sub> gene disarrangement, apo A<sub>I</sub> frameshift mutation or specific Apo-A<sub>I</sub> point mutation like Apo-A<sub>I</sub>ZAVALLA (Leu<sub>159</sub>→Pro) and Apo-A<sub>I</sub>PISA (Leu<sub>141</sub>→Arg) because the other forms of hypoalphalipoproteinemias are not associated with CAD.

Key words: Coronary atherosclerosis, hypoalphalipoproteinemia

#### **Aortic Root Abscess With Fistula Formation into Right Ventricular Myocardium**

*K. Kıralı, S.N. Ömeroğlu, D. Mansuroğlu, G. İpek, C.Yakut*

A fistula between aorta and right ventricular outflow tract is one of the uncommon complications of periannular abscess, which develops after aortic valve endocarditis. Operation for infective aortic valve endocarditis with associated periannular abscess has high mortality and morbidity rates. After 2-month-long antibiotic therapy for infective aortic valve endocarditis, a 34-year-old man underwent operation for severe aortic valve stenosis and insufficiency with associated aortico-right ventricular myocardial fistula in 1999. Reconstruction of the aortic wall and the right ventricular outflow tract was performed by primary closure of these defects following radical resection of the abscess cavity. Aortic valve replacement was applied with 23 mm St. Jude mechanical, bileaflet prosthetic valve. Postoperative course was uneventful, and he remained asymptomatic during follow-up controls. Because it is the most serious complication, when a fistula is diagnosed after active infective aortic valve endocarditis, surgical repair should be performed.

Key words: infective endocarditis, aortic root abscess

#### **Extraanatomic Correction for the Long-Interrupted Segment of the Isthmic Aorta in Adult Patients**

*K. Kıralı, N. Yakut, A. Tuncer, C. Yakut*

Interruption of aorta in adult patients is an uncommon congenital vascular anomaly, because it requires a corrective operation in the pediatric age group. Three adult patients were operated on at our clinic for the long-interrupted segment of the aorta. Tube graft interposition in place of the interrupted segment of the isthmic aorta was performed in all patients. They had no residual gradient at the corrected segment. Bypass grafting is a safe and easy method for the treatment of interruption of the aorta in adult patients.

Key words: Interruption of the aorta, extraanatomic bypass