Background: The multifactorial pathogenesis of ischemic heart disease (IHD) includes a combination of environmental and genetic factors. Activation of inflammatory pathways is common in IHD, but mechanisms are still unknown. We and others have recently proposed that a polymorphism in the CD14 receptor gene of monocytes may be involved in IHD. In this study, we assessed whether other polymorphisms of genes coding for pro-inflammatory mediators are involved in the inflammatory response observed in IHD.

Methods: We studied 87 pts with Braunwald class IIIb unstable angina (Group 1) and 32 pts with stable angina (Group 2). The following polymorphisms were detected by polymerase chain reaction and restriction analysis: -174 C/G of IL6, Thr/Asp26 of TNF-β and four polymorphisms of TNF-α (-375 G/A, -308 G/A, -244 G/A, -238 G/A). Genotype and allele frequencies were correlated with C-reactive protein (CRP) levels and IL-6 production by circulating monocyte in response to LPS-challenge (1ng/ml for 4 hours).

Results: Genotype and allele frequencies of the investigated polymorphisms were not different among groups. However, elevated levels of CRP (>3mg/L) were observed in 61% of the overall carriers of thr/thr genotype of TNF-β gene and 31% of the same carriers (p=0.05). Moreover, IL-6 production in response to LPS was higher in GG homozygotes of IL-6 gene than in GT heterozygotes (4.4 ng/ml vs 2.0 ng/ml; p=0.06). No correlation was found between CRP levels, IL-6 production and polymorphisms of TNF-α gene.

Conclusions: Our study suggests that in a polygenic and multifactorial syndrome such as IHD, polymorphisms of TNF-β and IL-6 genes, but not of TNF-α, are related with an enhanced pro-inflammatory response.

1025-35 The 894G T Polymorphism In the Endothelial Nitric Oxide Synthase Gene Influences Risk for Acute Myocardial Infarction Only in Subjects With Low Risk for Coronary Events

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Background: Homozygosity for the 894 G-T polymorphism in the Endothelial Nitric Oxide Synthase gene, which encodes a Gln298Asp substitution in eNOS, has been related to increased risk of acute myocardial infarction (AMI). We examined the role of this genetic variant in the pathogenesis of AMI in a relatively homogeneous, low coronary risk Caucasian population. Methods: 1629 consecutive AMI patients (mean age 62±13 years), enrolled into the GEMIG study were recruited on admission from 9 Cardiac Departments located in three cities. The GEMIG study is a multicentre prospective study, specifically designed to investigate the genetic background of ischemic heart disease in the Greek population. The control group (n=805, mean age 58±15 years) was derived from an epidemiological study that investigated the frequency of the same genetic variant in a representative sample of the general adult population. Results: The frequency of the Asp298 variant was not significantly higher in AMI patients compared to controls (11.2% vs 10.4%, P=0.342). Adjustment for age and gender did not alter these results, but subgroup analysis showed an excess of homozygotes for the Asp298 allele among cases (12.7% vs 7.8%, P=0.033) in subjects with low risk for CAD (non-smokers without hypercholesterolemia). The Asp/Asp genotype was more frequent in younger patients with AMI and multivariate analysis showed that older age was independently associated with homozygosity for the Asp298 allele among patients (OR=0.986, 95% CI 0.974-0.999, P=0.031) but not in controls (P=0.386). Univariate and multivariate analysis failed to demonstrate any relationship of the Asp298 variant with the extent of coronary artery disease on angiography or with in-hospital mortality after AMI. Conclusion: The 894G-T polymorphism of the eNOS gene is related to individual risk of AMI in younger subjects with low coronary risk as estimated by the major conventional risk factors, but not in the total population. Given the key role of eNOS in the pathogenesis of ischemic heart disease in humans, our results do emphasize the need for further evaluation of the possible influence of its genetic variants on the phenotypic expression of the disease.

1025-36 Outcome for Coronary Artery Disease: Observational Data 1986-2000


Background: Patients with significant (>75% stenosis) coronary artery disease (CAD) were prospectively evaluated for all-cause mortality with adjustment for cardiac risk, morbidity and propensity to select one of three initial treatment options. Methods: 18,481 patients were treated between 1986 and 2000 and assigned to one of three groups based on the initial treatment strategy of either medical therapy (MED N=6882), percutaneous intervention (PCI N=6293) or coronary bypass (CABG N=5327). The results are stratified according to the extent of CAD into 9 groups ranging from one-vessel (no proximal LAD involvement, group 1) to three-vessel (with 95% proximal LAD obstruction, group 9) using the Duke CAD Index. Results: The initial treatment strategy has changed from 1986 (42%MED, 23%PCI, 35%CABG) to 2000 (25%MED, 47%PCI, 28%CABG). Significantly improved survival in all treatment groups for all degrees of CAD has occurred over time. Conclusions: PCI and CABG continue to show significant long-term benefit compared to MED for all degrees of CAD. CABG remains the most robust and effective therapy for patients with multi-vessel disease and LAD involvement. CABG advantage over PCI begins with CAD more severe than group 5 (2-vessel CAD with 95% proximal LAD or 3-vessel CAD). Despite advances in PCI during the enrollment period, a developing advantage compared to CABG for more extensive CAD could not be demonstrated.

1026-27 Evolving Etiological and Prognostic Factors in Acute Coronary Syndromes

Sunday, March 17, 2002, Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

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Background: The presenting symptoms and electrocardiograph (EKG) changes identified with acute coronary syndromes (ACS) are not uniform and may be influenced by several factors. We examined the influence of age on these manifestations. Methods: Data collected on 2133 consecutive ACS pts, 51% with ST-elevation (STE) and 49% with non-ST-elevation (NSTEMI) in the framework of a national survey conducted in all 26 hospitals in Israel during Feb-Mar 2000 were used in this analysis. The pts were divided in 2 age groups: <65 (n=974), 65-74 (n=500), and >75 (n=639). Results: With advancing age, female gender, prior MI, previous angina, hypertension and Killip class >1 on admission became more frequent, whereas current smoking and hyperlipidemia became less frequent (p for trend <0.0001, for all). The frequency of no chest pain/typical symptoms on presentation increased with age for all ACS pts (14, 21, 32%, respectively, p for trend <0.0001). The corresponding figures in pts with STE were: 10, 18, 27%, respectively; in pts with no STE were: 20, 24, 35%, respectively; and in pts with ST-depression (STD) were: 17, 25, 32%, respectively (p for trend <0.0001, for all). In ACS pts, STE on admission ECG decreased with advancing age (p<0.0001). In multivariate analysis, independent predictors of no chest pain/typical symptoms on presentation increased with age for all ACS pts (14, 21, 32%, respectively, p for trend <0.0001). The corresponding figures in pts with STE were: 10, 18, 27%, respectively; in pts with no STE were: 20, 24, 35%, respectively; and in pts with ST-depression (STD) were: 17, 25, 32%, respectively (p for trend <0.0001). In multivariate analysis, independent predictors of no chest pain/typical symptoms on presentation (in decreasing order) were: age, history of heart failure, lack of past angina, diabetes and non-smoking. STE was negatively and independently associated with no chest pain/typical symptoms on admission (OR=0.48; 95%CI 0.37-0.63). The use of acute reperfusion therapy (thrombolysis or primary PCI) declined with advancing age (39, 25, 14%, respectively; p for trend <0.0001). No chest pain/typical symptoms was an independent predictor of 30-day mortality (18.1 vs. 6.7%. OR=1.43; 95% CI 1.01-2.06). Conclusions: In ACS pts with increasing age, no chest pain/typical symptoms are increasing in frequency. In the older age groups, STE is becoming gradually less frequent, while STD is more frequent. These findings partially explain the lower use of reperfusion therapy with advancing age.