

POSTER SESSION

1172 Stable Ischemic Syndrome IV:
Pathogenesis, Diagnosis, and Prognosis

Tuesday, March 19, 2002, Noon-2:00 p.m.

Georgia World Congress Center, Hall G

Presentation Hour: 1:00 p.m.-2:00 p.m.

1172-38

The *Scal* Atrial Natriuretic Peptide Gene Variants Are
Associated With the Extent of Coronary Artery Disease

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Background Atrial natriuretic peptide (ANP) is a circulating hormone mainly of cardiac origin whose biological actions include promotion of natriuresis and vasodilatation, inhibition of growth, and suppression of the renin-angiotensin and endothelin-1 (ET-1) systems. Transition T2238→C leading to the loss of the *Scal* restriction site in the *atrial natriuretic peptide (ANP)* precursor gene and potentially to the translation of ANP with two additional arginines, has been suggested to be associated with salt-sensitive hypertension. The aim of our study was to investigate whether there is an association between the *Scal* ANP gene polymorphism and extent of coronary artery disease among patients with significant coronary artery stenosis confirmed by means of angiography (at least one coronary artery with ≥50% lumen narrowing).

Methods The study was performed in 847 consecutive, Caucasian patients: 719 males and 128 females (mean age 47±11 years) with significant coronary artery stenosis confirmed by elective coronary angiography. Screening for the T2238→C substitution was performed by polymerase chain reaction of genomic DNA, followed by *Scal* digestion and agarose gel electrophoresis.

Results We observed increasing prevalence of homozygous A2A2 genotype from 23% in single-vessel disease patients to 28% and 31% in two- and three-vessel disease subjects, respectively. In a logistic regression model adjusting for other coronary risk factors the odds ratio for the association of the A2A2 genotype and multiple-vessel coronary atherosclerosis was 1.45 (95%CI 1.02-2.06, p<0.04). The *Scal* ANP genotypes distribution did not differ in terms of age, sex, body mass index, plasma lipids, hypertension, diabetes mellitus and family CAD history in studied group.

Conclusion Our results from this relatively large sample of Caucasian patients with significant coronary artery stenosis suggest that the A2A2 genotype of *Scal* ANP polymorphism may be associated with more severe coronary atherosclerosis.

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Interleukin-6 Concentration Predicts Coronary Artery
Disease Better Than High-Sensitivity C-Reactive Protein

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Background: Interleukin (IL)-1 beta and tumor necrosis factor alpha (TNF-alpha) are cytokines primarily produced during inflammatory responses. They induce IL-6 which in turn potentiates the biosynthesis of acute phase proteins (e.g. fibrinogen, C-reactive protein [CRP]) by hepatocytes. Elevated CRP increases the risk of coronary artery disease (CAD), and preliminary evidence suggests IL-6 may predict CAD independent of high-sensitivity (hs)CRP. The objective of this study was to determine the predictive value of these three related cytokines and hsCRP for CAD.

Methods: Levels of IL-1 beta, IL-6, TNF-alpha, and hsCRP were measured (automated DPC Immulite platform) in 434 patients. Cases (n=217) had angiographically proven CAD (>1 lesion of >70% stenosis) and controls (n=217) had no stenosis (all <10%). Cases were matched 1:1 to controls by age, gender, and time period of angiogram. Other risk factors were recorded at angiography in a cross-sectional study design that was analyzed by logistic regression.

Results: Average patient age was 62±11 years and 51% were male. In univariate analysis, elevated risk for CAD was associated with high hsCRP (hazard ratio [HR]=1.59, 95% confidence interval [CI]=1.02-2.5, p=0.04) and high IL-6 (HR=1.92, CI=1.2-3.0, p=0.004), but not IL-1 beta or TNF-alpha. IL-6 concentration was mildly correlated with hsCRP (r=0.29), but not with IL-1 or TNF. In models entering both, high IL-6 (HR=1.83, p=0.01) but not high hsCRP (HR=1.48, p=0.10) predicted CAD. Modeled as continuous variables, the result more strongly favored IL-6 (univariate: p=0.02, multivariate: p=0.02) compared to hsCRP (univariate: p=0.08, multivariate: p=0.46). In the final multivariate model, only high IL-6 remained a significant predictor of CAD (HR=1.91, CI=1.2-3.0, p=0.006).

Conclusion: IL-6 significantly predicted CAD, but also appeared to account for the predictive value of hsCRP. This supports a previous finding that IL-6 predicts CAD, but also suggests that IL-6 may be a more sensitive descriptor of risk than is hsCRP. Further studies are required to explore the relationship between hsCRP and IL-6 and determine the utility of measuring IL-6 on an automated assay in a clinical setting.

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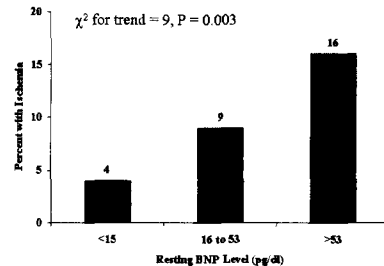
Brain Natriuretic Peptide Levels Are Associated With
Dobutamine Induced Myocardial Ischemia

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Background: Plasma Brain Natriuretic Peptide (BNP) levels have been associated with resting LV systolic dysfunction and exercise-induced ischemia. It is not known whether BNP correlates with pharmacologically induced ischemia.

Methods: We obtained BNP levels before and after dobutamine stress in 317 patients (age 68±11, 46% female) who had creatinine < 1.5 mg/dl and did not have valve disease. Echocardiogram readings were blinded to BNP levels. Ischemia was defined as new wall motion abnormalities with stress.

Results: Median BNP level at rest was 29 pg/ml (25th and 75th percentiles 12 and 70 pg/ml), while median BNP level just after stress was similar at 29 pg/ml (25th and 75th percentiles 10 and 72 pg/ml). Ischemia was noted in 31 patients (10%) while scar was present in 81 (26%). Both ischemia and scar were more common as the resting or exercise BNP levels increased; the Figure shows rates for tertiles of rest BNP. After adjusting



for age, gender, and left ventricular ejection fraction, BNP before and after stress was predictive of ischemia (for both measures one SD increase in the log of BNP adjusted odds ratio [OR] 2.0, 95% CI 1.3 to 3.0, P=0.002). Similarly, after adjusting for age, sex, and ejection fraction, BNP at rest predicted scar (for one SD increase in log of BNP adjusted OR 2.1, 95% CI 1.3 to 2.6, P=0.006). The change in BNP with stress was not correlated with the presence of ischemia. **Conclusion:** Resting BNP levels are predictive of dobutamine-induced ischemia. Larger studies are needed to confirm this finding.

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Does the Gender of the Cardiologist Have an Impact on
the Noninvasive Diagnosis of Coronary Artery Disease
in Women and Men?

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BACKGROUND: It is unknown if female physicians are better suited to take a patient history in female patients than their male colleagues. - **METHODS.** We investigated the impact of the gender of physicians and patients on accuracy of diagnosing coronary artery disease (CAD) based on patient history only in a prospective study conducted from September 2000 to January 2001 screening 1,082 patients undergoing coronary angiography for suspected CAD; known CAD was an exclusion criterion. The inclusion criteria were met by 144 consecutive patients (47 females); CAD was present in 20 females (43%) and 70 males (72%). All patients were interviewed by both an experienced male and female cardiologist who had to state before coronary angiography if CAD was present relying solely on the patient interview. All subjects answered a questionnaire covering their symptoms, risk factors, and own illness perception. Then, diagnostic accuracy for CAD of history-taking of male and female cardiologists, exercise testing, self-assessment of patients, and questionnaire were compared. - **RESULTS.** Diagnostic accuracy was not different between male (79%) and female (79%) cardiologists, comparable to results of exercise testing (74%) but better than self-assessment by patients (65%; p=0.01) or by a questionnaire (68%; p=0.01). Accuracy of female cardiologists was significantly better in male than in female patients (85% versus 66%, p=0.01), while the accuracy of male physicians was not influenced by patient gender (p=0.93) as female cardiologists tended to overestimate the presence of CAD in female patients (specificity 48% versus 74%, p=0.04), but had a better specificity in male patients than their male colleagues (79% versus 59%, p=0.51). - **CONCLUSIONS.** Female cardiologists do not assess female patients more accurately than their male colleagues. Diagnostic accuracy of male and female cardiologists is excellent. Both tend to better assess patients of the opposite gender - especially female cardiologists. The diagnostic accuracy of history taking is better than assessment by a questionnaire or self-assessment of patients. An impact of the gender of the physician on the accuracy to diagnose CAD by history taking may exist.

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Value of Noninvasive Testing for the Detection of
Coronary Artery Disease and Assessment of Cardiac
Risk in Renal Transplant Candidates

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Background: the purpose of the study was to evaluate the usefulness of dobutamine stress echocardiography (DSE) and of radionuclide perfusion imaging (dipyridamole single photon emission computed tomography, SPECT) for the detection of coronary artery disease (CAD) and assessment of cardiac risk in renal transplant candidates (RTC) using coronary angiography (CA) as gold standard.

Methods: eighty (80) high-risk RTC (55 + 8 years old, time on dialysis 58 + 30 months, 62 males, 56 Caucasians, 69 hypertensives, 26 smokers, 19 diabetics, 22 with serum total-cholesterol higher than 200 mg/100 ml, 78 with LV hypertrophy (Echo), 22 with angina, 10 with previous stroke and 7 with previous myocardial infarction (MI) were studied by DSE, SPECT and CA, in this order. CAD was defined as at least 70% stenosis in one or more epicardial arteries.