POSTER SESSION

1050 Prognostic Features in Stable Angina Pectoris

Sunday, March 30, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 3:00 p.m.-4:00 p.m.

1050-100 Prediction of Major Coronary Events in Stable Angina: The IONA Study

Alex D. McMahon, Henry J. Dargie, Ian Ford, Stewart Hillis, Kim M. Fox, University of Glasgow, Glasgow, United Kingdom, Royal Brompton Hospital, London, United Kingdom

Background: The Impact Of Nicorandil in Angina study ***(IONA)*** was a randomized controlled trial in 5126 patients with stable angina. Nicorandil, a potassium channel activator, reduced the incidence of the primary end point (CHD death, non fatal MI or unplanned hospitalization for angina) by 17%, HR 0.83 (0.72, 0.97), p = 0.014 and is the first anti anginal agent to be shown to improve clinical outcome in stable angina.
Methods: We interrogated the IONA database to identify factors related to outcome in order to inform clinical decision making about prognosis. Candidate factors were age, gender, Canadian Cardiovascular Society Functional status (CCSF), smoking, systolic blood pressure (SBP), heart rate, body mass index and histories of myocardial infarction, coronary artery bypass grafting (CABG), hypertension, diabetes, left ventricular hypertrophy on EKG and left ventricular systolic dysfunction. These were entered into a Cox proportional hazards model.
Results: All risk factors with the exception of gender, SBP, CABG, diabetes and hypertension were univariate predictors of the primary end point. The strongest multivariate predictors of outcome were, in descending order of importance, CCSF score IV, HR 5.49 (3.10, 10.00), p < 0.001; CCSF score III, HR 2.13 (1.67, 2.71), p < 0.001; CCSF II, HR 1.25 (1.04, 1.51), p = 0.021; previous MI, HR 1.54 (1.30, 1.83), p < 0.001; current smoking, HR 1.32 (1.10, 1.60), p = 0.004; age, HR 1.05 (1.00, 1.11), p = 0.035; treatment with nicorandil, HR 0.82 (0.71, 0.95), p = 0.009.
Conclusions: In the presence of medication which reduces major coronary events the profile of risk factors in patients with stable angina changes considerably. Traditionally strong factors including previous CABG, male gender, hypertension and diabetes were no longer even univariately predictive of outcome. By far the strongest predictor was clinical severity of angina (CCSF score) while smoking and previous MI also remain independently though less predictive than symptoms. These data could have an important influence on clinical assignment of risk and therefore on future clinical practice.

1050-101 Cumulative Infectious Burden (but Not Any Single Past Infection) Is Interrelated With Traditional Risk Factors to Cause Coronary Artery Disease

Einat Cotter-Metzkor, Ricardo Krakover, Gad Cotter, Miriam Ben-Yaakov, Tzilia Lazarovich, Zehava Chen-Levy, Ronit Zaidenstein, Shlomo Fytlovich, Ida Boldur, Ahuva Golik, Assaf-Harofeh Medical Center, Zerifin, Israel

The causative role of past infections in the pathogenesis of coronary artery disease (CAD) is uncertain.
Methods: We evaluated 179 consecutive patients, admitted electively for coronary angiography, for traditional atherosclerotic risk factors, serologic markers for prior infections with Chlamydia pneumonia, Helicobacter pylori, Cytomegalovirus (CMV), Epstein-Barr virus (EBV), Mycoplasma pneumonia, Hepatitis A virus (HAV), Hepatitis B virus (HBV), Hepatitis C virus (HCV), fibrinogen and ferritin. Patients underwent coronary angiography. Patients with CAD were compared to patients with angiograpicaly normal coronary arteries (NCA).
Results: Serologic markers of past infection with Chlamydia pneumonia (IgG, IgA) and serologic marker of past infection with Helicobacter pylori (IgG) were more prevalent in the CAD patients group compared to NCA patients. However, after adjustment for traditional risk factors none of the serologic markers for infectious agents remained an independent risk factor for CAD, while the cumulative effect of numerous past infections was found to progressively increase the risk for CAD. Having 3-4 positive serologic markers confers a risk for CAD of 7.5 (CI 1.4-39.1) compared having 0-2 serologic markers. Having more than 5 serologic markers was shown to confer an even greater risk for CAD (16.8; CI 2.8-99).
Conclusions: The cumulative infections burden rather than any specific infection is related to an increased risk of coronary artery disease, implying that increased inflammatory burden over long periods of time might contribute to the pathogenesis of ischemic heart disease.

1050-102 Relation of Testosterone With Inflammatory Cytokines in Men With Coronary Artery Disease

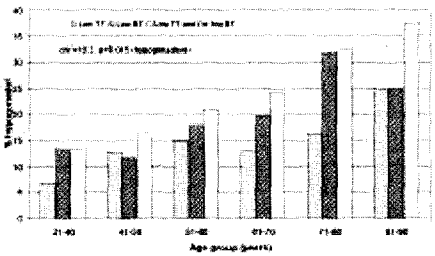
Peter J. Pugh, Chris J. Malkin, Paul D. Morris, Joanne Nettleship, Richard D. Jones, T. H. Jones, Kevin S. Channer, Royal Hallamshire Hospital, Sheffield, United Kingdom, University of Sheffield Medical School, Sheffield, United Kingdom

Background: Various cytokines have been identified as mediating the inflammatory process of atherosclerosis. Testosterone is known to possess anti-inflammatory properties and has been suggested as a therapy for some inflammatory conditions. Men with coronary artery disease have reduced levels of testosterone. Animal studies suggest that androgens may retard the progression of atherosclerosis. The mechanism of benefit is unknown but could involve immune modulation. In this study, we examined the relation between circulating levels of testosterone and inflammatory cytokines in men with established coronary artery disease.
Methods: Seventy five men with angiographically proven coronary artery disease (≥ 70% stenosis in ≥ 1 coronary artery) were studied. Blood samples were taken between 8 and 9.30am. Serum was removed by centrifugation and stored at -80° C until assayed. Serum levels of total and bio-available testosterone were measured, together with the pro-inflammatory cytokines tumour necrosis factor-α (TNF), interleukin- (Il-) 1β and Il-6, and the anti-inflammatory cytokine Il-10. Comparisons were made between eugonadal men and those with total testosterone level ≤ 7.5nmol/L or bio-available testosterone ≤ 2.5nmol/L, using the Mann Whitney U test.
Results: Eighteen subjects had low androgen levels. Compared with eugonadal subjects, levels of Il-1β were significantly elevated (516 ± 127fg/ml *v* 253 ± 42fg/ml, p=0.030). Levels of TNF, Il-6 and Il-10 did not differ significantly between groups (TNF 2.59 ± 0.75pg/ml *v* 2.35 ± 0.34pg/ml, p=0.785; Il-6 3.58 ± 0.61pg/ml *v* 6.66 ± 2.72pg/ml, p=0.190; Il-10 2.42 ± 1.04pg/ml *v* 1.68 ± 0.19pg/ml, p=0.613). There was a significant inverse relationship of both total and bio-available testosterone with Il-1β (r_S=-0.262, p=0.024; r_S=-0.283, p=0.015), but not with other cytokines.
Conclusion: In men with coronary artery disease, low testosterone levels are associated with pro-inflammatory cytokine activation. Whether this represents cause or effect is unclear but the data may support a rationale for androgen replacement therapy in men with coronary artery disease.

1050-103 Prevalence of Hypogonadism in Men With Coronary Artery Disease

Peter J. Pugh, Chris J. Malkin, Paul D. Morris, Sonia Asif, Richard D. Jones, T. H. Jones, Kevin S. Channer, Royal Hallamshire Hospital, Sheffield, United Kingdom, University of Sheffield Medical School, Sheffield, United Kingdom

Background: Low serum testosterone level has been associated with numerous risk factors for coronary artery disease (CAD) and men with CAD have lower androgen levels than controls. Testosterone administration has a beneficial effect on various coronary risk factors and has been shown to reduce symptoms and ischaemia in men with angina, with greatest effect in hypogonadal men. Men with CAD therefore represent a population prone to testosterone deficiency who may especially benefit from hormone treatment. The purpose of this study was to determine the size of the problem. **Methods:** Blood samples were taken between 0800 and 0930hours from 900 men with proven CAD (≥ 70% stenosis in ≥ 1 epicardial coronary artery). 69 subjects with evidence of inflammation or elevated C-reactive protein were excluded. Serum levels of total (TT) and bio-available testosterone (BT) were measured in the remaining 831. Hypogonadism was defined as TT ≤ 7.5nmol/L and / or BT ≤ 2.5nmol/L. **Results:** TT was low in 117 subjects (14.1%). BT was low in 165 (19.9%). 194 had low TT and / or BT. The prevalence of hypogonadism therefore was 23.4%. It was more frequent in the obese (BMI>30) (33.3% *v* 19.1%, χ^2=15.8, p<0.0001) and less frequent in smokers (13.8% *v* 24.7%, χ^2=5.5, p=0.02). There was a significant relationship of hypogonadism with age (figure).



Conclusion: Using strict criteria, nearly a quarter of men with significant CAD are hypogonadal. Further trials are required to determine the benefits and safety of hormone replacement in these patients.

1050-104 Which Features of the Metabolic Syndrome Predict the Presence of Angiographic Coronary Artery Disease?

Sandra P. Reyna, Joseph B. Muhlestein, John F. Carlquist, Dale G. Renlund, Donald L. Lappé, Tami L. Bair, Robert R. Pearson, Benjamin D. Horne, Chloe A. Allen Maycock, Stephanie V. Moore, Jeffrey L. Anderson, LDS Hospital, Salt Lake City, UT, University of Utah, Salt Lake City, UT

Background: The metabolic syndrome (MS), a cluster of vascular risk factors, is growing in prevalence. The Adult Treatment Panel III Guidelines provide a uniform clinical definition of MS but offer no information about the individual and combined predictive value (PV) of its components for CAD.
Methods: We tested the PV of the MS and its components for CAD in a consecutive series of consenting, prospectively entered subjects undergoing coronary angiography for suspected cardiac disease. Acute MI at presentation was excluded. Components of the MS were assessed at the time of study entry (angiography) and included: 1) fasting glucose (FG) ≥110 mg/dL, 2) triglyceride (TG) ≥150 mg/dL, 3) high density lipoprotein cholesterol (HDL) <40 mg/dL in men or <50 mg/dL in women, and 4) systolic blood pressure (SBP) ≥130 and/or diastolic (D) BP ≥85 mmHg. MS was defined as ≥3 features. Waist circumference was not captured in the database, so body mass index (BMI; >27 kg/m2) was explored as a surrogate fifth measure. Angiographic assessment was

blinded to presence of MS. Associations were assessed by logistic regression.
Results: The study included 3,528 subjects; 67% were male; age averaged 63±12 years; 57.7% had significant (≥70% stenosis), 11.1% mild/moderate, and 31.0% no CAD (<10% stenosis). MS was present in 48% of patients; specifically, 39% had high FG; 52% high TG; 71% low HDL; 76% high S/DBP; and 58% high BMI. MS predicted increased risk of significant CAD (odds ratio [OR] of significant vs. no CAD= 1.40, 95% CI 1.21-1.62, p<0.001). High FG (OR=1.91, CI 1.63-2.23, p<0.001) and low HDL (OR=1.38, CI 1.18-1.62, p<0.001), but not TG, BP, or BMI, were individually predictive of CAD. In multivariable modeling, CAD was predicted by age, gender, high FG (OR=1.75, CI 1.48-2.06), and low HDL (OR=1.45, CI 1.22-1.72)(all p<0.001). Similar results (with somewhat greater OR for FG, HDL) were found when restricting analysis to younger subjects (males<55 years, females <65 years).
Conclusion: In a large, prospective observational study, the MS was predictive of CAD, and PV was carried by high FG and low HDL. FG and HDL deserve particular attention in risk factor assessment and prevention in subjects at risk for CAD.

1050-105 **The Medicine, Angioplasty, or Surgery Study (MASS II Registry): A Comparison of Diabetic and Nondiabetic Patient's Outcome in Medical Therapy, Coronary Angioplasty, and Bypass Surgery During the First Year Follow-Up**

Paulo R. Soares, Whady Hueb, Bernard J. Gersh, Desiderio Favarato, Luiz M. Cesar, Protasio L. Luz, Sergio A. Oliveira, Jose F. Ramires, Heart Institute Medical School University of Sao Paulo, Sao Paulo, Brazil, Mayo Clinic, Rochester, MN

Diabetes is known to have a worse prognosis among patients with coronary artery disease. In MASS II Registry we compared medical treatment (MT), surgery (CABG) and angioplasty (PCI) in patients with multivessel coronary disease. The present study compared the one-year outcome of the patients divided in two subgroups: diabetic (D) and non-diabetic (ND) patients in each of the therapeutic options. 1080 patients were treated with CABG (451), PCI (305) and MT (324). The primary end point was considering as the composite events (CE) of cardiac-related deaths, myocardial infarction (MI) and new revascularization (NR) in the first year of follow-up. The results are presented in the table 1.
Conclusion: In MASS II Registry during the first year follow-up study there were no statistical differences in the frequency of composite events between diabetic and non-diabetic patients in each of the three therapeutic groups. On the other hand, when outcomes were compared among patients undergoing PCI, CABG or MT, there was a statistically significant benefit for CABG on the therapy in diabetic patients..

Table 1

Group		N	Death %	MI %	NR %	CE %
PCI	D	75	5.3	2.7	8.0	16.0
	ND	230	2.6	6.5	10.9	20.0
	Total	305	3.3	5.6	10.2	19.0
CABG	D	154	3.9	0.6	0.0	4.5*
	ND	297	2.7	1.0	0.3	4.0
	Total	451	3.1	0.9	0.2	4.2
MT	D	115	5.2	1.7	6.1	13.0
	ND	209	1.4	1.9	5.7	9.1
	Total	324	2.8	1.9	5.9	10.5

*CABG vs MT vs PCI, p=0.0028

POSTER SESSION

1068A-MP Moderated Poster Session...Hyperglycemia and Diabetes in Acute Coronary Syndromes II

Sunday, March 30, 2003, 3:00 p.m.-4:00 p.m.
McCormick Place, Hall A

3:00 p.m.

1068A-MP-203 **Acute Hyperglycemia Abolishes Ischemic Preconditioning: A Possible Mechanism for Adverse Outcome of Patients With Acute Myocardial Infarction and Acute Hyperglycemia**

Masaharu Ishihara, Ichiro Inoue, Takuji Kawagoe, Yuji Shimatani, Satoshi Kurisu, Kenji Nishioka, Takashi Umemura, Shuji Nakamura, Masashi Yoshida, Hiroshima City Hospital, Hiroshima, Japan

Background. Acute hyperglycemia has been shown to be an independent predictor of adverse outcome after acute myocardial infarction (AMI). Prodromal angina occurring shortly before the onset of AMI has cardioprotective effect by the mechanism of ischemic preconditioning. Ischemic preconditioning is promoted by opening of mitochondrial K_{ATP} channel. K_{ATP} channel is also located in pancreas ß cells. K_{ATP} channel in pancreas ß cells is closed by glucose and regulates insulin release.
Purpose. This study was undertaken to assess the interaction between acute hyperglycemia and ischemic preconditioning in patients with AMI.**Methods.** We studied 549 patients with a first anterior wall AMI who underwent coronary angiography within 12 hours after the onset of AMI. Acute hyperglycemia was considered to be present if patients had plasma glucose>11.1 mmol/L (200 mg/dl) on hospital admission. Prodromal angina was defined as angina episode(s) occurring within 24 hours before the onset of AMI. Serial measurements of left ventricular ejection fraction (LVEF) were obtained in 434 patients (79%) before reperfusion therapy and before discharge.
Results. In 377 patients without acute hyperglycemia, prodromal angina was associated with significantly larger improvement of LVEF (10.1±13.6% vs 5.9±13.3%, p=0.015) and lower 30-day mortality (0% (95% CI 0-3.0) vs 6.7% (4.2-10.5), p=0.001). However, in the presence of acute hyperglycemia (n=172), there was no significant difference in the change in LVEF (5.6±9.9% vs 5.4±13.3%, p=0.94) and 30-day mortality (8.1% (95% CI 3.5-17.5) vs 8.2% (4.4-14.8), p=0.98) between patients with prodromal angina and patients without. Multivariate analysis showed that prodromal angina was an independent predictor of predischarge LVEF in patients without acute hyperglycemia (p=0.019) and not in patients with acute hyperglycemia (p=0.96).
Conclusion. Acute hyperglycemia abolished ischemic preconditioning effect of prodromal angina. Our findings may provide a potential explanation for the adverse outcome of patients with AMI and acute hyperglycemia.

3:15 p.m.

1068A-MP-204 **Impact of Diabetes on Clinical, Echocardiographic, and Electrocardiographic Characteristics of Myocardial Infarction**

Costantina Manes Marc A. Pfeffer, John D. Rutherford, Sally Greaves, Jean-Lucien Rouleau, Scott D. Solomon, Brigham & Women's Hospital, Boston, MA

Background: Diabetes influences the clinical presentation and course of acute myocardial infarction (AMI). We investigated the impact of diabetes on clinical, echocardiographic and electrocardiographic characteristics of 272 pts with Q-wave anterior AMI enrolled in the Healing and Early Afterload Reducing Therapy (HEART) Trial . **Methods:** Patients underwent ECG testing within 24h (baseline) and at predischarge (median day 7) after AMI, and echocardiography at baseline and at 14 days. From both ECGs we calculated the Selvester QRS score, the sum of ST segment elevation and the number of negative T waves in leads I, avL, V1-V6. Left ventricular ejection fraction (LVEF) and infarct segment length were assessed by echocardiography. **Results:** Diabetics (n=56, 20.6%) were similar to non-diabetics (n=216, 79.4%) with respect to initial and 14-day infarct size as evidenced by maximal CK, ejection fraction and infarct segment length (Table). However, diabetics demonstrated a higher Killip class, greater QRS score at baseline and predischarge and fewer negative T waves on predischarge ECG, even after excluding patients with prior myocardial infarction (n=43, 16%). **Conclusion:** Diabetes may modify the clinical and electrocardiographic response to myocardial infarction independently of infarct size or ventricular function.

	Diabetics (n=56)	Non-Diabetics (n=216)	P value
Age, yr	60.8 ± 10.9	59.6 ± 13.1	0.5
Killip Class >1, %	34%	19%	0.01
Maximal CK, mU/mL	2593 ± 1887	2484 ± 2012	0.71
Baseline LVEF, %	51.6 ± 10.1	52.2 ± 9.4	0.67
Baseline Infarct Segment Length, %	27.2 ± 9.8	25.8 ± 11.0	0.36
Day 14 LVEF, %	54.5 ± 10.3	56.5 ± 8.9	0.14
Day 14 Infarct Segment Length, %	20.6 ± 12.2	17.9 ± 13.0	0.16
Baseline Sum ST Elevation, mm	11.5 ± 9.2	10.5 ± 7.9	0.44
Baseline Number Negative T waves	0.7 ± 1.4	0.8 ± 3.2	0.85
Baseline QRS Score	4.3 ± 2.9	3.4 ± 2.6	0.03
Predischarge Sum ST Elevation, mm	4.5 ± 3.0	4.6 ± 3.3	0.9
Predischarge Number Negative T waves	1.4 ± 1.7	2.6 ± 2.2	0.001
Predischarge QRS Score	5.2 ± 3.1	4.0 ± 2.5	0.01

3:30 p.m.

1068A-MP-205 **Impact of Known and Newly Diagnosed Diabetes Mellitus After a Myocardial Infarction**

David Aguilar, Scott D. Solomon, Lars Kober, Jean-Lucien Rouleau, Hicham Skali, John J. McMurray, Gary S. Francis, Marc Henis, Rafael Diaz, Yuri N. Belenkov, Sergei Varshavsky, Jeffrey D. Leimberger, Robert M. Califf, Marc A. Pfeffer, Brigham & Women's Hospital, Boston, MA

Background: Diabetes mellitus (DM) is associated with adverse outcomes in patients (pts) presenting with an acute myocardial infarction (AMI), but little is known of the risk of newly diagnosed DM.
Methods: The VALsartan In Acute myocardial iNfarcTion (VALIANT) trial identified 14,808 pts with an AMI complicated by either clinical or radiologic signs of heart failure and/or evidence of left ventricular (LV) systolic dysfunction. Assessment of diabetic sta-