POSTER SESSION

1002 Novel Biomarkers in Acute Coronary Syndromes

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1002-203 The Relationship between the Framingham Cardiovascular Risk Score and C-reactive Protein Levels Among Women of Various Race/Ethnic Groups

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Background: While data exists on the relationship between the Framingham Cardiovascular Risk Score (FCRS) and C-reactive protein levels (CRP) among Whites, little data are available in different racial/ethnic groups.
Methods and Results: CRP levels were compared to the calculated 10-year FCRS and its components among apparently healthy White (n=24,465), Hispanic (n=254), and Black (n=475) women enrolled in the Women's Health Study. Compared to White and Hispanic women, Black women had the highest prevalence of diabetes (7.4%), body mass index (28.6 kg/m2), were more likely to be smokers (16.2%), and to have a history of hypertension (44.6%), and had the lowest triglyceride levels (122mg/dL ± 75 mg/dL). Median CRP levels were higher among Black women (2.96 mg/L, interquartile range [IQR] 1.19 to 5.86) than in Hispanic (2.06 mg/L , IQR 0.88 to 4.88) and White (2.01 mg/L, IQR 0.81 to 4.36) women. The relationship between CRP and 10-year Framingham Risk Categories were significant and similar in magnitude among all racial/ethnic groups, among women not taking any hormone replacement therapy (HRT) [White r=0.34; Hispanic r=0.25; Black r=0.30; all p<0.001]. Among White women, statistically significant associations were observed between CRP levels and age (r=0.16,), total cholesterol (r=0.17), HDL cholesterol (HDL-C) (r=-0.33), and history of hypertension (r=0.25)[all p<0.01]. However, among Hispanic and Black women, CRP was only significantly associated with HDL-C ($r_{Hispanic}$=-0.25, r_{Black}= -0.26; p<0.01) and history of hypertension ($r_{Hispanic}$=0.35, r_{Black}=0.21; p<0.01). Among women taking HRT, the relationship between CRP and Framingham Cardiovascular risk categories was similar in magnitude to those not taking HRT.
Conclusions: Overall, CRP levels significantly correlated with the calculated 10-year FCRS among White, Hispanic, and Black women. HDL-C and history of hypertension were the components of the FCRS that had the strongest correlations with CRP in all three ethnic groups.

1002-204 Identification of Polymorphisms in the Microsomal Triglyceride Transfer Protein and Glutamate-Cysteine Ligase Catalytic Subunit Genes as Susceptibility Loci for Myocardial Infarction

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Background: We previously showed that polymorphisms in the connexin 37, plasminogen-activator inhibitor 1, and stromelysin-1 genes are significantly associated with myocardial infarction (MI) (N Engl J Med 2002). The aim of the present study was to further identify genes that confer susceptibility to MI.
Methods: The study population comprised a total of 6120 unrelated Japanese individuals (3845 men and 2275 women), including 3364 patients with MI (2118 men and 1246 women) and 2756 controls (1727 men and 1029 women). We selected 43 polymorphisms of 40 candidate genes that were not examined in our population.
Results: The two-step analysis was performed for men and women independently. In an initial screening of the relation between 43 polymorphisms and MI in 860 subjects (430 men and 430 women), multivariate logistic regression analysis with adjustment for age, body mass index, and the prevalence of smoking, hypertension, diabetes mellitus, hypercholesterolemia and hyperuricemia revealed that 6 and 8 single nucleotide polymorphisms (SNPs) were related (P <0.05) to MI in men and women, respectively. A large-scale association study with these SNPs was then performed in the remaining 5260 subjects (2793 men and 1109 women). Similar multivariate logistic regression analysis revealed that the -493G/T SNP of the microsomal triglyceride transfer protein (MTTP) in men (odds ratio, 0.75; P = 0.002), and the -129C/T SNP of the glutamate-cysteine ligase catalytic subunit (GCLC) in women (odds ratio, 1.58; P = 0.009) were significantly associated with MI.**Conclusions:** We identified the MTP gene in men and the GCLC gene in women as susceptibility loci for MI, respectively. Genotyping of these polymorphisms may prove informative for prediction of the genetic risk for MI, and thereby contribute to the primary prevention of this condition.

1002-205 A Polymorphism in the Metabotropic Glutamate Receptor 8 Gene is Strongly Associated with Myocardial Infarction in Two Independent Studies

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Background: Myocardial infarction (MI) is a multi-factorial disease associated with both environmental and genetic factors. Although major clinical risk factors are associated with most MI events, some patients are at higher risk than indicated by traditional risk analysis. Identification of genetic polymorphisms associated with MI could lead to a more accurate prediction of risk and provide a mechanistic basis for individualized therapy.
Methods: To identify genetic markers associated with MI, we interrogated approximately one fifth of the known human genes by determining the allele frequencies of about 8,000 single nucleotide polymorphisms (SNPs) expected to alter the amount, activity, or stability of encoded proteins. Allele frequencies were determined in pooled DNA samples from 1494 males and females collected by the University of California San Francisco Genomic Resource (835 MI cases and 659 controls). The 574 SNPs associated with MI in that study (unadjusted p<0.05), were tested in pooled DNA from a second study of 1051 subjects collected at the Cleveland Clinic Foundation Heart Center (445 MI cases and 606 controls).
Results: Of the 574 SNPs associated with MI in the first study, 36 SNPs in 35 genes were also associated with MI in the second sample set (unadjusted p<0.05, same risk allele). The most significant association, verified by individually genotyping the samples in the second study, was with a SNP in the gene coding for metabotropic glutamate receptor 8 (GRM8, p=0.00001, OR=1.62). This unadjusted p value remained significant even after conservative multiple testing correction.
Conclusions: The identification of a GRM8 variant associated with MI by testing putative functional SNPs in two large sample sets is a step in creating an improved genetic risk assessment for MI. GRM8 encodes a group III metabotropic receptor for which in-vitro studies have suggested a potential role in regulating glucose homeostasis. The strong and plausible association of this GRM8 variant with MI would not have been discovered in a candidate gene study; this underlines the importance of extending genetic association studies to broad gene scans.

1002-206 Platelet-activating Factor-acetylhydrolase G994t (exon 9) And Its Receptor V379 Allele (exon 11) Gene Polymorphisms In Relation To The Onset Of Premature Myocardial Infarction In Taiwan

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Background: Oxidation of low density lipoproteins is an initial step of atherogenesis that generates pro-inflammatory phospholipids, including platelet-activating factor (PAF) and its analogs. PAF is degraded by PAF-acetylhydrolase (PAF-AH), a circulating enzyme having both pro- and anti-inflammatory activities. PAF-AH activity has been postulated to be a risk factor for premature myocardial infarction (MI); however, whether PAF-AH has a causal role or is simply a marker of risk for MI is unclear.
Methods: All polymorphisms located in putatively functional regions were investigated in a cohort of premature MI patients onset less than 46 years of age (n = 150) and a sex-age-matched control group (n = 150). Their PAF-AH activities were evaluated by ELISA assay.
Results: The frequency of the G994T (exon 9) mutation on PAF-AH gene was similar among premature MI and the control group (p>0.1). The V379 allele mutation (exon 11) on PAF-receptor gene was less frequent in premature MI patients than in controls (p=0.02) and was associated with a lower risk of future cardiovascular events, suggesting that this allele might be protective against the development of premature MI or CAD. The V379 allele was also associated with a weak increase of plasma PAF-AH activity. The modification of the enzyme function towards a more anti-atherogenic form by this A379V genetic mutation might help explain this paradoxical gene-phenotype association. Multiple logistic regression analysis showed that the V379 allele polymorphism was an independent risk factor (Odds Ratio (OR) 1.7, 95% CI 1.2 to 7.3, p=0.04) as were as smoking (OR 3.6, 95% CI 1.4 to 5.8, p=0.001), diabetes mellitus (OR 3.5, 95% CI 1.5 to 6.7, p=0.003) and hypertension (OR 1.9, 95% CI 1.7 to 7.7, p=0.001) for the onset of premature MI.
Conclusion: We conclude that a functional and significant association between the V379 allele polymorphism on exon 9 of PAF-receptor gene and premature MI exists in this Taiwanese population. This allele may be protective partially via modifying the PAF-HA enzyme towards a more anti-atherogenic function.

1002-207 The Polymorphisms in the Interleukin-1 Gene Cluster as Protective Factors Against Myocardial Infarction in Patients with Coronary Artery Disease

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Objectives: Acute myocardial infarction (MI) is caused by ruptured of unstable plaque, where macrophages releases several cytokines (including interleukin-1, IL-1) and matrix metalloproteinase. The relationship between polymorphisms of IL-1 gene cluster and the risk of MI remains unsettled. We want to elucidate the effect of these polymorphisms on the risk of MI in coronary artery disease (CAD) patients.
Methods: We recruited 410 subjects with angiographically-proven CAD, and carried out a matched case-control study which consisted of 205 cases with a history of MI and 205 matched controls without MI. Gensini score was applied to evaluate the severity of coronary atherosclerosis. Genotyping of IL-1ß +3954C>T,-31C>T, -511C>T and IL-1 Receptor Antagonist intron 2 VNTR (IL1RN) were performed. Plasma level of CRP and IL-1ß were assayed.
Results: After adjustment for age, sex, diabetes, hypertension, hypercholesterolemia, hypertriglyceridemia and smoking habit, the genotype IL-1ß -31 C>C is protective against MI (OR=0.54, 95%CI:0.32,0.86, p=0.02), independent of the severity of coronary atherosclerosis. This result is supported by haplotype analysis (omnibus likelihood ratio, p=0.01), Estimated haplotypes showed that the haplotype frequency of IL-1ß +3954C/-31C/-511C is 2 times higher in the controls than in the cases (12.7% vs 6.4%, respectively, p=0.006). In addition, IL-1ß -31 allele C had significant effect on the plasma CRP level (carrier vs non-carrier: 8.1± 17.2 vs 15.0± 28.1 mg/L respectively, p=0.004). Likewise, IL1RN*2 repeat allele is also protective

against MI (Allele *2 repeat carrier vs non carrier: OR:0.38, 95% CI: 0.18,0.79, p=0.008) after adjustment for the afore-mentioned clinical factors.
Conclusion: This study demonstrates that the polymorphism of IL-1 gene cluster is associated with the risk of MI. IL-1ß-31 C/C genotype and IL1RN*2 repeat allele are protective factors against MI.

1002-208 NT-proBNP In Symptom Limited Exercise Myocardial Perfusion Scintigraphy: Sustained Elevation After Exercise And Independent Association With Myocardial Ischemia Extent

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Background. In patients with overt heart failure, levels of N-terminal pro-BNP (NT-proBNP) are associated with ventricular dysfunction. Increased levels are also found in acute coronary syndromes, suggesting that other mechanisms such as myocardial ischemia may also cause elevations of NT-proBNP.
Methods. 38 patients were included undergoing symptom limited exercise myocardial perfusion scintigraphy according to a two-day stress/rest protocol using 99m Technetium Tetrofosmin and ECG gated single photon emission tomography. Stress and rest perfusion images were scored using a 5-point semi-quantitative score for each of 17 myocardial segments, classifying each segment as normal (0), equivocal abnormal (1), mildly abnormal (2), moderately abnormal (3) or severely abnormal (4). The summed difference score (SDS) was calculated as the difference between summed stress score and summed rest score. A SDS of three or greater was arbitrarily considered to indicate clinically relevant ischemia. Left ventricular ejection fraction (LVEF) was calculated using a completely automated algorithm. Blood samples were drawn at baseline, at maximum exercise (at least 85% of the age predicted heartrate), and at 1, 2, 3, 4, and 6 hours after maximum exercise, for assessment of levels of NT-proBNP and creatinine (baseline only). For analysis, NT-proBNP levels were logtransformed to a normal distribution.
Results. 15 patients were classified as having myocardial ischemia. Baseline NT-proBNP levels were 75 pg/mL (33-236) (median, IQ range), and were increased at maximum exercise (137% of baseline (99-176)) (p<0.001), with a second peak 4 hours later (137% (118-173)) (p<0.001). In a multivariate analysis, NT-proBNP levels were independently associated with creatinine clearance (Cockroft and Gault), LVEF, and SDS, as assessed from the samples at baseline (adjusted R^2 of model = 0.537), maximum exercise (adj.R^2 = 0.561), and 4 hours later (adj.R^2 =,0.476).
Conclusion. Baseline levels of NT-proBNP, as well as the sustained elevations after symptom limited exercise testing are independently associated with extent of inducible myocardial ischemia, LVEF and creatinine clearance.

POSTER SESSION

1003 Treatment Approaches in Unstable Coronary Syndrome

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1003-195 Comparison Of Infarct Size In 1200 NSTE-ACS Patients With An Elevated Troponin T Randomized To An Early Invasive Or A Selective Invasive Treatment Strategy (subanalyses Of The ICTUS Trial)

Fons Windhausen, Jan Tijssen, Jan Hein Cornel, F. W. Verheugt, Peter H. Dunselman, Pim de Feyter, H. R. Michels, Robbert J. de Winter, for the ICTUS investigators, Academic Medical Center, Amsterdam, The Netherlands

Background: The ICTUS trial compared an early invasive (EI) management aiming at coronary angiography (CAG) and revascularization within 24-48 hrs, with a "selective invasive" (SI) management, in 1200 nSTE-ACS patients with an abnormal cTnT. In the SI group, CAG and revascularization was performed in the event of refractory angina or ischemia on the pre-discharge exercise test . The primary endpoint, the composite of death, myocardial infarction (MI) and rehospitalization for angina at one year, was reached in 21.7% in the EI group versus 20.4% in the SI group (p=0.59). However, there were significantly more MIs in the EI group compared to the SI group(14.6 % versus 9.4%, RR 1.55; p=0.006).
Methods: We compared infarct size in spontaneous-, and PCI related MIs between the two treatment strategies. Infarct size is expressed as peak CK-MB ratios (peak CK-MB level/upper limit of normal [ULN]). Patients with a MI after an episode of chest pain or after PCI were stratified into categories by peak CK-MB ratios of 1-3, 3-6, and >6 × ULN.
Results: The median CK-MB ratio for all MIs in the early invasive (EI) group was 2,3 (IQR 1.3-5.3) versus 2.3 (IQR 1.4-6.6) in the selective invasive (SI) group (p=0.9). In the EI group, the median CK-MB ratio for PCI related MI was 2.25 (IQR 1.5-4.9) and 2.46 (IQR 1.1-9.4) for spontaneous MI (p=0.94). In the selective invasive group, the median CK-MB ratio for PCI related MI was 2.26 (IQR 1.3-6.3) and 2.5 (IQR (1.4-6.8) for spontaneous MI (p=0.74). The incidence of MI (spontaneous and PCI related) with peak CK-MB ratios between 1 and 3 was 7.3% in the EI-group versus 4.9% in the SI group (p=0.08). In the EI group 3.0% had a CK-MB ratio between 3 and 6 versus 1.3% in the SI group (p=0.05). In 3.5% of patients in the EI group versus 2.7% in the SI group a CK-MB ratio > 6 was observed (p=0.424).
Conclusion: Median infarct size and infarct size categories were similar in both treatment groups. Moreover, there was no difference in infarct size between spontaneous and PCI related MIs. The higher incidence of MI in both treatment groups compared to previous strategy trials is explained by the incidence of small MIs (CK-MB ratio 1-3). The prognostic value of these small MIs requires long-term follow-up.

1003-196 Despite the Temporal Increases, Coronary Angiography and Revascularization Remain Paradoxically Directed Towards Low Risk Non-ST Elevation Acute Coronary Syndrome Patients

Andrew T. Yan, Raymond T. Yan, Mary Tan, Anthony Y. Fung, Chi-Ming Chow, Warren J. Cantor, Eric A. Cohen, David H. Fitchett, Anatoly Langer, Shaun G. Goodman, for the Canadian ACS Registry Investigators, St. Michael's Hospital, Toronto, ON, Canada, Canadian Heart Research Centre, Toronto, ON, Canada

Background: Randomized clinical trials support early invasive risk stratification for high risk non-ST elevation (NSTE) acute coronary syndromes (ACS).
Objective: To examine the temporal use of invasive strategy in the "real world" management of NSTE ACS.
Methods: The Canadian ACS Registries were prospective multicentre observational studies of less selected ACS patients. ACS I enrolled 2778 NSTE ACS patients from Sept 99 to June 01; ACS II enrolled 2063 patients from Oct 02 to Jan 04. We evaluated the use of in-hospital coronary angiography and revascularization in ACS I and II patients stratified into low, intermediate and high risk groups, according to tertiles of their GRACE risk scores (validated predictor of in-hospital mortality).
Results: Overall, the calculated GRACE scores (median 114 vs 117) and in-hospital death/MI rates (5.6% vs 5.9%) were similar in both ACS I and II. However, ACS II patients more frequently underwent coronary angiography (40.5% vs 60.9%, P<0.001), PCI (14.3% vs 26.8%, P<0.001), and CABG (4.0% vs 9.5%, P<0.001).

	Registry	Low-risk	Intermediate-risk	High-risk	P value
Coronary angio (%)	ACS I	47.6	41.4	32.5	<0.001
	ACS II	69.7	63.0	49.9	<0.001
Time to cath (days) *	ACS I	5 (3, 7)	5 (3, 8)	5 (3, 8)	NS
	ACS II	3 (2, 5)	3 (2,6)	4 (2, 6)	0.01
PCI (%)	ACS I	16.7	14.5	11.8	0.01
	ACS II	33.1	28.5	18.8	<0.001
CABG (%)	ACS I	3.8	4.1	4.1	NS
	ACS II	8.5	10.2	9.8	NS
In-hospital Death/MI (%)	ACS I	2.8	4.1	9.0	<0.001
	ACS II	3.1	4.4	9.6	<0.001

* median (25^{th}, 75^{th} percentiles)

Conclusions: The use of in-hospital coronary angiography and revascularization has increased substantially in the management of NSTE ACS. However, this temporal increase was not specifically targeted towards high risk patients, who remained least likely to undergo early invasive risk stratification, with an associated worse outcome. Future study is needed to elucidate the reasons for less frequent intervention in these patients.

1003-197 Use of the Early Invasive Strategy in Older Patients With Acute Coronary Syndromes: Insights from the PREMIER Registry

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Background: Although guidelines recommend an early invasive strategy (EIS) for patients with NSTEMI, it is not known if this approach is utilized equally across the age spectrum.
Methods: We studied consecutive NSTEMI patients in 19 US centers in the PREMIER registry between 1/2003-6/2004. The use of EIS (defined as pre-discharge coronary angiography without antecedent stress testing) was assessed in strata according to age and TIMI NSTEMI risk scores. In multivariable models, we assessed the relationship between age group and EIS, adjusting for TIMI scores and in-hospital events (rest angina, heart failure, VT/VF or shock) and accounting for patient clustering by center.
Results: Among all patients, 74.1% were treated with EIS. This strategy was implemented more commonly in younger patients in all TIMI categories (Table). After adjustment, EIS was used less frequently in patients age 65-74 (OR=0.61, 95% CI 0.44-0.84) and age ≥75 (OR 0.21, 95% CI 0.13-0.32) compared to patients ≤64 years old (1.00 referent). TIMI score was not associated with EIS in all patients (p=0.3) or in age strata (TIMI score*age interaction p-value=0.8). Analyses defining EIS as angiography within 48 hours of admission yielded comparable results.
Conclusions: Older patients with NSTEMI are less likely to be treated with EIS, even after accounting for site-specific differences and clinical risk features. The implications of this practice pattern on clinical outcomes warrant further investigation.

Percentage of Patients Undergoing Early Invasive Strategy

% receiving EIS	Age Groups			
	All Ages (n=2,210)	<=64 years(n=1,142)	65-74 years(n=505)	>=75 years(n=563)
TIMI Risk Scores				
All Risk Scores	74.1%	79.0%	78.0%	60.8%
1-2	74.1%	77.2%	72.7%	51.9%
3	72.7%	76.5%	80.8%	57.6%
4	74.8%	85.2%	78.2%	67.8%
5	76.2%	86.8%	78.4%	67.8%
6-7	73.0%	84.6%	76.8%	66.7%

1003-198 Clinical Correlates, Management and Outcome in Myocardial Infarction Complicated by Cardiogenic Shock at Hospital Admission - A Report from the SHOCK Trial and Registry

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Background Up to 25% of cardiogenic shock (CS) cases are diagnosed at hospital admission. Characteristics, outcome, and effect of early revascularization (ERV) may differ between CS on admission (CSA) and delayed CS (CSD) pts, but data are conflicting.
Methods Characteristics and in-hospital mortality in both SHOCK trial and registry pts with predominantly left ventricular failure were compared for CSA *vs* CSD. Trial pts were randomized to a strategy of ERV (≤18 hrs post CS) *vs* initial medical stabilization (IMS) and followed for 1 year. Pts with suspected CS but not eligible for the trial were enrolled in a registry.
Results Overall (n=1053), 20% had CSA. The median time from MI to CS was shorter in CSA (1.5, interquartile range 0.5, 4.1, *vs* 8.1, interquartile range 2.8, 21.0 hrs; p<0.001) *vs* CSD pts. Lowest systolic blood pressure (64±19 *vs* 69±15mmHg; p=0.008) and hemodynamic variables on support measures, *ie,* systolic blood pressure (84±27 *vs* 89±21mmHg; p=0.017), cardiac output (3.3±1.0 *vs* 3.7±1.5L/min; p=0.001), cardiac power output (0.5±0.2 *vs* 0.6±0.3W; p=0.002), and stroke volume (33±12 *vs* 40±18ml; p<0.001) were lower in CSA *vs* CSD pts. In contrast, left ventricular ejection fraction, cardiac index, cardiac power index, systemic vascular resistance, pulmonary capillary wedge pressure, or baseline demographic characteristics did not differ. In-hospital mortality was higher in CSA (75 *vs* 56%; p<0.001) *vs* CSD pts with lower mortality in ERV *vs* IMS in CSA (60 *vs.* 82%; p=0.001) and CSD pts (46 *vs* 62%; p<0.001), *ie,* without interaction between CS onset and treatment assignment. Estimated 1-week mortality was higher in CSA (59 *vs.* 42%) *vs* CSD pts. In trial pts (n=263) similar hemodynamic differences between CSA and CSD pts were observed as were mortality differences (73 vs. 57% at 1 year; p=0.081) despite similar rates of coronary angiography and revascularization in both ERV and IMS assigned CSA and CSD pts.
Conclusion CSA pts have a more severe hemodynamic derangement and higher mortality. They benefit equally from ERV for which their precipitous presentation demands rapid stabilization. This suggests the need for direct transport to hospitals with interventional facilities.

1003-199 Do Patients With Acute Coronary Syndromes Admitted to Non-PCI Hospitals Have Worse Outcome? Results From the PL-ACS Registry

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Background: Guidelines recommend early invasive strategy in unstable angina (UA) / non ST-elevation myocardial infarction (NSTEMI) and primary angioplasty in ST-elevation myocardial infarction (STEMI). We set up a prospective, population-based registry of acute coronary syndromes (ACS) in Poland to assess treatment strategy and determine the outcome in unselected pts.
Methods: Between October 2003 and June 2004 a total of 81 hospitals in Silesia (population of 4,8 million) prospectively collected data of each pt admitted with ACS.
Results: There were 10753 reported admissions of ACS pts in all hospitals. Pts were hospitalised for UA in 49.8%, NSTEMI in 15.4%, and STEMI in 34.8%. Seventy-five hospitals without PCI facilities admitted 65.1% of pts; 14.9% of them were transferred to one of the 6 PCI centres for further treatment within 48 hours. The remaining 34.9% of patients were directly admitted to PCI centres and early angiography was performed in 94.3% of them. The rates of in-hospital deaths or myocardial infarctions in relation to treatment strategy and type of ACS are shown in the table.

Table

N = 10 753	Non-PCI Hospitals		PCI Hospitals	
	Conservative (N= 5 955)	Transport to PCI(N= 1 045)	Conservative (N= 215)	Immediate coronary angio (N= 3 538)
Unstable angina [N=5 361]	56.5%	6.2%	2.5%	34.9%
Death or MI	3.9%	1.8%	1.5%	0.8%
NSTEMI [N=1 610]	76.7%	7.1%	1.2%	15.0%
Death or MI	13.4%	7.0%	15.0%	4.6%
STEMI [N=3 728]	44.7%	15.9%	1.6%	37.8%
Death or MI	20.5%	6.0%	24.2%	5.5%

Conclusion: Patients with STEMI admitted to non-PCI hospitals and transported to PCI have similar in-hospital outcome to those admitted directly to PCI hospitals. Oppositely, patients with UA and NSTEMI have worse outcome in non-PCI hospitals and transport to PCI only partially improves the outcome.

1003-200 Major Access Site Bleeding in Acute Coronary Syndrome Patients Undergoing Early Invasive Management Can Be Reduced With Radial Access and Smaller Sheath Sizes. Observations From the SYNERGY Trial

Warren J. Cantor, Shaun G. Goodman, Dianne Gallup, Kenneth W. Mahaffey, Dietrich C. Gulba, Marc Cohen, Elliott M. Antman, Anatoly Langer, Neal S. Kleiman, Harvey D. White, Robert J. Chisholm, Robert A. Harrington, James J. Ferguson, III, Robert M. Califf, on behalf of the SYNERGY Investigators, St. Michael's Hospital, University of Toronto, Toronto, ON, Canada, Duke Clinical Research Institute, Durham, NC

Background: An early invasive strategy improves outcomes after acute coronary syndromes (ACS), but may be associated with increased bleeding, particularly at the arterial access site. The impact of radial access and sheath size has not been evaluated in this setting.
Methods: In the SYNERGY trial, 9978 patients with non-ST elevation ACS were randomly assigned to enoxaparin or unfractionated heparin. Of these, 9164 patients underwent angiography within 22 (6, 43) hours and 4683 (51%) had PCI within 22 (6, 48) hours of enrollment. Glycoprotein IIb/IIIa inhibitors were used in 57% of patients. Access site and sheath size were left to operators discretion. Major access site bleeds were those which met criteria for GUSTO severe or TIMI major bleeding.
Results: Radial access was associated with less major access bleeding and less transfusions. The unadjusted rates of major access site bleeding by sheath size was 2.6% for 4/5F, 2.2% for 6F, 3.5% for 7F and 3.6% for ≥8F (p=0.01). After adjusting for baseline characteristics, radial access was an independent predictor of transfusions (OR 0.62, p=0.002).
Conclusion: In this nonrandomized comparison, major access-site bleeding and the need for transfusion occurred less often with an early invasive strategy when radial access and smaller sheath sizes were used. In selected patients, smaller sheaths and radial access may mitigate the bleeding risk associated with potent antithrombotic therapy and early catheterization.

	Radial (n=413) (4.4%)	Femoral (n=8922) (94.9%)	p-value
Male	72%	66%	0.02
Caucasian	93%	85%	<0.0001
Age	66 (60, 73)	67 (60, 74)	0.24
PCI Success	241/245 (98%)	4231/4376 (97%)	0.15
TIMI Major Bleed (Any Site)	5.8%	8.8%	0.03
Transfusions	13%	19%	0.002
No Access Site Bleed	77%	81%	0.04
Minor Access Site Bleed	21%	17%	
Major Access Site Bleed	1.7%	2.5%	

1003-201 Cardiogenic Shock Complicating Non St Segment Elevation Myocardial Infarction. Data From Rico Survey

Marianne Zeller, Jack Ravisy, Gilles Rioufol, Sonia Salmi-Belmihoub, Mohamed Jolak, Jean-Claude Beer, Michel Vincent-Martin, Isabelle L'Huillier, Hamib Makki, Philippe Buffet, Nawal Moreau, Alexandra Oudot, Yves Cottin, on behalf of the RICO survey working group, University of Burgundy, Dijon, France

Background. Many studies have examined the clinical outcome of cardiogenic shock complicating ST segment elevation myocardial infarction (STEMI), but its occurrence and impact among patients with non STEMI (NSTEMI) remains limited.
Patients. Among the 1945 patients admitted for acute MI in the RICO survey (French regional survey for acute MI) between 1st January 2001 and 23rd September 2003, 148 (7.6%) patients with primary cardiogenic shock complicating acute MI were included in the study. Patients with causes of shock other than left ventricle failure were excluded from the study. Patients with NSTEMI were compared with STEMI patients.
Results. Among the 148 patients with cardiogenic shock complicating myocardial infarction, 35(23%) had a NSTEMI and 113(76%) had a STEMI. Patients from the NSTEMI group were older (median 78 vs 73 y, p<0.001) than those in the STEMI group and had diabetes mellitus and peripheral arterial disease more frequently (respectively 49 vs 27%, p=0.025 and 29 vs 3%, p<0.01). The time delay from symptom onset to admission was higher for the NSTEMI group (median 247 vs 165 min, p=0.003). Other risk factors and clinical variables were similar for the 2 groups, except for LVEF which was significantly higher in NSTEMI patients (median 45 vs 34 %, p=0.048). Despite more recurrent MI or angina (29 vs 11%, p=0.019), NSTEMI patients had similar recourse to acute therapeutics such as IIb/IIIa receptor blockers or coronary angiography. With regard to the proportion of patients undergoing primary PCI, there was no significant difference between the 2 groups (23 vs 14%, p=0.057). In-hospital mortality was similar for the NSTEMI and STEMI groups (46 vs 58 %, p=0.032).
Conclusion. Patients with cardiogenic shock and NSTEMI have a higher risk profile than STEMI patients, in particular for age and diabetes. More recurrent angina or MI provides opportunities for earlier intervention in this group of patients without ST segment elevation. In-hospital mortality from cardiogenic shock was equally high for patients with and without ST segment elevation.

1003-202 **Complications During Spasm Provocation Tests Of Acetylcholine - From The Experience Of 927 Consecutive Cases**

Shozo Sueda, Yousuke Izoe, Hiroshi Fukuda, Saiseikai Saijo Hospital, Saijo City,Ehime, Japan

Backgroud: There were some reports concerning the severe complications during nonselective spasm provocation test of ergonovine and its complication rate was 0.16-4.72%.
Objectives: The purpose of this study was to clarify the complications during spasm provocation test of acetylcholine (ACh), retrospectively.
Methods: From 1991 January to 2003 September, we performed 927 consecutive provocation tests of ACh to evaluate coronary spasm. ACh was injected in incremental doses of 20, 50 and 80 μg into the right coronary artery and of 20,50 and 100 μg into the left coronary artery.
Results: (1) Severe complications were observed in 14 patients (1.5%). However, no death and no serious irreversible complications were determined. (2) Ten patients (1.1%) developed ventricular tachycardia/fibrillation. Two was reversed by direct cardioversion, three by thump version and five resolved quickly with the intracoronary administration of ISDN. In all ten patients, spasm occurred. (3) There were three patients (0.3%) who developed severe hypotension, loss of consciousness and shock. In three patients coronary spasm occurred in both just proximal left anterior descending artery and just proximal circumflex artery, like the spasm of left main trunks by intracoronary injection of 50/100 mg ACh. By the administration of both norepinephrine and ISDN, coronary spasm was relieved gradually and they recovered from hypotension and shock. (4) Surgical drainage was performed in one patient who complicated with cardiac tamponade by inserting the temporary pace maker. (5) Paroxysmal atrial fibrillation occurred in 149 patients (16.6%) out of 886 patients who had sinus rhythm before the provocation test. Intravenous administration of anti-arrhythmic agents were necessary to recover sinus rhythm in 44 patients, while 105 patients were recovered to sinus rhythm within a few minutes.
Conclusions: Although the spasm provocation test of ACh was safe and reliable method, we should be take care of performing it in spite of selective procedure.

POSTER SESSION

1004 Guidelines and Quality of Care Issues in ST-Elevation Myocardial Infarction

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1004-226 **Relative 36% Reduction of Hospital Mortality in Diabetics with ST-Elevation Myocardial Infarction Between 1994 and 2002 due to Adherence to Guidelines in Clinical Practice: Results of MITRA PLUS**

Anselm K. Gitt, Harm Wienbergen, Ralph Winkler, Tobias Heer, Rudolf Schiele, Ralf Zahn, Martin G. Gottwik, MITRA-PLUS-Study-Group, Herzzentrum Ludwigshafen, Ludwigshafen, Germany, Klinikum Nuernberg Sued, Nuernberg, Germany

Background - Diabetics are known to have a high mortality after acute myocardial ST-elevation myocardial infarction (STEMI). We analysed if the implementation of guidelines for the treatment of STEMI improved outcome in diabetics from 1994 to 2002.
Methods - Since 1994 consecutive patients with STEMI were enrolled into German MI-registries in 319 hospitals (MITRA PLUS). Acute reperfusion and adjunctive treatment of STEMI and hospital mortality in diabetics were analysed using 2-year periods.
Results - Between 1994 and 2002, 8516 consecutive diabetics with STEMI were enrolled into MITRA PLUS. The prevalence of prior MI slightly decreased, known hypertension increased within time. Acute reperfusion increased from 47% to 65% with a more frequent use of primary PCI replacing thrombolysis. Adjunctive treatment with betablockers, ACE-I. and statins was administered more often in diabetics. This improvement in acute treatment was associated with a decrease in hospital mortality from initial 20.5% in 1994/96 to 13.2% in 2001/2002 (p<0.001 for trend).
Conclusion - Between 1994 and 2002 the acute treatment of STEMI in diabetics in Germany significantly improved according to existing guidelines. This improvement in acute treatment was associated with a 36% relative reduction in hospital mortality for diabetics with STEMI.

Hospital Mortality of STEMI in Diabetics

	1994-96 (n=1078)	1997-98 (n=4197)	1999-2000 (n=1632)	2001-02 (n=1609)
Age (years)	71	72	71	69
Male Gender	52.3 %	52.5 %	56.7 %	61.0 %
Reperfusion	47.2 %	38.0 %	54.7 %	65.0 %
Thrombolysis	39.1 %	28.0 %	31.7 %	18.7 %
Primary PCI	8.1 %	10.0 %	23.0 %	46.3 %
Betablockers	51.6 %	51.0 %	72.2 %	75.5 %
ACE-Inhibitors	63.8 %	62.9 %	71.2 %	66.6 %
Statins	na	46.5 %	47.9 %	62.7 %
Hospital Mortality	20.5 %	20.1 %	18.8 %	13.2 %

1004-227 **Bypassing the Emergency Room (ER) impacts care and outcomes in ST Elevation Myocardial Infarction (STEMI)**

Philippe Gabriel Steg, Olivier Fondard, Patrick Sauval, Didier Blanchard, Jean-Marc Lablanche, Jean-Pierre Cambou, Guy Hanania, Laurent Vaur, Nicolas Danchin, for the USIK 2000 investigators, Hopital Bichat, Paris, France, HEGP, Paris, France

Background: Most STEMI patients identified in a pre-hospital setting are initially brought to the ER before being admitted in a Coronary Care Unit (CCU). We decided to study the impact of direct admission to the CCU (bypassing the ER) vs admission via the ER.

Methods: The USIK 2000 registry was a nationwide registry of acute STEMI collected in 369 centers (83% of french CCUs) in November 2000. 1000 patients with STEMI < 24 h from onset were categorized on the basis of the initial management pathway (direct transfer to CCU, vs transfer to CCU via ER).
Patients admitted via the ER had more severe baseline characteristics than those who bypassed the ER (Table). Direct transfer to the CCU was associated with a shorter time to CCU admission (5.8 vs 7.2 h, p<0.001), a greater frequency of reperfusion therapy (70.1 vs 56.8%, p<0.01), a greater use of beta blockers at 48 h and a lower short-term mortality. Among patients treated with primary PCI (n=671), there was a greater difference in mortality between those who bypassed the ER and those who did not (4.2% vs 17.1%, p=0.009). Multivariate analysis showed that admission via the ER was an independent predictor of short-term mortality (OR: 3.079, p=0.005).
Conclusions: In this registry, bypassing the ER appeared associated with improved processes of care and outcomes, especially among patients treated with primary PCI. This suggests that pathways should be established for patients with STEMI to bypass the ER.

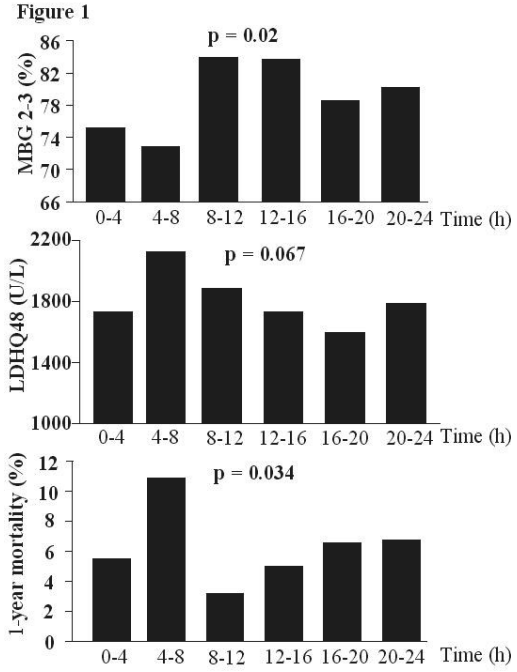
	Direct to CCU	CCU via ER	p
N	787	213	
Male gender (%)	77.6	69	0.005
Age > 70 years	36.2	47.9	0.002
Delay call to CCU (h)	2.7	4.2	0.0001
Lytic therapy (%)	37.2	40.4	0.001
Primary PCI (%)	32.9	16.4	0.001
beta-blockers at 48 h (%)	75.2	67.1	0.032
Death at day 5 (%)	5.1	9.4	0.019

1004-229 **Circadian Variation In Myocardial Perfusion And Mortality In Patients With ST-Segment Elevation Myocardial Infarction Treated By Primary Angioplasty**

Giuseppe De Luca, Harry Suryapranata, Arnoud WJ van't Hof, Jan Paul Ottervanger, Jan CA Hoorntje, AT Marcel Gosselink, Jan-Henk E. Dambrink, Menko-Jan de Boer, De Weezenlanden Hospital, Zwolle, The Netherlands

Background. Little is known about whether the physiologic factors, that determine the circadian variation in STEMI onset and thrombolyis efficacy, may affect myocardial perfusion and long-term outcome of patients with STEMI treated with primary angioplasty.
Methods. Our study population consisted of 1548 consecutive patients with STEMI treated by primary angioplasty between April 1997 and October 2001. All clinical, angiographic and follow-up data were collected.
Results. Most of the patients (65.2%) were treated at daytime (between 8 a.m. and 8 p.m.). Patients treated between 1 and 12 p.m. had a lower prevalence of anterior infarction and longer door-to-balloon time, whereas the shortest ischemic time and the highest use of stent was observed in patients treated between 0 and 4 a.m. Patients treated between 4 and 8 a.m. showed the worst outcome in terms of myocardial perfusion, enzymatic infarct size and 1-year outcome, whereas patients treated between 8 a.m. and 4 p.m. had the best myocardial perfusion and lowest 1-year mortality rate (Figure 1). After correction for baseline confounding factors, the time of treatment (between 4 and 8 a.m.) was still significantly associated with 1-year mortality (relative risk [95% CI] = 1.92 [1.13-3.26], p = 0.016).
Conclusions. This is the first study showing a significant relationship between the time of treatment, myocardial perfusion and long-term mortality in patients with STEMI undergoing mechanical reperfusion.

Figure 1



1004-230 **High Mortality In Patients With ST Elevation Myocardial Infarction And Prehospital Cardiopulmonary Resuscitation Despite Aggressive Reperfusion Therapy. Results Of PREMIR.**

Uwe Zeymer, Lutz Nibbe, Ralf Zahn, Hans-Richard Arntz, Klaus Ellinger, Harald Genzwürker, Burkhard Dirks, Jochen Senges, Herzzentrum Ludwigshafen, Ludwigshafen, Germany

Background: Recent studies and registries suggest a low mortality in patients with ST elevation myocardial infarction treated with early reperfusion therapy. Little is known about the outcome of patients with STEMI and pre-hospital cardiopulmonary resuscitation (CPR)treated with early reperfusion therapy.
Methods: In a nationwide prospective registry (PREMIR : PREhospital acute Myocardial Infarction Registry) data of consecutive patients with STEMI already diagnosed pre-hospital in the ambulance by emergency physicans by obtaining a 12-lead ECG were collected and processed centrally. A total of 64 ambulance systems in Germany were in involved in PREMIR. Patient characteristics, pre- as well as in-hospital treatments and events were recorded.
Results: So far 1503 patients with STEMI were included, of whom 197 needed pre-hospital CPR (13.1%). The mean age of the latter was 64 years, 74% were men, 26% had a previos myocardial infarction, 27% were diabetics and 40% were smokers. The median time interval between symptom-onset and arrival of the ambulance was 25 minutes. In the pre-hospital ECG 41% had an anterior, 54% an inferior infarct and 5% left bundle branch block. Over 90% of the patients were given aspirin and heparin. 116 (58.9%) patients were treated with pre-hospital thrombolysis. 51 (26%) died before hospital arrival, 46 of the latter were treated with pre-hospital thrombolysis. Addional in-hospital reperfusion therapy with thrombolysis (n=16) and/or percutaneous coronary intervention (n=77) was performed, leaving only 17 (8.6%) patients without any early reperfusion therapy. The in-hospital mortality of admitted patients was 33%. In total 96 of 197 patients (48.7%)with STEMI and pre-hospital CPR died.
Conclusion: Patients with STEMI already diagnosed in the ambulance by emergency physicans and pre-hospital CPR have a high mortality despite an over 90% rate of early reperfusion therapy. Therefore the real world mortality of patients with STEMI is higher than recent clinical trials and in-hospital registries suggest.

1004-231 **Acute Myocardial Infarction: Improving Trends in Patient Care**

Alan K. Berger, Susan J. Duval, Christopher Armstrong, Patricia A. Janey, Russell V. Luepker, University of Minnesota, Minneapolis, MN, Health Evaluation Research Foundation, St. Paul, MN

Background: Prior studies have documented poor physician compliance with the American College of Cardiology/American Heart Association guidelines for acute myocardial infarction (AMI). Regional and nationwide quality improvement programs have sought to improve the utilization of aspirin (ASA), beta blockers (BB), and angiotensin converting enzyme inhibitors (ACE-I) in AMI but few studies have demonstrated significant change in real-world practice.
Hypothesis: Among patients hospitalized in the Minneapolis-St. Paul metropolitan area with AMI, the utilization of ASA, BB, and ACE-I improved between 1995 and 2001.
Methods: We analyzed data from the Minnesota Heart Survey, a population-based study that abstracted random samples of all medical records of hospitalized AMI patients in 1995 and 2001 in the Minneapolis-St. Paul metropolitan area. AMI was defined using an algorithm requiring either elevated serum cardiac biomarkers or ST elevation on the electrocardiogram. The utilization of ASA, BB, and ACE-I or angiotensin receptor blocker (ARB) in-hospital and at discharge was assessed using a linear regression model adjusting for age and gender.
Results: We identified 1,298 patients with an AMI in 1995 and 1,348 patients in 2001. The in-hospital use of ASA (91.8 vs 95.7%, p=0.0013), BB(70.1 vs 84.8%, p<0.0001), and combined ACE-I/ARB(35.5 vs 63.9%, p<0.0001) increased between 1995 and 2001. Similarly, the prescription of ASA (83.7 vs 85.0%, p=0.48), BB (54.4 vs 78.6%, p<0.0001), and combined ACE-I/ARB (27.5 vs 57.4%, p<0.0001) at discharge increased between 1995 and 2001. In-hospital mortality declined from 7.2% in 1995 to 5.4% in 2001 (p=0.136).
Conclusions: The utilization of standard AMI therapies improved between 1995 and 2001. This improved quality of care may be partially responsible for the trend toward a reduction in hospital mortality.

1004-232 **Does Facilitated Percutaneous Coronary Intervention Extend Optimal Door-to-Balloon Time in Patients With ST-Segment Elevation Myocardial Infarction Presenting in Community Hospitals?**

Georgios I. Papaioannou, Haris Athar, Sanjeev B. Patel, Marcin R. Dada, Fawad A. Kazi, Justin B. Lundbye, Joseph E. Thomas, Leo Marcoff, Roger A. Mennett, Jeffrey F. Mather, Edcar D. Messer, Joseph F. Mitchell, Daniel B. Fram, Charles A. Primiano, Jeffrey A. Hirst, Francis J. Kiernan, William E. Boden, Raymond G. McKay, Hartford Hospital, Hartford, CT, Athens Medical Center, Athens, Greece

Background: Prolonged door-to-balloon (DTB) time >=120 min has a negative impact in patients with ST-segment elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI). Whether Facilitated PCI extends optimal DTB time in community-hospital STEMI patients remains unclear.
Methods: We compared baseline characteristics, and in-hospital major adverse cardiac events (MACE) (death, re-infarction, stroke and emergency revascularization), between 808 consecutive, community STEMI patients, presented within 12 hours of symptom onset, without cardiogenic shock, treated either with Facilitated PCI (antecedent use of bolus fibrinolytics and/or glycoprotein (GP) IIb/IIIa inhibitors followed by transfer for PCI, n=349), or Primary PCI (PCI without antecedent use of thrombolytic or GP IIb/IIIa therapy, n=459). Patients in both groups were further divided according to DTB times <=120 minutes or >120 minutes.
Results: There were no differences among the 4 groups (stenting >90%). Primary PCI patients with DTB <=120 min had lower in-hospital mortality and MACE compared to patients with DTB >120 min. Facilitated PCI patients had similar outcomes compared to Primary PCI patients with DTB <=120 min, irrespective of DTB time (Table).
Conclusion: Facilitated PCI in STEMI patients transferred from community hospitals results in similar clinical outcomes to that achieved in STEMI patients treated with Primary PCI with optimal DTB time, irrespective of transfer delay.

Table

	I: Primary PCI/DTB<=120 min (n=249)	II: Primary PCI/DTB>120 min (n=210)	III: Facilitated PCI/DTB<=120 min (n=90)	IV: Facilitated PCI/DTB>120 min (n=259)	P value
Death	1/249 (0.4%)[a,e]	10/210 (4.8%)[b]	1/90 (1.1%)[d]	5/259 (1.9%)	[a]p=0.002 (I vs. II); [b]p=0.08 (II vs. IV); [c]p=0.006 (II vs IV)
MACE	6/249 (2.4%)[a,e]	19/210 (9%)[c]	2/90 (2.2%)[d]	8/259 (3.1%)	[d]p=NS (III vs. IV); [e]p=NS (I vs. III and IV)

1004-233 **The Feasibility Of Transport For Primary PCI In The Treatment Of STEMI In A Rural American Setting**

Thomas A. Haldis, Jr., James C. Blankenship, Geisinger Medical Center, Danville, PA

Background: ACC/AHA guidelines suggest that patients with STEMI transferred for primary PCI should undergo PCI within 90 minutes of initial presentation. The feasibility of meeting these goals in a rural American setting has not been proven.
Methods: Geisinger Medical Center is the only tertiary care facility in north central Pennsylvania. Patients are transferred for PCI from hospitals up to 74 miles away. They are routinely re-evaluated by our inpatient service on arrival before the catheterization team is called. We retrospectively analyzed all patients transferred for primary PCI to our facility between January 1-July 31, 2004. All times from the symptom onset to balloon inflation were collected from emergency room notes, helicopter dispatch logs, and catheterization laboratory logs. We compared the specific time intervals in our region to those from recent randomized controlled trials.
Results: 61 patients with STEMI who were transferred to our facility underwent primary PCI over a 7-month period. The mean flight distance from referring hospital to our center was 29.2 miles (range 10-74 miles).

Median Time Intervals In Recent Trials Compared To Rural Pennsylvania

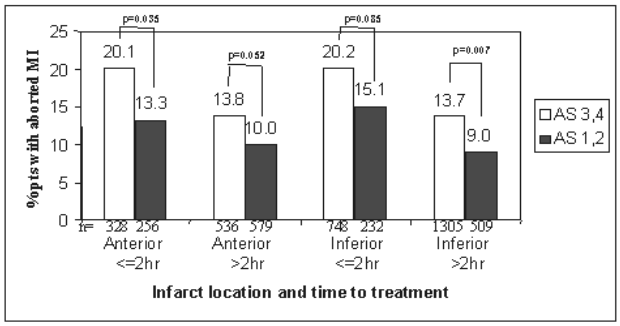
	n	Presentation time	Admission-dispatch time	Transport time	Arrival-balloon time	Presentation-balloon time	30-day Mortality
PRAGUE	215	120	15	52	28	95	7%
PRAGUE 2	429	183	20	48	26	94	6.8%
AIR PAMI	71	na	35	58	25	118	8.4%
DANAMI 2	567	106	22	67	26	115	6.5%
Rural Pennsylvania (95% CI)	61	71 (60, 92)	39 (33, 46)	54 (48,61)	89 (76, 99)	183 (157, 206)	3.3%(0.4%, 11.9%)

Conclusions: Patients with STEMI in rural Pennsylvania present sooner after onset of symptoms than in recent trials. Despite its rural location, transport times are similar to those in the clinical trials. A policy of re-evaluation at the receiving center leads to unacceptable delays in reperfusion. Even with a door to balloon time under 30 minutes, it would be difficult to meet ACC/AHA guideline goals.

1004-234 The ECG Adds Value to Time to Treatment in Predicting Aborted Myocardial Infarction

Taha Taher, Suhaib Al-Kurtass, Yuling Fu, Galen Wagner, Shaun G. Goodman, Robert Welsh, Christopher Granger, Lars Wallentin, Frans Van de Werf, Paul W. Armstrong, University of Alberta, Edmonton, AB, Canada, Duke Clinical Research Institute, Durham, NC

Background: Faster time to treatment enhances the success of pharmacologic reperfusion of ST MI. We recently demonstrated it also increases the likelihood of aborted MI. Since time from symptom onset may be an imprecise measure of when ischemic injury begins we utilized baseline ECG measures of infarct acuteness score (AS) to further explore this.
Objective: To determine if an objective measure i.e. ECG AS (algorithm incorporating relative amounts of excess T amplitude and Q duration in ST leads: AS range 4.0 earliest to 1.0 latest) predicts reperfusion success, aborted MI and large MI.
Methods: ECGs (at baseline, 60 min after lysis) of STEMI pts in ASSENT3 and 3+ analyzed by a core lab. Baseline demographics and outcomes were analyzed to determine associations with AS.
Results: Of 6,617 pts with CK and ECG data, 14.3% had an aborted MI. Compared to pts with AS<3, pts with AS≥3 had more frequent aborted MI (15.6% vs 12.4%, p=0.002) and fewer large infarcts ie. CK>5x normal (61.3% vs 71.7%, p<0.001). A multivariate analysis showed both time to treatment ≤2h (OR=1.68, CI=1.41-2.00) and AS≥3 (OR=1.46, CI=1.20-1.77) are independent predictors of aborted MI. In all pts, complete ie. ≥70% ST resolution at 60 min was more likely in pts with higher AS.
Conclusion: The AS adds value to time to treatment in predicting reperfusion, aborted MI and large MI's. A high AS even in pts presenting >2h increased likelihood of successful reperfusion and aborted MI thereby broadening the potentially successful treatment window.



1004-235 Hospital Stay After Uncomplicated Acute Myocardial Infarction in Europe can Be Significantly Reduced; Observations from The Euro Heart Survey of Acute Coronary Syndromes

Maureen J. van der Vlugt, Sanne Hoeks, Eric Boersma, Maarten L. Simoons, Erasmus Medical Center, Rotterdam, The Netherlands

Background: Since efficient use of medical resources is a priority for society, early hospital discharge after myocardial infarction (MI) has been studied extensively. The aim of the study was to evaluate the length of hospital stay (LOS) in patients (pts) with an uncomplicated MI across Europe, and to identify pts eligible for earlier discharge.
Methods: During 2001 the Euro Heart Survey of ACS enrolled 6,086 pts with acute MI (103 hospitals, 25 countries). During admission the most serious post MI adverse events were recorded, including death, asystole, ventricular fibrillation or -tachycardia, heart failure, re-infarction and high-graded AV-block. For each hospital day we determined the daily event rate and the amount of pts free of any of these events.
Results: The mean age was 65 years, 70 % were male. The median LOS was 9 days (6-13). Table demonstrates a significant decrease of the event rate during the first 6 days. From day 7 on daily event rates stabilized around 1.0 %. At day 7 still 40 % were admitted, pts eligible for early discharge. Then, 13,588 days (21 % of all hospital days) spend in hospital would have been avoided.
Conclusion: Current ACC/AHA/ESC guidelines recommend discharge within 4 days in pts with uncomplicated MI. Our data suggested that this might be too early, since the event rate (death) decreased further beyond this 4 day period. However, even if pts will be discharged within 7 days a considerable reduction in LOS can be achieved. Such policy might contribute to an extensive reduction in costs.

hospital day	1	2	3	4	5	6	7	8	9
pts still admitted	6,086	3,948	3,601	3,348	3,117	2,777	2,414	1,998	1,615
death (%)	1.8	0.6	0.3	0.2	0.3	0.3	0.2	0.2	0.1
any event (%)	33.9	6.9	3.9	2.9	2.4	1.8	1.4	1.3	1.0
discharged (%)	0.3	1.9	3.1	4.0	8.5	10.6	14.7	17.9	19.3

1004-236 Participation In Thrombolytic Trials Delays Reperfusion Therapy In Acute Myocardial Infarction.

Wojtek C. Wasek, Sebastian Stec, Tomasz Mazurek, Andrzej Budaj, Beata Klosiewicz-Wasek, Pawel Maciejewski, Bronislaw Bednarz, Cardiology Department, Postgraduate Medical School, Warsaw, Poland

Background: Shortening of time delay to the beginning of treatment in ST-segment elevation myocardial infarction (STEMI) is proven to be clinically essential. However, invasive vs thrombolytic treatment strategy is currently under investigation, particularly in terms of time from the onset of chest pain to treatment initiation. It is likely, that enrolment to the trials in STEMI may paradoxically prolong the time delay to treatment if randomisation procedures are too complex.
Aim: Evaluation of door-to-needle time (DtN) to the onset of reperfusion therapy in patients (pts) randomised to trials or treated routinely with thrombolytics (Thrx).
Methods: We evaluated DtN in a group of 189 consecutive STEMI pts (trials n=96, Thrx n=93). The inclusion criteria for the analysis were the same in three groups: 1. STEMI diagnosis was given on admission. 2. Pts had no signs of heart failure. 3. There were no contraindications for immediate reperfusion therapy. The comparison of DtN between evaluated groups was analysed. DtN was separately compared in a subgroup of pts admitted within the first hour from the onset of chest pain.
Results: DtN was significantly longer in pts participated in trials. No differences in DtN were found between groups of pts enrolled to various trials.
Conclusion:(1) The participation in trials delays the beginning of reperfusion therapy. (2) The delay may be clinically important particularly in pts hospitalized very early from the onset of symptoms.

Door-to-needle time (minutes)

	Thrx mean ± SD	Trials mean ± SD	p <
all patients	22 ± 8	41 ± 18	0.0001
Subgroup of pts with chest pain < 1h	22 ± 8	42 ± 22	0.001

POSTER SESSION

1005 Novel Predictors of Outcome After an Acute Coronary Syndrome

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1005-219 Does Plasma Homocysteine Levels Have An Independent Impact On Long-term Cardiovascular Mortality In Patients With Acute Coronary Syndromes. Results From The Biochemical Indices and outcome in Acute coronary Syndromes (Bias) Study.

Michael N. Zairis, Demetrios Beldekos, Charalambos Apostolatos, Dionissis Xenos, George Bibis, Olga Ampartzidou, Stamatis Makrygiannis, Paraskevi Psarogianni, George Psaltiras, Evdokia Adamopoulou, John Hatzissavas, Stefanos Foussas, Tzanio Hospital, Piraeus, Greece

Background-Although an elevated plasma total homocysteine (tHcy) level has been considered as a cardiovascular disease risk factor, its impact on the long term prognosis in patients with acute coronary syndromes remains controversial. We evaluated this possible association in the BIAS (Biochemical Indices and outcome in Acute coronary Syndromes) study.
Methods-The BIOS study was designed to evaluate prospectively the impact of several biochemical indices including tHcy on the long term cardiovascular mortality in patients who hospitalised due to either ST elevation myocardial infarction (STEMI) or non-ST elevation acute coronary syndromes (NSTACS). For the purpose of this study 934 consecutive pts with STEMI (458 pts) and NSTACS (476) who admitted in the first 12 and 24 hrs of index pain respectively, were recruited. All biochemical indices were estimated upon pts' admission and cardiovascular mortality during 5 years of follow up was the primary study endpoint.
Results-Plasma tHcy levels were significantly higher in pts with: diabetes (p=0.02); age>=70 years (p=0.01); history of coronary revascularization (p=0.001); and history of cerebrovascular or peripheral artery disease (p<0.001). The incidence of cardiovascular mortality at the end of the follow up was 23.1% and 21.4% in pts with STEMI and NSTACS respectively. By univariate regression analysis high plasma tHcy levels were significantly related with increased cardiovascular mortality in pts with either STEMI (p=0.01) or NSTACS (p=0.01). However by multivariate regression analysis, in which all univariate predictors of cardiovascular mortality were included, high plasma tHcy levels were no associated with the 5-year outcome in both STEMI (p=0.9) and NSTACS (p=0.8).
Conclusions-The results of the BIAS study suggest that plasma tHcy levels upon admission cannot be used as an index of early risk stratification in patients with either STEMI or NSTACS

1005-220 Serum 15-F_2-Isoprostane Predicts Future Cardiovascular Events In Patients With Acute Coronary Syndromes

Srikanth Sola, Patrick B. Caneer, W. Craig Hooper, Megan E. Price, Muhammad Q. Mir, Joshua M. Larned, Nadya Khan-Merchant, Bobby V. Khan, Emory University School of Medicine, Atlanta, GA, Rollins School of Public Health, Atlanta, GA

Background: Isoprostanes are free-radical dependent metabolites of arachidonic acid that are used as clinical biomarkers of lipid peroxidation and oxidative stress. Whether quantification of 15-F_2-isoprostane provides prognostic information in unstable coronary artery disease is unknown.
Methods: We measured plasma levels of 15- F_2-isoprostane, interleukin-6 (IL-6), and VCAM-1 on admission in patients who were admitted to the hospital with acute coronary syndrome (ACS). Patients were followed prospectively for the occurrence of the primary endpoint, which was a composite of cardiac death, non-fatal myocardial infarction (MI), revascularization, or hospitalization.
Results: We followed 136 patients for an average of 13 ± 1.3 months. Baseline plasma levels of 15-F_2-isoprostane, IL-6, and VCAM-1 predicted the risk of myocardial infarction, even in patients who are negative for troponin T (<0.1 ng per milliliter) at baseline (P<0.0001). Furthermore, the incidence of the primary outcome during the follow-up period was increased in patients in the highest tertile of 15-F_2-isoprostane levels compared with those in the lowest (see Table). The adjusted odds ratio for occurrence of the primary outcome was 1.67 (95% CI 1.32-2.12; p < 0.001) for each tertile of serum 15-F_2-isoprostane levels.
Conclusions: Serum levels of 15-F_2-isoprostane, a marker of oxidative stress, independently predicts long-term cardiovascular events in high risk patients admitted with ACS.

Outcome	Tertile (15-F_2-Isoprostane range, pg/mL			
	1 (< 51.20) n = 45	2 (51.20 -61.53) n = 46	3 (> 61.53) n = 45	*P*
Composite outcome	**7**	12	28	< 0.0001
Non-fatal MI	2	6	21	< 0.0001
Hospitalization for heart failure	2	3	8	0.03
Revascularization	4	11	25	< 0.0001
Cardiac death	2	2	2	1

1005-223 Living Alone Is an Independent Predictor of Future Cardiac Events Not in Female but in Male Elderly Patients After Acute Myocardial Infarction

Daisaku Nakatani, Hiroshi Sato, Yasuhiko Sakata, Kunihiro Kinjo, Hiroya Mizuno, Masahiko Shimizu, Hiroshi Ito, Masayoshi Mishima, Masatsugu Hori, Osaka University Graduate School of Medicine, Suita, Japan, Sakurabashi Watanabe Hospital, Osaka, Japan

Background: Although the number of the adults aged 65 years or older living alone has been increasing steadily, few data are available regarding the impact of living alone on cardiac events in elderly patients with AMI. Furthermore, there exists a sex difference in response to social isolation in rats.
Methods: To examine the impact of living alone on cardiac events in elderly patients with AMI and whether it differs between in men and women, we studied 1035 patients aged 65 years or older who discharged alive after AMI. Cardiac events were defined as composite of cardiac death, percutaneous coronary angioplasty, coronary aorta bypass surgery, readmission for heart failure, reinfarction, unstable angina, or arrhythmia.
Results: The mean follow up was 699±523 day. The incidence of cardiac events after AMI was higher in patients living alone than in those not living alone after AMI (36.2% vs. 28.0%, P=0.009). Interestingly, the rate of cardiac events was higher in male patients living alone than in the group not living alone (40.4% vs. 28.7%, P=0.002), while it was similar between female patients living alone and not alone (26.4% vs. 25.9%, P=0.943). Multivariate analysis revealed that living alone was an independent risk factor predicting future cardiac events in elderly patients after AMI (HR 1.64, 95% CI; 1.19-2.28, P=0.003). According to sex, living alone was independently associated with an increased risk of cardiac events in men (HR 1.86, 95% CI; 1.27-2.74, P=0.002), but not in women (HR 1.37, 95% CI; 0.71-2.62, P=0.345), suggesting sex difference in response to social isolation.
Conclusions: Living alone is associated with an increased risk of future cardiac events in elderly male patients after AMI, for whom social support may be needed.

1005-224 Baseline Urinary Albumin Concentration Predicts Long-Term Cardiovascular Risk in Acute Coronary Syndrome Patients: A PROVE IT-TIMI 22 Substudy

Kausik K. Ray, David A. Morrow, Sabina Murphy, Carolyn H. McCabe, C. Michael Gibson, Christopher P. Cannon, Brigham and Women's Hospital, Boston, Harvard Medical School, Boston, MA

Background: Urinary microalbuminuria (MA) is postulated to be a marker of vascular health and correlates with cardiovascular (CV) risk in patients with diabetes and hypertension. Statins have been shown to improve markers of vascular health such as flow mediated dilatation and adhesion molecule expression in patients with stable coronary artery disease (CAD).
Aims and Methods: Among ACS patients, we assessed whether urinary albumin concentration (UAC) (µg/ml) identified patients at risk of future CV events, and the effect of intensive statin therapy on UAC in the PROVE IT-TIMI 22 study. UAC was measured using a spot urine sample at enrollment and at the end of study.
Results: We measured UAC in 3280 patients. A higher baseline UAC was associated with MI, stroke and death or MI during a mean follow up of 2 years (fig1). The % of patients with death, MI, stroke or the composite of death, MI or stroke at 2 years each increased incrementally with increasing UAC (figure 2). In 1204 patients who had UAC determined at a mean of 2 years after enrollment, neither statin regime significantly reduced urinary MA.
Conclusions: Urinary albumin concentration peri-ACS predicts CV risk during long term follow up, but is not significantly influenced by statin therapy at 2 years. Measurement of vascular health using urinary albumin concentration may be a useful as an additional risk predictor in ACS.

Fig 1
Median urinary albumin concentration at enrollment and CV events at 2 years

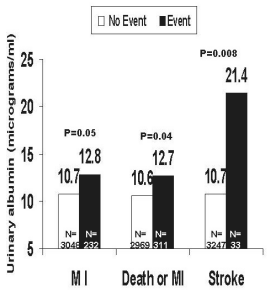
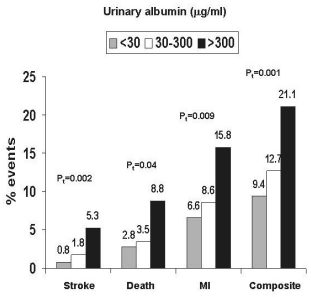


Fig 2
2 year event rate by baseline urinary albumin concentration



1005-225 Cystatin C is the Most Powerful Predictor of Long-term Mortality in Patients With Acute Coronary Syndromes

Stefan K. James, Bertil Lindahl, Anders Larsson, Lars-Olof Hansson, Paul Armstrong, Robert Califf, Maarten Simoons, Lars Wallentin, Institute of Medical Sciences, Uppsala, Sweden

Background: Measurements of renal function, such as creatinine and creatinine clearance (creacl) carry independent prognostic information in patients with acute coronary syndromes (ACS). Cystatin-C is a cysteine protease inhibitor involved in the catabolism of proteins and a more reliable endogenous marker of glomerular filtration rate.
Methods: The GUSTO IV trial, evaluating abciximab as the medical treatment in non-ST elevation ACS without early revascularization, included 7800 patients. Levels of cystatin-C at randomization were analyzed in 785 patients and creacl was calculated from creatinine with the Cockroft-Gault equation. The results were related to 1-year mortality.
Results: The median of cystatin-C was 0.99 (cystatin-C derived GFR 75 ml/min). There was a significant correlation between cystatin-C and creacl, creatinine, Nt-proBNP, CRP and troponin T ; r=0.53, 0.47, 0.41, 0.25 and 0.1 respectively.
In a multiple logistic regression analysis including a large number of riskfactors Cystatin-C above the median of 0.99 had the highest Odds ratio 3.3 (95% C.I: 1.4-7.75). When creacl was added, Cystatin-C remained significant with O.R 2.8 (95% C.I: 1.2-6.9) while creacl was not; O.R 1.8 (95% C.I: 0.7-4.5).
Conclusion: In non-ST elevation ACS, a single measurement of Cystatin-C at admission provides prognostic information on long-term mortality beyond creatinine clearance. In combination with NT-proBNP and Troponin-T the risk stratification is further improved.

One-year mortality

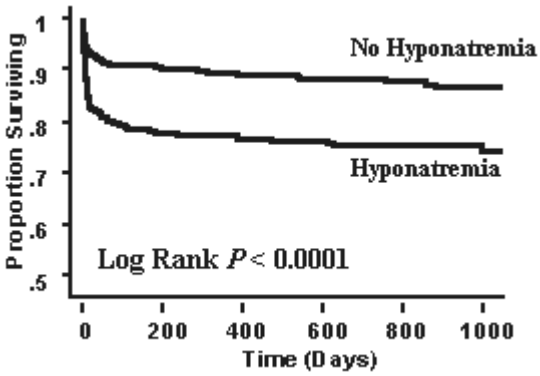
%		Troponin-T, ug/L		p	Nt-proBNP, ng/L		p
		<=0.01	>0.01		<=669	>669	
Cystatin-C, mg/L	<0.86	1.2	6.1	0.09	0.7	13.7	<0.001
Quartiles	086-0.99	1.4	5.6	0.14	0.9	9.1	0.007
	0.99-1.21	7.0	10.3	0.4	7.1	11.2	0.2
	>1.21	9.0	24.4	0.009	7.7	24.6	0.006
		0.046	<0.001		0.04	0.08	

1005-228 Long-term Prognosis of Patients who Developed Hyponatremia During the Acute Phase of ST-elevation Myocardial Infarction

Alexander Goldberg, Haim Hammerman, Sergey Yalonetski, Sirouch Petcherski, Alexander Zdorovyak, Michael Kapeliovich, Walter Markiewicz, Doron Aronson, Rambam Medical Center, Haifa, Israel

Background: Hyponatremia (HNa) is common in hospitalized patients (pts) and is associated with adverse short-term prognosis. The prognostic significance of HNa in acute coronary syndromes, especially beyond the index hospitalization, is not known.
Methods: We studied 1345 pts presenting with ST-elevation myocardial infarction (STEMI). Plasma sodium levels (PNa) were obtained on admission and at 24-h, 48-h, and 72-h. All pts were followed in hospital and following discharge (median follow-up 568 days). Cox proportional hazards analysis analyses were performed to determine the relation between HNa and mortality adjusting for age, sex, diabetes, hypertension, smoking, Killip class on admission, SBP and heart rate on admission, anterior infarction, use of diuretics, previous heart failure and reperfusion therapy.
Results: HNa (PNa < 135 mmol/L) was present on admission in 168 pts (12.5%) and developed in 234 (17.4%) during the first 72-h. Cox analysis revealed that pts with HNa were at increased risk of mortality (adjusted RR 2.4; 95% CI 1.8-3.2; *P* < 0.0001) (Figure). Similar results were obtained when analyzing only pts who survived the index hospitalization (adjusted RR 1.7; 95% CI 1.1-2.7; P = 0.03). The risk associated with severe HNa (≤130 mmol/L) was larger than that of mild (131-134 mmol/L) HNa (adjusted RR 4.4 [95% CI 3.0-6.6] vs. 1.8 [95% CI 1.3-2.5]).

Conclusion: HNa on admission or developing within 72 h from admission is a strong independent risk factor for long-term mortality in pts with STEMI.



POSTER SESSION

1006 Genetic and Hormonal Influences on Vascular Functions

Sunday, March 06, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 11:00 a.m.-Noon

1006-215 Effects of Dehydroepiandrosterone Supplementation on Coronary Reserve in Men with Coronary Artery Disease

Jerzy Krzysztof Wranicz, Iwona Cygankiewicz, M. Rosiak, J. Slowikowska-Hilczer, P. Dejak, M. Maciejewski, W. Koniarek, M. Lipinski, M. Wrona, P. Kukla, I. Poprawska, J. H. Goch, K. Kukla, Wojciech Zareba, Medical University of Lodz, Lodz, Poland, University of Rochester Medical Center, Rochester, NY

Background. Dietary supplementation with dehydroepiandrosterone (DHEA) has been considered as therapeutic modality in coronary patients. We aimed to determine the effect of daily supplementation of DHEA on coronary reserve, assessed by clinical evaluation, exercise-treadmill test (ETT), and quality of life in men with coronary disease.
Methods. A randomized double blind placebo-controlled crossover trial was designed involving 36 coronary patients (mean age 58+/-9 years) who received 12 weeks of 50 mg/day oral therapy of DHEA and placebo interrupted by a 4-week washout period. Blood levels of DHEA sulfate, testosterone, and estradiol were measured and cardiac status of the patients was evaluated by quantifying weekly usage of nitroglycerine and by ETT: exercise duration and workload. Quality of life was evaluated using SF-36 questionnaire.
Results. Median values of measured parameters after DHEA treatment indicated improvement in cardiac status (Table). SF-36 questionnaires also showed significant ($p<0.05$) improvement in quality of life (physical function, vitality, bodily pain, limitations related to physical and emotional problems).
Conclusions. Administration of DHEA in dose 50 mg per day is associated with significant improvement of several clinical measures reflecting coronary reserve and quality of life in coronary patients. This clinically detectable improvement probably relates to an increase of DHEAS blood levels together with elevation of blood testosterone and estradiol.

Parameters	Baseline	Placebo	DHEA
DHEA (ug/dl)	103	106	191†
Estradiol (pmol/l)	99	97	196*
Testosterone (nmol/l)	11.9	12.6	16.9*
Nitroglicerine use (tabl/week)	6.1	4.7*	2.9*
ETT workload (METs)	7.5	7.0	9.5*
ETT duration (min)	6.8	6.4	8.2*
* significantly different than placebo			
† -p=0.07 when comparing to placebo			

1006-216 Endothelin-1 Gene LYS198ASN Polymorphism in Human Variant Angina Pectoris

Juyong Lee, Jeong-Uk Kim, Kyung Il Song, Yunseok Choi, Sang-sig Cheong, Gangneung Asan Hospital, Gangneung-si, South Korea

Background; Endothelin-1 (ET-1) is increased in patients with variant angina pectoris (VAP) occurring chest pain. The imbalance of blood vasoconstrictor and vasodilator, such as endothelium derived relaxation factor (EDRF) was assumed to be one of the key factors causing VAP. Recently, the polymorphisms of EDRF and other vasoreactants have been reported for VAP patients. However, there has been no data about genetic polymorphism of ET-1 in the patients with VAP. We investigated the frequency of a G/T polymorphism with an amino acid substitution (Lys-Asn) at codon 198 in exon 5 of the ET-1 gene in the VAP patients and its possible association with coronary spasm.
Methods: Polymerase chain reaction (PCR) restriction fragment length polymorphism (RFLP) method was performed in 103 VAP patients and 111 controls. VAP was diagnosed with ergonovin (ERG) provocation coronary angiography (CAG)(n=58, 56.3%) and ERG stress echocardiography (n=45, 43.7%). Absence of the fixed coronary artery disease (CAD) (> 50% of diameter stenosis) was confirmed in the finding of ERG provocation CAG group with normal or minimal CAG result and in ERG stress echocardiography group with negative result of treadmill test, thallium scan, normal or minimal CAG result. Age, sex matched control who has no history of any angina like chest pain was randomly selected from health care screening department. The control has no diabetes mellitus, hypertension, hypercholesterolemia, current systemic infection, and elevated SGOT/SGPT. High-sensitivity C-reactive protein concentration was checked by immunonephelometry in two groups.
Results: Genotype frequency of Lys198Asn polymorphism of ET-1 in VAP (GG 46(44.7%), GT 42(40.8%), TT 15(14.6%)) was significantly higher than control group (GG 64(57.7), GT 41(36.9%), TT 6(5.4%))(p=0.038). Multiple logistic regression analysis using risk factors and the Lys198Asn polymorphism showed that the significant risk factors for VAP were hs CRP(odds ratio 20.68, p=0.03) and the Lys198Asn polymorphism(odds ratio 1.736, p=0.04).
Conclusion: The frequency of Lys198Asn polymorphism of ET-1 gene is higher in VAP than normal. It might associate with VAP and seems to be a susceptablity gene for VAP.

1006-217 GLU27 Variant of Beta 2 Adrenergic receptor polymorphism is a Risk Factor for Coronary Artery Disease

Emanuele Barbato, Alexandre Berger, Leen Delrue, Ganesh Manoharan, Eddy van Schuerbeeck, William Wijns, Hans De Beenhouwer, Quirino Ciampi, Jozef Bartunek, O.L.V. Clinic, Cardiovascular Center, Aalst, Belgium, Fatebenefratelli Hospital, Cardiology, Benevento, Italy

Background. Glu-27 variant of β2-adrenergic receptor (β2-AR) polymorphism is associated with several risk factors of coronary atherosclerotic disease (CAD) like obesity, high level of plasma trygliceride and hypertension. We tested the hypothesis that Gln27Glu β2-AR polymorphism is directly related to coronary artery disease (CAD).
Methods. Seven hundred and fifty-five consecutive patients were genotyped for Gln27Glu polymorphism of β2-AR. Pts were divided into 2 groups: No CAD patients with angiographically smooth coronary arteries (n=278) and CAD patients with presence of diameter stenosis (DS) >30% in at least one coronary artery (n=477). Control population consisted of 110 volunteers from the blood donor center.
Results. In control population, Glu27 allele frequency was 39%. In No CAD patients, allele frequency was similar to controls (40%, OR:1.0, 95%CI: 0.6-1.5, NS). In CAD patients, incidence of Glu 27 variant was significantly higher (47%, OR:1.4, 95%CI: 1.1-1.7, p<0.01 vs controls and no CAD). The risk for CAD was 1.9 fold higher for Glu 27 heterozygotes and 2.4 fold higher for Glu 27 homozygotes Glu 27 patients (Table).
Conclusion. The incidence of coronary artery disease is higher in patients with Glu 27 variant of the β2- adrenergic receptor. The present data suggest that Glu27 polymorphism may play a role in the progression of coronary atherosclerosis and represent a novel risk factor for coronary artery disease.

β2AR-27 (n=755)	**Coronary Stenosis (DS ≥ 30%)**	**Coronary Stenosis (DS ≥ 30%)**	
	YES	NO	
GLN/GLN	58% (134)	42% (95)	
GLN/GLU	66% (247)	34% (128)	**χ^2=6.56, p=0.038**
GLU/GLU	71% (107)	29% (44)	

1006-218 The C161T Polymorphism of Peroxisome Proliferator-Activated Receptor Gamma Gene Is Associated With the Occurrence and Severity of Coronary Artery Disease

Ting-Hsing Chao, Yi-Heng Li, Shih-Hung Chan, Jyh-Hong Chen, Hwa-Lin Wu, Guey-Yueh Shi, Liang-Miin Tsai, Li-Jen Lin, National Cheng Kung University Medical Center, Tainan, Taiwan,ROC

Background: Peroxisome proliferator-activated receptor (PPAR) is a nuclear receptor. Activation of PPAR γ with ligands could modulate some gene transcription, thereby leading to multiple antiatherogenic and fibrinolytic effects. According to our study, an association between PPAR γ C161T polymorphism and premature myocardial infarction was observed. Lipid peroxidation was significantly influenced with T allele. We hypothesized that C161T polymorphism of the exon 6 of PPAR γ is associated with the occurrence and severity of coronary artery disease (CAD).
Methods: We recruited 338 patients with angiographically documented CAD (≥ 50% diameter narrowing in one major coronary artery or its major branches) and 310 controls in our hospital. The C161T polymorphism was examined using polymerase chain reaction and restriction fragment length polymorphism.
Results: The frequencies of the CC, CT, and TT genotypes in controls were 50.3%, 43.9%, and 5.8%, respectively, which were in Hardy-Weinberg equilibrium. The frequency of the PPAR γ CT+TT genotype among patients with CAD was significantly higher than that in controls (59.8% vs. 49.7%, p=0.01). By a simple χ^2 comparison, there was a significant association between PPAR γ genotypes and the number of significant diseased vessels (p=0.002). This association was still significant after adjustment of conventional coronary risk factors. In multivariate logistic regression analyses, we found CT+TT genotypes (OR 1.7, 95% CI 1.2 to 2.4), smoking (OR 2.4, 95% CI 1.7 to 3.6), hypertension (OR 3.0, 95% CI 2.1 to 4.3), and diabetes mellitus (OR 2.9, 95% CI 1.8 to 4.6) were the independent risk factors for the occurrence of CAD.
Conclusions: T allele carriers of C161T polymorphism of the PPAR γ gene had a significantly higher risk for CAD in terms of the occurrence and severity.

1006-221 **Effects of Sarpogrelate HCl, a Selective 5-HT2A Antagonist, on Endothelial Function and Aortic Stiffness in Diabetic Patients With Stable Angina**

Hideki Watanabe, Kinu Medical Association Hospital, Mitsukaido, Japan, Makabe-Silvertopia Facilities for Geriatric Care, Makabe, Japan

Background: Sarpogrelate HCl is a novel serotonin blocker, which specifically antagonizes 5-HT2A receptors, and it has potential as an antianginal drug. We assessed the effects of sarpogrelate HCl on endothelial function and aortic stiffness in diabetic patients with stable angina.
Methods: Twenty patients with type 2 diabetic mellitus (DM) and stable angina were randomized to receive sarpogrelate HCl (sarpogrelate group, 300mg/day, n=10) or not to receive sarpogrelate HCl (control group, n=10) after the standard treatment. Flow-mediated dilatation (FMD) and Nitroglycerin-induced dilatation (NID) of brachial artery were measured by using ultrasound system to evaluate endothelium - dependent and - independent vasodilation. We also measured aortic pulse wave velocity (PWV) to evaluate aortic stiffness by using oscilometric technique (form PWV/ABI, COLIN). These measurements were performed at baseline, and then at 3 and 6 months after the treatment. **Results:** At baseline, there was no difference in fasting glucose level, HbA1c, FMD, NID, and PWV between two groups. There is no difference in fasting glucose level and HbA1c at 3 and 6 months between two groups. FMD was significantly increased after 3 and 6 months in the sarpogrelate group. PWV was significantly decreased after 6 months in the sarpogrelate group. NID did not change during the study in two groups. **Conclusion:** Sarpogrelate HCl, a serotonin blocker, improves endothelial function and aortic stiffness in diabetic patients with stable angina.

		Baseline	3 months	6 months
FMD (%)	Sarpogrelate	5.7+/-0.4	7.5+/-0.9*#	8.1+/-0.6*#
	Control	5.8+/-0.5	5.8+/-0.4	5.8+/-0.5
NID (%)	Sarpogrelate	14.9+/-1.0	14.9+/-0.8	14.9+/-0.7
	Control	14.8+/-0.8	14.7+/-0.8	14.9+/-0.8
PWV (cm/sec)	Sarpogrelate	1750+/-99	1705+/-73	1506+/-62*#
	Control	1760+/-105	1712+/-93	1706+/-54
Data are means+/-SD. *p<0.01 vs Baseline, #p<0.01 vs Control				

1006-222 **Rosiglitazone Improves Myocardial Glucose Uptake in Ischemic Regions in Patients With Type 2 Diabetes. A 16 Week Randomised, Double-Blind, Placebo-Controlled Study**

Riikka Lautamäki, K.E.Juhani Airaksinen, Marko Seppänen, Jyri Toikka, Matti Luotolahti, Elizabeth Ball, Ronald Borra, Risto Härkönen, Juhani Knuuti, Murray Stewart, Pirjo Nuutila, University of Turku, Turku, Finland, GlaxoSmithKline, United Kingdom

Background: Rosiglitazone improves insulin sensitivity and skeletal muscle glucose uptake in patients with uncomplicated type 2 diabetes. In patients with ischemic coronary artery disease, glucose is an important source of energy and preserved myocardial glucose uptake is essential for the viability of the jeopardised myocardium. The effect of rosiglitazone on myocardial metabolism in type 2 diabetic patients with coronary artery disease was thus studied.
Methods: The study was randomized, double-blind and placebo-controlled. Post-hoc analysis was conducted excluding 4 subjects who were considered violators. 54 patients (38 men, 16 women) with type 2 diabetes (HbA1c 7.2+0.9%) and coronary artery disease were studied with PET and [18F]FDG during hyperinsulinemic euglycemic clamp before and after 16 week intervention period with rosiglitazone (n=27) or placebo (n=27). Ischemic regions of myocardium were determined with rest-stress 99m Tc-SPECT imaging and coronary angiography.Statistical analysis was carried out using Analysis of Covariance, adjusting for gender and baseline.
Results: Myocardial glucose uptake increased by 6.12 [0.89, 11.34] µmol/100g/min in ischemic regions (P=0.023) and by 8.40 [2.99, 13.81] µmol/100g/min in non-ischemic regions (P=0.003) on rosiglitazone as compared to placebo. The treatment effect of myocardial glucose uptake in ischemic regions based on all subjects was smaller, 4.77 [-0.37, 9.90] µmol/100g/min. In addition, whole body insulin sensitivity and glycemic control were significantly improved on rosiglitazone compared to placebo.
Conclusion: Rosiglitazone therapy significantly improves myocardial glucose uptake in type 2 diabetic patients with ischemic coronary artery disease. These results suggest that rosiglitazone therapy may facilitate myocardial glucose storage and utilization in these patients.

POSTER SESSION

1032 Myocardial Regeneration/ Revascularization

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1032-203 **Effects of Cell Transplantation Using Vascular Endothelial Growth Factor-Expressing Mesenchymal Stem Cells for Myocardial Infarction**

Ryo Matsumoto, Takashi Omura, Minoru Yoshiyama, Tetsuya Hayashi, Yasukatsu Izumi, Yasuhiro Nakamura, Kaname Akioka, Kazuhide Takeuchi, Junichi Yoshikawa, Osaka City University Medical School, Osaka, Japan

Background: Vascular endothelial growth factor (VEGF) is known to play an important role in inducing angiogenesis in ischemic regions. Mesenchymal stem cells (MSCs) may have therapeutic potential for restoring cardiac function after irreversible injury. Then, we hypothesized that transplantation of VEGF-expressing MSCs could effectively treat acute myocardial infarction (MI) by providing enhanced cardioprotective effects, followed by angiogenic effects in salvaging ischemic myocardium.
Methods: Bone marrow mononuclear cells of Lewis rats were cultured with low glucose DMEM for MSCs outgrowth. The human $VEGF_{165}$ gene was transfected to cultured MSCs using an adenoviral vector. Six million of VEGF- and LacZ-transfected MSCs (VEGF group), LacZ-transfected MSCs (Control group), or serum-free medium only (Medium group) were injected into syngeneic rat hearts one hour after left coronary artery occlusion.
Results: At one week after MI, the transplanted MSCs were detected by X-gal staining in the infarcted region. High expression of VEGF was immunohistochemically observed in the VEGF group. At 28 days after MI, infarct size, left ventricular end-diastolic and end-systolic dimensions, ejection fraction, E wave velocity / A wave velocity ratio were most improved in the VEGF group, compared with the Medium group. Under electron microscopy, small cells containing myofilaments and many interstitial cells were observed adjacent to the infarcted area, in both the VEGF and Control groups. In addition, immunohistochemically stained α-smooth muscle actin-positive cells and capillary density of the infarcted region were most increased in the VEGF group.
Conclusions: This combined strategy of cell transplantation with gene therapy could be a useful therapy for the treatment of acute MI.

1032-204 **Enhancement of The Functional Benefits of Pretreated Mesenchymal Stem Cells(MSCs) in a Rat Myocardial Infarct Model**

Jihyun Yoon, Young Hoon Kim, Wan Joo Shim, Young Moo Ro, Do-Sun Lim, Korea University Medical Center, Seoul, South Korea

Background: Mesenchymal stem cells (MSCs) offer a novel therapeutic option in the treatment of acute myocardial infarction. MSCs are able to differentiate into myogenic cells after 5-azacytitinde treatment. However, 5-azacytidine might have genotoxic effects. Recently, it was reported that combined treatment with **bone morphogenetic protein-2**(BMP-2) and **fibroblast growth factor-4**(FGF-4) caused cardiac differentiation in non-precardiac mesoderm explants. Therefore, we investigated whether MSCs treated with combined BMP-2 and FGF-4 showed evidence of myogenic differentiation in vitro, and whether these cells resulted in sustained engraftment, myogenic differentiation, and improved cardiac function after implantation in infarcted myocardium.
Methods and Results: In vitro study: MSCs were treated with BMP-2 + FGF-4 (GF-MSCs) and myogenic phenotype was evaluated immunohistochemically. Cell growth curve was used to compare MSC proliferative capacity between the growth factors and 5-azacytidine treatments. **In vivo study:** Two weeks after coronary artery occlusion, GF-MSCs (n = 15), MSCs (n = 5) labeled with PKH26 were injected into infarcted myocardium. Control animals (n = 5) received a culture medium into the infarcted myocardium. Two weeks after implantation, some engrafted GF-MSCs or MSCs expressed sarcomeric-a-actinin and cardiac myosin heavy chain, as was observed in culture. Echocardiography showed that GF-MSC group had better (p<0.05) left ventricular performance than the other groups.
Conclusion: GF-MSCs were induced myogenic differentiation in vitro. Moreover, GF-MSCs engrafted into the infarcted myocardium appeared to myogenic differentiation, prevented dilation of the infarcted region, and eventually improved heart function.

1032-205 **Early Treatment With Fluvastatin Enhances the Mobilization of $CD34^+$, $CD117^+$, $CXCR4^+$, $C\text{-}met^+$ Stem Cells Into Peripheral Blood in Patients With Acute Myocardial Infarction: LAVA Trial**

Wojciech Wojakowski, Anna Michalowska, Marcin Majka, Katarzyna Maslankiewicz, Rafal Wyderka, Marek Krol, Andrzej Ochala, Mariusz Z. Ratajczak, Michal Tendera, SIlesian School of Medicine, Polish-American Childrens Hospital, Katowice, Krakow, Poland, Stem Cell Biology Program at James Graham Brown Cancer Center, University of Louisville, Louisville, KY

BACKGROUND: Stem cells can be mobilized into the peripheral blood in the setting of acute myocardial infarction. Statins use is associated with improved survival in patients with acute coronary syndromes. Aim of the study was to assess the influence of early (< 12 hours) and late (first dose given on 4.-5. day after admission) treatment with 80 mg of fluvastatin on the dynamics and magnitude of stem cell mobilization in patients with STEMI.
METHODS: 25 patients with STEMI (< 12 hours after chest pain onset) and randomized to early treatment (group A, n=13) and late treatment (group B, n=12) with 80 mg of

fluvastatin. 20 patients with stable angina were the controls. Peripheral blood samples were drawn on admission, after 7 and 30 days. FACSCalibur flow-cytometer was used for stem cells assay. **RESULTS:** *Table 1* shows the changes in absolute number of stem cells in both groups of STEMI patients in comparison to patients with stable angina. Stem cells numbers were significantly higher at baseline and after 7 days in all STEMI groups in comparison to stable angina and comparable after 30 days. Fluvastatin started early was associated with significantly higher number of stem cells after 7 days in comparison to group treated with fluvastatin later (day 4.-5.). There were no differences in SDF-1, VEGF, IL-6 and HFG levels between groups A and B.
CONCLUSION: Early administration of 80 mg fluvastatin significantly increases the mobilization of $CD34^+$, $CD117^+$, $c\text{-}met^+$, $CXCR4^+$ stem cells in acute myocardial infarction.

Table. Data expressed as median and range;
*p<0.05 vs. group B

	STABLE ANGINA	STEMI BASELINE	STEMI BASELINE	STEMI DAY 7	STEMI DAY 7	STEMI DAY 30	STEMI DAY 30
		GROUP A	GROUP B	GROUP A	GROUP B	GROUP A	GROUP B
$CD34^+$	430 (0-821)	930 (0-1549)	890 (0-1489)	1423 (0-1870)*	860 (0-1584)	571 (131-1121)	498 (0-821)
$CD117^+$	412 (13-3745)	824 (0-2311)	865 (0-2298)	1031 (0-2087)*	721 (0-1547)	602 (0-1599)	576 (0-2105)
$CXCR4^+$	1512 (211-2897)	2689 (321-2989)	2543 (0-3011)	2434 (0-2979)*	1724 (0-2475)	1438 (176-2265)	1232 (0-3033)
$c\text{-}met^+$	507 (34-2734)	1789 (0-2458)	1853 (0-2189)	1571 (132-2567)*	932 (0-2312)	677 (0-2060)	729 (283-2120)

Myocardial Ischemia and Infarction

1032-206 **Autologous Transplantation of a new Generated Pluripotent Cells Type of Monocytic Origin Improves Damaged Heart Function**

Nour Eddine El Mokhtari, Bettina Dresske, Hendrik Ungefroren, Maren Ruhnke, Volker Plate, Dirk Janssen, Reiner Siebert, Alexander Reinecke, Fred Fandrich, Rudiger Simon, Clinic of Cardiology, Kiel, Germany, Clinic of General and Thoracic Surgery, Kiel, Germany

Aims: Stem cell transplantation has been well demonstrated to improve cardiac function after myocardial infarction (MI). Recently, we could generate $CD34^+$,$CD90^+$ and $CD117^+$ cells from blood monocytes with pluripotent characteristics that in vitro differentiate into various somatic cell types. This study investigated wether these programmable cells of monocytic origin (PCMO) succeed to restore LV function postinfarction.
Methods: MI was induced in female LEW rats by ligation of the left coronary artery. PCMO of male LEW donors were injected either intramyocardially in the infarcted area or i.v. 24 hours or 6 days after MI. Infarcted animals receiving no cell treatment or autologous naive blood monocytes of male origin served as control. 6 weeks after transplantation, all animals underwent transthoracic echocardiography for assessment of LV dimensions and cardiac function. Additionally, PCR for the rat sex determing region of the Y-chromosome was performed of the different areas of infarcted heart muscle using microdissection technique.
Results: Intramyocardial injection of PCMO significantly improved LV function of infarcted hearts (ejection fraction (EF) 53.0 ± 15.2% in animals injected 24 hours postinfarction and EF 50.8 ± 4.3 % in animals injected after 6 days versus EF 38.3 ± 8.7% in untreated rats, p< 0.05) while transplantation of naive blood monocytes failed to restore damaged heart function (EF 39.3 ± 17.2%). Interestingly, early i.v. cell transplantation had the same effect as intramyocardial injection and improved the ejection fraction to 54.1 ± 14.2%. 6 days after myocardial infarction systemic application was ineffective in the rat model (EF 30.3 ± 2.1%). PCR for the Y-chromosome was positive solely in the area beside the infarction while no DNA could be detected in the infarcted area or in the right ventricle.
Conclusions: Intramyocardial transplantation of autologous PCMO significantly improved damaged heart function after MI. Moreover, this study demonstrated that also systemic application of these cells succeed to restore cardiac function. In combination with the superior availability, the transplantation of PCMO promise effective clinical appproach.

1032-207 **Dose-Dependent Contribution of CD34-positive Cell Transplantation to Cardiomyogenesis, Vasculogenesis and Arteriogenesis with Functional Recovery Post-Myocardial Infarction**

Hiroto Iwasaki, Atsuhiko Kawamoto, Masakazu Ishikawa, Akira Oyamada, Shuko Nakamori, Hiromi Nishimura, Kazuyo Sadamoto, Miki Horii, Satoshi Murasawa, Toshihiko Shibata, Shigefumi Suehiro, Takayuki Asahara, RIKEN, Kobe Institution of Biomedical Research and Innovation, Kobe, Japan, RIKEN Center for Developmental Biology, Kobe, Japan

Background: Transformation capacity of the CD34+ cells into cardiomyocyte (CMCs) and smooth muscle cells (SMCs) is still controversial. Here, we performed a series of experiments to prove our hypothesis that cardiomyogenesis and arteriogenesis post myocardial infarction (MI) may be dose-dependently enhanced following CD34+ cell transplantation.
Methods: Peripheral blood CD34+ cells were isolated from total mononuclear cells of a patient with critical limb ischemia by apheresis after 5-day administration of G-CSF, using a magnetic cell sorting system. PBS, $1x10^3$ CD34+ cells (Low), $1x10^5$ CD34+ cells (Mid) or $5x10^5$ CD34+ cells (High) were intramyocardially transplanted 20 min after ligating LAD of nude rats (n=12 in each group). Functional, histological and gene expression outcomes were compared among the groups.
Results: Functional assessments using echocardiography and a micro-tip conductance catheter at day 28 revealed dose-dependent preservation of LV function by CD34+ cell transplantation. Necropsy examination at day 28 disclosed dose-dependent augmentation of capillary density by isolectin B4 staining (High group, 714.3±25.0; Mid group, 535.8±31.0; Low group, 320.9±36.0; PBS group, 291.3±19.0 /mm^2 respectively. P<0.01 for High vs Mid and Mid vs Low) and dose-dependent inhibition of LV remodeling by assessing % fibrosis area (High group, 16.0±2.6; Mid group, 22.4±1.9; Low group, 30.7 ±3.9; PBS, 31.5±0.7% respectively. P<0.01 for High vs Mid and Mid vs Low groups). Immunohistochemistry for human-specific BNP demonstrated that human CMCs were more frequently observed in ischemic myocardium at day 28 in High and Mid groups than Low group. Immunostaining for smooth muscle actin and human leukocyte antigen or Ulex europaeus lectin type 1 also revealed dose-dependent vasculogenesis and arteriogenesis following CD34+ cell transplantation. RT-PCR indicated that human specific gene expression of CMC, SMC and endothelial cell markers were dose-dependently augmented in MI tissue.
Conclusion: CD34+ cell transplantation may have significant and dose-dependent potential for cardiomyogenesis, vasculogenesis and arteriogenesis with functional recovery from MI.

1032-208 **Paracrine Action Accounts for Marked Protection of Ischemic Heart by Akt Modified Mesenchymal Stem Cells**

Massimiliano Gnecchi, Huamei He, Nicolas Noiseux, Olin D. Liang, Lunan Zhang, Luis G. Melo, Richard E. Pratt, Joanne S. Ingwall, Victor J. Dzau, Brigham and Women's Hospital, Boston, MA, Duke University Medical Center, Durham, NC

Background: We reported that transplantation of rat mesenchymal stem cells overexpressing Akt (Akt-MSC) limits ventricular remodeling and restores cardiac function 2 weeks following myocardial infarction. Moreover we showed that the same therapeutic effects occur in less than 72 hours. Since this early protective effect cannot be attributed to myocardial regeneration, we hypothesised that a paracrine mechanism mediated by factor(s) secreted from Akt-MSC is involved. Accordingly, we tested the protective effect of conditioned medium from Akt-MSC both *in vitro* and *in vivo*.
Methods: Conditioned medium was collected from control MSC (GFP-MSC) and Akt-MSC grown in normoxia (N-M) or exposed for 12 hours to hypoxia (H-M). Isolated adult rat ventricular cardiomyocytes (ARVC) were exposed to 24 hours of hypoxia in presence of either standard growth medium (CTR-M), N-M or H-M from GFP-MSC and N-M or H-M from Akt-MSC. Myocardial infarction was induced in rats by permanent ligation of the left coronary artery. After 30 minutes H-M from GFP- or Akt-MSC was injected in the heart. Sham and PBS-injected animals served as controls. At 72 hours cardiac function was measured with Langendorff preparation and infarct size was determined with TTC staining.
Results: Maximal protection on hypoxic ARVC was seen with H-M. Both GFP- and Akt-MSC H-M significantly decreased caspase 3 activity compared with CTR-M. However, the effect of Akt-MSC H-M was greater: compared with CTR-M and GFP H-M a reduction respectively of 78% (p<0.05) and 66% (p<0.05) was observed. Moreover, compared with CTR-M and GFP-MSCs H-M in the presence of Akt-MSC H-M there were respectively 62% (p<0.05) and 54% (p<0.05) fewer TUNEL-positive ARVC. *In vivo,* Akt-MSC H-M significantly increased left ventricular systolic pressure (Sham: 108±5; PBS: 72±6; GFP-MSC H-M: 75±5; Akt-MSC H-M: 96±2, p<0.05 vs PBS and GFP-MSC H-M; values in mmHg). Infarct size was significantly smaller in Akt-MSC H-M group (PBS: 33±5%; GFP-MSC H-M: 29±4%; AKT-MSC H-M: 15±4%: p<0.05 vs PBS and GFP-MSC H-M).
Conclusion: We conclude that paracrine protective action by released factor(s) is a major mechanism in post-infarction healing process observed after Akt-MSC transplantation.

POSTER SESSION

1033 Predictors and Markers for Acute Ischemic Syndrome

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1033-215 **Impact of Prediabetic State on Clinical Outcomes in Patients With Acute Coronary Syndrome**

Richard Otten, Eva Kline-Rogers, David J. Meier, Rupal Dumasia, Niquole May, Yuri Resin, Ranya Sweis, Jianming Fang, Fadi Saab, Mircea Petrina, Kim A. Eagle, Debabrata Mukherjee, University of Michigan, Ann Arbor, MI

Background: The American Diabetes Association [ADA] recently redefined the cutpoint for normal fasting blood glucose levels from 110 mg/dl to 100 mg/dl, meaning that a value of 100 mg/dl or above would lead to a diagnosis of impaired fasting glucose (IFG), which is included in the term pre-diabetes. We assessed the impact of the prediabetic state on clinical outcomes in patients presenting with acute coronary syndrome [ACS] incorporating the new ADA definition.
Methods: 1763 patients with ACS between Jan 1999 and Aug 2002 were stratified based on their fasting glucose levels as non-diabetic, prediabetic or with known diabetes. We compared in-hospital outcomes including death, re-infarction, stroke, cardiogenic shock, pulmonary edema, cardiac arrest, atrial dysrythmias and MACE in the different groups.
Results: Adverse clinical events were significantly higher in prediabetic and diabetic patients compared to those with normal fasting glucose [Table]. Multivariate risk adjustment demonstrated a gradient of risk in patients with prediabetes proportional to fasting glucose levels.
Conclusions: This pilot study suggests that prediabetic state is a marker for worse prognosis in patients with ACS. The new ADA definition identifies more patients with impaired fasting glucose who may be targeted for optimal therapies to improve clinical outcomes. This study validated the higher risk profile in patients with impaired fasting glucose identified by the new ADA definition.

Clinical event rates in pre-diabetic patients

	Fasting glucose < 100 mg/dl; n=579	Fasting glucose 100 -110 mg/dl; n=215	Fasting glucose 110 -126 mg/dl; n=215	Diabetic; n=277	P value [4-way]
Death	1.04%	0.93%	1.56%	6.69%	<0.001
Reinfarction	0.49%	2.21%	0%	0.96%	0.194
Stroke	0.17%	0%	0%	1.16%	0.033
Pulmonary edma	2.21%	3.68%	3.36%	10.8%	<0.001
MACE	6.74%	8.84%	14.58%	19.95%	**<0.001**
Multivariate Risk adjusted effect of fasting blood glucose levels on clinical outcome					
Fasting glucose 100 -110 mg/dl		1.308 [95% CI 0.728 - 2.350]		P=0.369	
Fasting glucose 110 -126 mg/dl		1.850 [95% CI 1.086 - 3.153]		P=0.023	
Diabetic		2.982 [95% CI 2.034 - 4.371]		P<0.001	

1033-216 Impact Of Fasting Glucose Abnormality On Heart Failure In Patients With Acute Myocardial Infarction. Data From Rico Survey

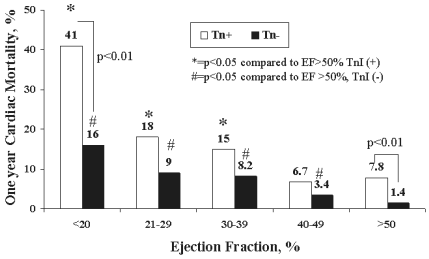
Marianne Zeller, Jack Ravisy, Gilles Rioufol, Hamib Makki, Mohamed Jolak, Alexandra Oudot, Luc Janin-Manificat, Isabelle L'Huillier, Jean Eric Wolf, Bruno Verges, Luc Rochette, Yves Cottin, on behalf of the RICO survey working group, University of Burgundy, Dijon, France

Objectives: Recent works have described the major effects of fasting glucose abnormality, including diabetes mellitus (DM) and Impaired Fasting Glucose (IFG), on the onset of in-hospital cardiogenic shock development and mortality after acute myocardial infarction (MI). However, very few studies have investigated the influence of abnormal fasting glycemia on the occurrence of heart failure (HF) after MI.
Methods: Between January 2001 and July 2003, all patients hospitalized with acute MI in one region of France were included. Patients with prior HF or cardiogenic shock during the in-hospital stay were excluded from the study. Patients with HF (Killip class II or III) were compared with patients without HF. Mean fasting blood glucose (FG) was determined at day 4 and 5 after admission. FG abnormality was defined for patients with either DM (FG > 7 mm/L or clinical history of DM) or IFG (FG 6.1 to 7 mmole/L). **Results :** Among the 894 patients, 202 (22%) had HF. Median age was significantly higher in the HF group than in patients without HF (75 vs 63 y, p<0.0001). Moreover, patients with HF had significantly higher rate of cardiovascular risk factors. Patients with HF were more likely to have a FG abnormality (69 vs 45 %, p<0.001), and had higher HbA1c median level (6.1 vs 5.7 %, p<0.01). The incidence of MI with ST elevation (STEMI) or with anterior location was similar for the 2 groups (p=ns). Patients with HF had increased median pulse measured at the time of admission (85 vs 74 b/min, p<0.01) and higher incidence of altered LVEF (≤40%) (28 vs 10%, p<0.05). There was a significant increase in hospital mortality in the HF group (12 vs 3 %, p<0.001). By logistic regression analysis, HF was a strong independent predictor of hospital death (OR, 4.53; 99% CI, 2.01-10.17, p<0.0001). FG abnormality was an independent predictor of HF, even after adjustment for covariates (age, gender (male is reference), hypertension, prior MI, STEMI, LVEF, and creatinine level) (OR, 2.58; 99% CI, 1.58-3.96, p<0.0001). **Conclusion.** Abnormal FG was associated with an increased risk of developing heart failure in the setting of acute myocardial infarction. Further studies are needed to evaluate the specific strategies for this population.

1033-217 Does Ejection Fraction Still Predict Mortality in the Era of the Troponin-Based Definition of Myocardial Infarction?

Michael C. Kontos, Rajat Garg, F Philip Anderson, Joseph P. Ornato, James L. Tatum, Robert L. Jesse, Virginia Commonwealth Univeristy, Richmond, VA

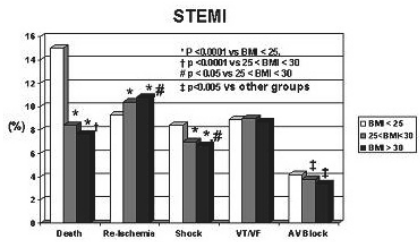
BACKGROUND: A curvilinear relationship between ejection fraction (EF) and mortality has been shown in patients (pts) with myocardial infarction (MI). However, most data were derived from multi-center randomized controlled trials that included only pts with ST elevation MI, and used CK as the MI gold standard. We questioned whether a similar relationship holds when troponin is used as the diagnostic criteria for MI in non-ST elevation ACS pts.
METHODS: Consecutive pts without ST elevation admitted from the ED for exclusion of ACS underwent serial assessment of cardiac markers (CK, CK-MB, TnI). EF was assessed using gated SPECT, coronary angiography, or echocardiography during admission. An elevated TnI was defined using the ACC/ESC criteria. One year cardiac mortality was compared in those with and without TnI elevations.
RESULTS: Among the 3,074 consecutive pts admitted without ST elevation MI who had EF assessed, MI was diagnosed by TnI elevations in 545 pts (18%). AMI pts were more likely to have any systolic dysfunction (EF <50%: 51% vs 30%, p<0.001) and an EF <35% (25% vs 11%, p<0.001) than those without TnI elevations. There was a stepwise increase in mortality based on both TnI status and EF (Figure).
CONCLUSIONS: EF is a powerful predictor of mortality in pts admitted for exclusion of MI. The presence of TnI elevations increases mortality 2 fold or more for any given EF, even when EF is normal. Pts presenting with possible ACS should have EF assessed routinely, even in those without troponin elevations.



1033-218 Obesity Is Associated With Reduced Mortality And Complication Rates In Stemi: Results From The National Registry For Myocardial Infarction 4

R. Scott Wright, Joseph G. Murphy, Paul Frederick, Allan S. Jaffe, William J. French, Mayo Clinic, Rochester, MN, Harbor UCLA Medical Center, Los Angeles, CA

Background: Obesity is a public health crisis in the United States and many parts of the world. Preliminary reports suggest an "obesity paradox" in acute myocardial infarction (AMI) in that obesity is associated with lower mortality risks.
Methods: Using the National Registry for Myocardial Infarction (NRMI)-4 database, we identified 172,061 patients with STEMI dividing into obese (BMI > 30 kg/m2 n=52,674), overweight (25< BMI < 30, n=63,747) and lean (BMI < 25, n=55,640) patients.
Results: Age was significantly lower in obese (61.7± 12.1˙,† years) versus overweight (65.4± 13.0˙) and lean patients (71.4± 13.6), (* p<0.0001 vs lean, † p <0.0001 vs overweight). TIMI Risk Scores (TRS), calculated in non-transfer STEMI patients (n=120,739), revealed Low risk TRS in 17.9% of lean patients, 33.5% of overweight patients and 41.7% of obese patients. High risk TRS were observed in 55.8 % of lean patients, 37.2% of overweight patients and 30.3% of obese patients (p<0.00001 across groups). Use of reperfusion therapy was higher in obese (63.6%˙,†) and overweight patients (62.4%˙) compared to lean patients (47.7%). Risks of death, shock and high-grade AV block were significantly lower in obese and overweight patients (See figure).
Conclusion: The "obesity paradox" may reflect that obese patients are younger and have lower TRS at time of presentation for STEMI. They indeed suffer lower risks for death, shock and high-grade AV block yet this may reflect younger age and risk profile at time of STEMI.



1033-219 Chest Pain At Presentation And Delayed Resolution Of Pain In Patients Admitted With Non- ST Segment Elevation Acute Coronary Syndromes Predicts Short-term Outcomes

Benjamin Scirica, Sabina Murphy, Stephen Wiviott, David Morrow, Marc Sabatine, C. Micheal Gibson, Christopher Cannon, Brigham and Women's Hospital, Boston, MA

Background: Ischemic chest pain is the hallmark of non- ST segment elevation acute coronary syndromes (NSTEACS). Although the duration of pain is often deemed clinical important, there is limited data to suggest that the timing of chest pain resolution has prognostic value.
Methods: Time to chest pain resolution was evaluated in 6963 patients with NSTEACS enrolled in the Orbofiban in Patients with Unstable Coronary Syndromes (OPUS) - TIMI 16 trial. Outcomes included death, recurrent myocardial infarction (MI), recurrent ischemia at 30 days, and baseline levels of creatine kinase-MB(CKMB) .
Results: Patients who had chest pain on arrival to the hospital were at increased risk of death or recurrent MI (4.6% vs. 3.3%, p<0.001) and death/recurrent MI/recurrent ischemia (10.8% vs. 8.9%, p=0.01). In patients who presented with chest pain, a prolonged time to resolution of pain was associated with worse outcomes and increased baseline CKMB levels (Table). The groups were comparable in terms of aspirin, heparin, beta-blockers or nitrates use.

30 Day outcomes by time of chest pain resolution

Time when chest pain resolved	Death (%)	MI (%)	Death/MI (%)	Death/MI/Recurrent ischemia (%)
Pre-hospitalization (n=3426)	1.4	2.2	3.3	8.9
< 30 min after arrival (n=555)	0.7	2.3	2.7	7.0
> 30 min after arrival (n=2332)	**2.2**	**3.3**	**5.0**	**11.7**
P value	0.012	0.031	0.001	0.0001

Conclusion: In patients presenting with NSTEACS, resolution of chest pain before hospital arrival was associated with better outcomes. If the pain persisted beyond 30 minutes after hospital arrival, patients were more likely to have recurrent MI, ischemia, or die by 30 days.

1033-220 Genetic Polymorphisms C807T and A1648G on Platelet Glycoprotein Ia, are Associated With Premature Myocardial Infarction in Young Smokers

Charalambos Antoniades, Dimitris Tousoulis, Carmen Vasiliadou, Christos Pitsavos, Christina Chrysochoou, Marina Toutouza, Demos Panagiotakos, Costas Toutouzas, Kyriakoula Marinou, Christodoulos Stefanadis, Athens University Medical School, Athens, Greece

Background: Platelet membrane glycoprotein Ia (GPIa) has an important role in platelet function as a receptor for collagen. Silent genetic polymorphism C807T seems to affect the expression of GPIa, while A1648G polymorphism leads to a Glu/Lys substitution on GPIa. We investigated whether these polymorphisms affect the risk for premature myocardial infarction (MI) in young individuals.
Methods: This study enrolled 191 young patients with premature MI (46.6±5.2 years old) and 284 healthy controls (48.1±13.5 years old). Distributions of the C807T and A1648G polymorphisms were investigated by genotyping DNA by PCR. The allele and genotype frequencies in patients and controls were compared using chi-square test. There was no deviation from Hardy-Weinberg equilibrium for any of the considered polymorphisms.
Results: The prevalence of 807TT homozygotes was slightly higher among MI patients (30 patients, 15.7%) compared to healthy controls (35 subjects, 12.4%, p=NS). The 807CC genotype was present in 65 MI patients (34%) and in 88 controls (31.0%, p=NS), while the 807CT genotype was present in 96 MI patients (50.2%) and 161 controls (56.6%, p=NS). However, among smokers, the prevalence of 807TT was present in 27 of 174 MI patients (15.5%) and in 11 of 114 controls (9.6%, p<0.05). Homozygosity for the 1648A allele existed in 6 MI patients (3.2%) and in only 1 control (0.3%, p<0.05). 1648AG genotype was present in 38 MI patients (19.9%) and in 66 controls (23.2%, p=NS), while the 1648GG genotype was present in 147 MI patients (76.9%) and 217 controls (76.5%, p=NS). Among smokers, 1648AA genotype was observed in 6 MI patients (3.4%) and in none of the controls (p<0.05).
Conclusions: The present study supports that both genetic polymorphisms C807T and A1648G on platelet glycoprotein Ia, are associated with the development of premature myocardial infarction in young smokers

1033-221 Impact of Diabetes on In-Hospital Mortality Following Percutaneous Coronary Intervention for Acute Myocardial Infarction: A Report From the New York State Coronary Angioplasty Reporting System Database

Ramesh Gowda, David L. Brown, Beth Israel Medical Center, New York City, NY

Background: The presence of diabetes mellitus (DM) confers high risk for adverse clinical outcomes following acute myocardial infarction (AMI). Limited information exists regarding the impact of DM on short-term outcomes following percutaneous coronary intervention (PCI) for AMI.
Methods: We conducted a retrospective cohort study of all patients undergoing angioplasty within 24 hours of an AMI in New York State between 1997 and 1999. The primary end point was in-hospital mortality. Diabetes was defined by treatment with oral hypoglycemics or insulin.
Results: Of 9015 patients who underwent PCI for AMI, 1583 (17.6%) were diabetics. Diabetics were older (62 years vs. 60 years, P=<0.001), more often female (37.7% vs. 27.2%, P=<0.001) but less often current smokers (18.7% vs. 30.9%, P<0.001) than non-diabetics. Hypertension (72% vs. 52%, P=<0.001), congestive heart failure (CHF), (4.7% vs. 1.8%, P=<0.001), stroke (5.5% vs. 3.6%, P=<0.001), chronic renal insufficiency (2.2% vs. 0.6%, P=<0.001), dialysis (0.9% vs. 0.3%, P=<0.001), prior open heart surgery (10.9% vs. 5.9%, P=<0.001) and vascular disease (9.4% vs. 5.1%, P<0.001) were more common in diabetics. The mean ejection fraction was reduced in diabetics (45% vs. 47%, P<0.001). More patients with DM developed CHF (15.5% vs. 9.9%, P<0.001) and shock (5.4% vs. 3.6%, P=0.001). Use of stents was less common (74.2% vs. 79.2%, P<0.001) and intraaortic balloon pump more common (9.2% vs. 7.1%, P=0.004) in diabetics. Acute vessel closure was more common among diabetics (1.6% vs. 0.7%, P=0.001) while stent thrombosis and emergency bypass surgery did not differ significantly between groups. Unadjusted in-hospital mortality was higher in diabetics than non-diabetics (7.3% vs. 3.7%, P<0.001). On multivariate logistic regression analysis to adjust for differences in baseline characteristics, diabetes was associated with a 50% increase in the risk of in-hospital mortality (Odds Ratio 1.52, 95% CI 1.094-2.118, P<0.013).
Conclusion: Diabetics who undergo PCI for AMI are an extremely high-risk population. However, even after adjustment for their high-risk features, they maintain a 1.5-fold increased risk of in-hospital death.

1033-222 Impact of Cardiac Over-expression of Placental Growth Factor on the Improvement of Chronic Phase Left Ventricular Function in Patients with Acute Myocardial Infarction

Hajime Iwama, Shiro Uemura, Noriyuki Naya, Keiichi Imagawa, Kenji Onoue, Yasuhiro Takemoto, Osamu Asai, Satoshi Okayama, Yukiji Takeda, Yoshitomi Kida, Minoru Takaoka, Hiroyuki Kawata, Manabu Horii, Tamio Nakajima, Yoshihiko Saito, Nara medical university, Kashihara, Nara, Japan

Placental growth factor (PlGF), a specific ligand for flt-1, is known to stimulate the recruitment of monocyte from bone marrow into the injured tissue, and seems to enhance wound healing processes by activating monocyte and inducing arteriogenesis. However, clinical significance of PlGF in myocardial infarction (MI) has not been understood. This study investigated expression pattern of PlGF and the impact of PlGF on the clinical course in patients and mouse models of acute MI.
Methods and Results: Human study: Fifty five patients with acute MI and 43 controls were enrolled. Blood sampling was performed from peripheral vein, ostium of coronary artery (CA), and coronary sinus (CS), before and after recanalization (RC) of occluded CA. Plasma levels of PlGF were measured by ELISA. Transcardiac gradient of plasma PlGF ([CS]-[CA]) just after RC of the occluded CA was significantly higher than the value before RC (14.1±10.6 vs, 0.0±1.1pg/ml p<0.01), indicating cardiac production and release of PlGF from infarct heart. Peak plasma PlGF levels (3.2 ± 1.1 days) were significantly higher than those in control subjects (35.1±26.5 pg/ml vs 13.4±5.7 pg/ml, p<0.001). Peak plasma PlGF levels positively correlated with peak peripheral monocyte counts during acute phase of MI (r=0.42, p<0.005), although they did not correlated with age, gender, time to reperfusion, or peak CK-MB. Furthermore, multiple regression analysis revealed that PlGF was the strongest independent predictor for the restoration of left ventricular ejection fraction examined at 6-month follow-up study (p=0.0098). Mouse study: In mouse models of MI, tissue PlGF mRNA expression was increased 26.6 fold (p<0.001) compared with sham operated heart. Immunohistochemical staining showed that PlGF protein was over-expressed mainly in endothelial cells of coronary artery in the infarct region, but scarcely in non-infarct region.
Conclusion: PlGF is rapidly produced in the infarct myocardial tissue, especially endothelial cells of coronary artery in infarct region during acute phase of MI, and over-expressed PlGF seems to be involved in the improvement of left ventricular function in chronic phase probably by recruiting monocyte from bone marrow.

POSTER SESSION

1034 Mechanical and Pharmacologic Innovations for Acute Myocardial Ischemia and Infarction Care

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1034-195 Effectiveness of Distal Embolic Protection During Primary Angioplasty: Final 6-Month Results from the Prospective, Randomized, EMERALD Trial

Gregg W. Stone, John Webb, David A. Cox, Bruce R. Brodie, Mansoor Qureshi, Daniel Dulas, Anna Kalnych, Mark Turco, Heinz P. Schultheiss, Barry Rutherford, Mitchell W. Kruckoff, Raymond Gibbons, Alexandra J. Lansky, Allan Schwartz, Ramona Pop, Denise Jones, Roxana Mehran, Columbia University Medical Center, New York, NY, Cardiovascular Research Foundation, New York, NY

Background. Distal embolization during PCI for AMI is common, and may result in diminished myocardial perfusion, incomplete ST segment resolution (STR), impaired myocardial recovery and increased mortality. We therefore performed a multicenter randomized trial to determine whether retrieval of distal embolic debris translates into improved reperfusion success and clinical outcomes.
Methods. In the EMERALD trial, 501 pts w/i 6 hrs of pain onset with ≥2 mm ST elevation or LBBB undergoing primary or rescue PCI were prospectively randomized at 38 sites in 7 countries to stenting with vs. without distal protection with the 0.028" GuardWire Plus. The primary endpoints were STR 30 mins post procedure (measured by 24 hr continuous ECG monitoring) and infarct size assessed by tc-99m-sestamibi imaging at day 5-14.

Results. Median age was 59 years, 22% were women, 40% had anterior MI, and median peak ST elevation was 4.0 mm. Primary PCI was performed in 81.4% of pts and rescue PCI in 18.6%. Median symptom onset to ER time was 77 minutes. In the GuardWire arm, balloon occlusion was achieved in 95% of pts, aspiration was performed in 97%, and visible debris was retrieved in 72%. Results appear in the table.
Conclusions. The GuardWire distal protection device may be used safely as an adjunct to primary PCI in AMI, and effectively retrieves embolic debris in most patients. Nonetheless, distal embolic protection did not result in improved microvascular flow or function, nor was infarct size reduced or event-free survival improved.

	GuardWire (n=252)	Control (n=249)	P value
Final TIMI-3	91.6%	89.2%	0.44
Final blush grade 3	61.1%	52.9%	0.09
STR 30 mins	62.2%	60.6%	0.77
Infarct size (%LV)	18.3 ± 19.4	16.2 ± 19.1	0.26
6 mo death	3.5%	3.5%	0.90
6 mo reinfarction	2.5%	4.0%	0.37
6 mo disabling stroke	0.9%	1.8%	0.37
6 mo TVR	6.4%	6.0%	0.83
6 mo MACE	10.1%	11.5%	0.61

1034-196 Catheter-Based Trans-coronary Myocardial Hypothermia Attenuates Arrhythmia and Myocardial Necrosis in Pigs With Acute Myocardial Infarction

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Background: Although lowering myocardial temperature by 3-5°C is effective in attenuating myocardial infarction (MI), efficient myocardial cooling could not be obtained with systemic hypothermia. We invented a new idea that direct cold saline injection into MI-related coronary artery through the over the wire PTCA balloon (OTWB) lumen.

Methods: Anesthetized pigs received 60min of coronary artery occlusion with OTWB and 3hr reperfusion. After 15 min of occlusion, the pigs were randomly assigned to either: hypothermia group (H: n=13), or control group (N: n=15). In H animals, cold saline (4°C) was given to ischemic myocardium through the wire lumen of OTWB with150 ml/hr (determined with preliminary study). In N pigs, same volume of normothermal saline (36.5°C) was administered through OTWB. Myocardial and systemic temperature, incidence of ventricular tachycardia (VT), coronary flow reserve (CFR) by Doppler flow wire, serum troponin T variables, and ratio of necrosis to ischemic risk area using blue dye and triphenyltetrazolium chloride staining were evaluated.
Result: In H group, myocardial temperature significantly decreased from 36.3±1.0 to 33.1°C±0.5°C (p<0.001) without significant reduction of rectal temperature, while temperatures in N group did not change. Incidence of VT was 38% in H and 73% in N group. At 1hr reperfusion, CFR in H was significantly higher than that in N (H:2.44±0.5 vs N:1.75±02, p=0.010). The values of troponin T was significantly lower in H than in N (H:0.85±0.61µg/ml vs N:2.84±2.74, p=0.037). Although ischemic risk area were similar in both groups, the ratio of necrosis to risk area in H was significantly smaller than that in N (H:9±7% vs N:36±12%, p<0.001). It was 75% necrosis area reduction.
Conclusion: We successfully obtained regional hypothermia within only ischemic myocardium using OTWB. This method dramatically reduced arrhythmia and MI size without any complication and is simple enough to permit widespread clinical use.

1034-197 Multivessel Revascularization in the Setting of Primary Percutaneous Coronary Intervention for Acute ST-Elevation Myocardial Infarction

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Background: The goal of primary percutaneous coronary intervention (PCI) is to restore flow in the infarct related artery (IRA). The optimal management of severe stenoses in other major coronary artery distributions is not clear. We hypothesized that revascularization of severe non-IRA stenoses at the time, or within 60 days, of primary PCI is associated with improved mortality.
Methods: We retrospectively evaluated patients undergoing primary PCI for ST-elevation myocardial infarction between January 2000 and December 2003. Exclusion criteria included cardiogenic shock, CABG performed for complete revascularization, or non-IRA chronic total occlusions. The final study population consisted of 364 patients who underwent a PCI on the culprit lesion, and patients were divided into three groups based on their coronary anatomy and the strategy of further PCI: patients with attempted PCI of ≥1 non-IRA stenosis of 70-99% within 60 days (group A, n=52), patients with ≥1 non-IRA stenosis of 70-99% on which no PCI was attempted within 60 days (group B, n=50), and patients without any non-IRA stenoses of 70-99% (group C, n=262).
Results: In group A, 34 of the 52 patients (65.4%) underwent PCI on the non-culprit lesion during the index procedure. Among the 18 patients who had a staged procedure, the median interval between the two PCIs was 6 days. The patients in group A had a higher cumulative survival by Kaplan-Meier analysis compared to patients in groups B and C: 96.9% vs. 73.4% vs. 89.7% at 2 years, respectively, p=0.0006. Likewise, when groups A and C were combined into a group with more complete revascularization, the survival was higher compared to group B (less complete revascularization): 90.9% vs. 73.4% at 2 years, respectively, p=0.0004. This survival benefit remained significant (HR 0.34, p=0.017) in a multivariate analysis including important clinical and procedural variables.
Conclusions: Among patients undergoing primary PCI, treatment of non-IRA stenoses immediately, or within 60 days, of primary PCI appears to be associated with improved survival. Consideration should be given to this strategy in selected patients.

1034-198 Long-Term Follow-Up of Patients With ST-Segment Elevation Myocardial Infarction Treated With Sirolumis-Eluting Stents

Haris Athar, Rachid Elkoustaf, Justin B. Lundbye, Edcar D. Messer, Jeffrey F. Mather, Roger A. Mennett, Jill Cloutier-Jarvis, Daniel B. Fram, William E. Boden, Raymond G. McKay, Francis J. Kiernan, Hartford Hospital, University of Connecticut, Hartford, CT

Background: Sirolimus drug-elusting stents (DES) have been shown to confer superior long-term outcomes in patients undergoing elective percutaneous coronary intervention (PCI). To-date, however, the in-hospital and long-term safety and efficacy of Sirolimus DES in patients with ST-segment elevation myocardial infarction (STEMI) has been incompletely described.
Methods: We assessed baseline clinical and angiographic characteristics, in-hospital and 9-month major adverse cardiac events (MACE) in 429 consecutive STEMI patients without cardiogenic shock undergoing emergency PCI. STEMI patients were divided into 210 patients treated with one or more Sirolimus DES and 219 patients treated with non-DES (bare metal, heparin-coated). GP IIb/IIIa inhibitors were utilized in 88.8% of patients.
Results: Compared to non-DES STEMI patients, DES patients were younger and more likely to be Caucasian. Otherwise, there were no significant differences between DES and non-DES patients with respect to baseline demographics, cardiovascular risk factors, co-morbidities, peri-procedural medication use, extent of coronary artery disease and left ventricular ejection fraction. In-hospital and 9-month MACE are presented below.

		DES	Non-DES	P Value
In-Hospital	Death	2.9%	2.3%	NS
	Stent Thrombosis	0.0%	0.9%	NS
	Emergent Repeat PCI	0.5%	0.9%	NS
	Stroke	0.0%	0.5%	NS
	Renal Failure	0.0%	0.5%	NS
9-Month	Death	3.4%	4.6%	NS
	Recurrent Myocardial Infarction	1.9%	5.0%	NS
	Repeat Catheterization	12.4%	13.2%	NS
	Angiographic Restenosis	0.5%	4.1%	<0.02

Conclusions: In this single center study, implantation of Sirolimus DES in STEMI patients is not associated with any increased risks of adverse in-hospital outcomes, and may reduce the need for repeat target vessel revascularization at 9 month follow-up.

1034-199 The Impact of Coronary Stent Placement on Survival in Patients Undergoing Angioplasty for Acute Myocardial Infarction: A Report From the New York State Coronary Angioplasty Reporting System Database

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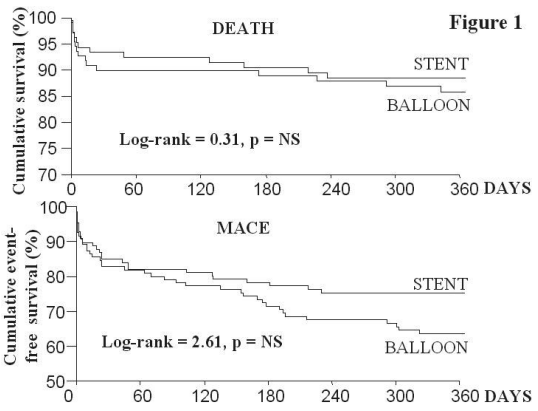
Background: Randomized trials have demonstrated the superiority of primary angioplasty with stent implantation over balloon angioplasty alone in the treatment of acute myocardial infarction (AMI). However, it remains unknown whether beneficial outcomes attained in clinical trials can be generalized to community-based practice. This study sought compare the outcome for patients with AMI undergoing coronary stent placement to those treated with balloon angioplasty alone.
Methods: We conducted a retrospective cohort study of all patients undergoing primary angioplasty for AMI in New York State in 1998 and 1999. A total of 6,010 consecutive patients who presented within 23 hours of an AMI were identified for this analysis. In-hospital mortality was the primary end point.
Results: Stents were placed in 5,225 (87%) patients. Patients receiving stents were younger (61 vs. 62 years, P=0.011) and less often female (29% vs. 33%, P=0.018). Patients receiving stents were less likely to have a history of hypertension (56% vs. 61%, P=0.013), diabetes (17% vs. 24%, P<0.001) and chronic kidney disease (0.8% vs. 2.0%, P=0.002) compared to patients not receiving stents. Sixty percent of patients in both groups presented within 6 hours of the onset of infarction. Ejection fraction was similar between groups (46% vs. 47%, P=NS). Patients receiving stents were less likely to present with 3-vessel disease (14% vs. 19%, P<0.001) and left main disease (2.4% vs. 4.6%, P<0.001). Glycoprotein IIb/IIIa inhibitor use was similar in both groups (56% vs. 53%, P=NS). Stent use was associated with a significant reduction in length of stay (5.9 vs. 8.1 days, P<0.001), major adverse cardiac events (4.1% vs. 12%, P<0.001) and in-hospital mortality (3.5% vs. 9.3%, P<0.001). After multivariate logistic regression analysis to adjust for differences in baseline characteristics, stent use was associated with a 50% reduction in the risk of in-hospital mortality (Odds Ratio 0.474, 95% confidence interval 0.311-0.723, P=0.001).
Conclusion: In a large unselected statewide database, stent use during angioplasty for AMI resulted in a significant reduction in length of stay, major adverse cardiac events and in-hospital mortality.

1034-200 Comparison Between Stent and Balloon in Patients Undergoing Primary Angioplasty for ST-Segment Elevation Myocardial Infarction due to Proximal Left Anterior Descending Coronary Artery Occlusion. A Substudy of the Zwolle-6 Randomized Trial

Giuseppe De Luca, Harry Suryapranata, Arnoud WJ van't Hof, Jan Paul Ottervanger, Jan CA Hoorntje, AT Marcel Gosselink, Jan-Henk E. Dambrink, Menko-Jan de Boer, De Weezenlanden Hospital, Zwolle, The Netherlands

Purpose. In the Zwolle 6 randomized trial 1683 patients were randomized before angiography to stent (S) or balloon (B), without any exclusion criteria. In this study we present data form the subanalysis in patients with proximal left anterior descending coronary artery (LAD) occlusion.
Methods. A total of 218 patients with STEMI underwent primary angioplasty of proximal LAD (107 randomized to S and 111 to B). All angiographic, clinical and 1-year follow-up data were prospectively collected.
Results. The cross-over rates from B to S and S to B were 35.1% and 13.1%, respectively (p < 0.0001). No difference was observed in 1-year mortality and MACE (Figure 1).
Conclusions. Our study is the first randomized trial comparing stenting and balloon angioplasty in a large cohort of unselected, consecutive patients. This subanalysis showed that routine stenting does not improve clinical outcome in patients undergoing primary angioplasty for proximal LAD occlusion.

Figure 1



1034-201 **Effects Of Hypothermia On Haemostasis And Inflammation During Myocardial Infarction**

Laurent Payot, Jean-Philippe Collet, Gilles Montalescot, Annick Ankri, Farzin Beygui, Remi Choussat, Jean-Philippe Metzger, Daniel Thomas, Institut du Coeur, Paris, France, Laboratoire d'hémostase, Paris, France

OBJECTIVES: To evaluate the effects of hypothermia on both haemostasis and inflammation markers during acute myocardial infarction (AMI)
BACKGROUND: Mild hypothermia has been shown to reduce metabolic demand and to limit infarct size in experimental models of AMI and in humans. The acute phase reactant proteins PAI-1 and vWf are independent predictors of survival in acute coronary syndromes
METHODS: Twelve consecutive patients with anterior AMI were cooled down (target core temperature 33°C) via the insertion of an intravascular heat-exchanger catheter (Icy®) placed in the common femoral. It was connected to an external temperature control system (CoolGard®). Hypothermia was initiated after primary angioplasty. Blood sampling was performed before angioplasty (T1), at the target core temperature after 3 hours of cooling (T2), and after passive rewarming to normothermia (T3). Von Willebrand factor (vWf) and plasminogen activator inhibitor-1 antigen (PAI-1), plasminogen, FVIIIc, tPA antigen, alpha 2-antiplasmin, antithrombin III, Protein C, protein S, Partial thromboplastin time, prothrombin time test, thrombin time, D-dimer were measured at each time point. The acute release of vWF and PAI-1 antigen was defined as the difference between their plasma concentrations at T3 and T1
RESULTS: The mean temperature obtained was 35,2°± 0,56. There was neither vascular access complication nor cardiac dysrhythmias during the cooling period. An increase of all biological parameters was observed between T1 and T2 followed by a decrease at T3, except for Ddimer and Protein S. These variations were found to be statistically significant for vWF, tPA antigen, and antithrombin III. We have paired our patients according to the age, the sex, the killip score, Timi flow at the end of PCI with patients who were not treated with endovascular cooling. Of interest, vWF and PAI-1 release (T3-T1) was found to be lower in patients who received endovascular cooling as compared to controls (1.0 vs 35.3; p=ns and - 4,2 vs 12.2; p=ns, respectively)
CONCLUSIONS: Therapeutic hypothermia in AMI seems to blunt the early rise and the release of acute phase reactant proteins in AMI. Our results need to be confirmed by a largest randomised trial

1034-202 **Superiority of Enoxaparin Low-Molecular-Weight Heparin Over Unfractionated Heparin in Patients With No Prior Antithrombin Therapy or Maintained on Consistent Antithrombin Therapy: Results From SYNERGY**

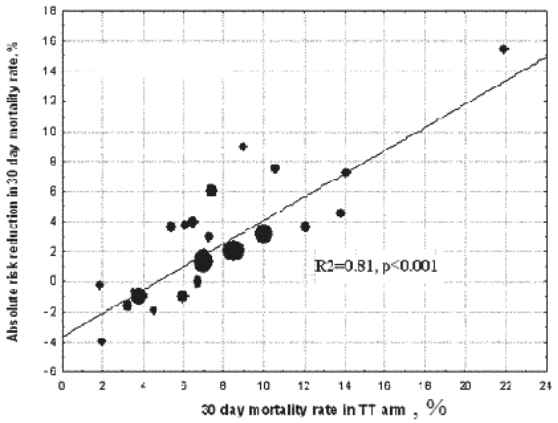
Marc Cohen, Kenneth W. Mahaffey, Lisa G. Berdan, Craig J. Reist, Louise Traylor, Anatoly Langer, Shaun G. Goodman, Elliott Antman, Flavia Dietrich, Robert M. Califf, James J. Ferguson, on behalf of the SYNERGY Trial Investigators, Newark Beth Israel Medical Center, Newark, NJ, Duke Clinical Research Institute, Durham, NC

Background: Previous trials demonstrated superiority of enoxaparin (Enox) over unfractionated heparin (UFH) in patients with non-ST-segment elevation (NSTE) acute coronary syndromes (ACS). The recent SYNERGY trial did not demonstrate a significant difference in outcomes between these 2 antithrombins, although noninferiority was shown. Unlike prior comparative trials, 75% of SYNERGY patients received open-label antithrombins prior to randomization. Our objective was to compare the outcomes of patients treated with Enox versus UFH in a consistent manner from hospital admission through randomization in the SYNERGY trial.
Methods: Of 9,978 SYNERGY patients, 2440 did not have any open label antithrombin therapy before randomization, and 3698 were randomly assigned to the same antithrombin therapy they were treated with prior to enrollment. The primary efficacy outcome was the composite of death or nonfatal MI during the first 30 days after randomization. Primary safety outcome was TIMI major and GUSTO severe bleeding.
Results: In the no-prior-treatment subgroup (n=2440), the primary endpoint occurred in 12.6% of patients assigned to Enox and 14.8% of patients assigned to UFH (relative risk ratio [RRR], 14.9%; odds ratio [OR], 0.84; 95% confidence interval [CI], 0.68-1.05). In the subgroup of 6138 patients receiving no prior antithrombin treatment or randomly assigned to the same antithrombin received before enrollment, the primary endpoint occurred in 13.3% versus 15.9% (Enox vs UFH), (RRR, 16.4%; p=0.0039; OR, 0.82; 95% CI, 0.72-0.94). Rates of TIMI major bleeding (Enox 9.3% vs UFH 7.9%, p=0.05) and GUSTO severe bleeding (Enox 2.9% vs UFH 2.1%, p=0.047) were more frequent with Enox.
Conclusions: While the overall trial results showed noninferiority, in the large subgroup of patients that had no prerandomization therapy or had the same treatment through randomization, Enox was superior to UFH in reducing death or nonfatal MI, with a modest excess in bleeding.

1034-233 **Survival Benefit Of Primary Angioplasty Over Thrombolytic Therapy In Patients With Acute Myocardial Infarction Varies According To The Baseline Mortality Risk Of Patients With Acute Myocardial Infarction. Modelling Across Trials**

Giuseppe Tarantini, Angelo Ramondo, Massimo Napodano, Gianbattista Isabella, Renato Razzolini, Sabino Iliceto, University of Padova, Padova, Italy

Background According to published meta-analysis, primary angioplasty (PCI) compared to thrombolityc therapy (TT) is associated with an absolute early mortality reduction of 2%. This result, however, is unlikely to be applied to all patients.
Methods To investigate the benefit of primary PCI as function of mortality risk, we examined the treatment effect of PCI compared to TT against the mortality rates in the TT groups across the 22 clinical randomized trials comparing PCI to TT in acute myocardial infarction, using meta regression technique. When the outcome is mortality, the control (TT) mortality rate can be interpreted as a proxy for mortality risk, so far we used control rate meta-regression for assessing differences in treatment effect across mortality risk that refers to the acute mortality in the TT arm.
Results. Across studies, absolute survival benefit ranged from -4% (favoring TT) to 22% (favoring PCI). The graph depicts the absolute benefit in percentage points in the included trials. The slope of the regression line is 0.77 and the x-axis intercept is 4.7%, indicating that populations at mortality risk below this level are unlikely to demonstrate benefit for PCI over TT in term of 30-day mortality and may show harm. These results are not modified by the exclusion of trials with lowest and highest risk of mortality with TT.
Conclusion. Most of the incremental benefit of primary PCI can be achieved by treating high risk patients, for which TT is difficult to justify, if nearby PCI is available.



1034-234 **Impact of Early Tirofiban Administration on Myocardial Salvage in Patients With Acute Myocardial Infarction Undergoing Infarct-Related Artery Stenting**

Ayse Emre, Ekrem Ucer, Ebru Onturk, Mahmut Cakmak, Dilaver Oz, Muhammed Gurdogan, Aycan Esen, Ali Buturak, Birsen Ersek, Siyami Ersek Thoracic& CV Surgery Center, Istanbul, Turkey

Background: The timing of GP IIb /IIIa inhibitor administration may be important in achieving early epicardial and myocardial reperfusion. We evaluated the effect of early tirofiban administration on myocardial salvage and cardiovascular outcome in patients with acute myocardial infarction (AMI) undergoing infarct-related artery (IRA) stenting.
Methods: Patients (n=42) with a first AMI presenting < 6hrs from onset of symptoms were randomized to either early administration of tirofiban (n=22) in the emergency room or later administration (n=20) in the catheterization laboratory (tirofiban bolus dose of 10 mcg/kg, followed by 0.15 mcg/kg for 24 hours). 16.5 mCi of Tc 99m sestamibi were injected to all patients in the emergency room. Imaging was performed within 6 hours after tracer injection. A follow-up study was performed 5-7 days after stenting. Risk area (initial perfusion defect), final infarction size (perfusion defect at follow-up study) and the salvage index (risk area-final infarction size/ risk area) were calculated. The primary end-point was the degree of myocardial salvage. Thirty-day major adverse cardiac events were also assessed.
Results: There were no significant differences in patient characteristics or in their presentation. The mean door-to-balloon time was similar in both groups (43+/-12 min and 53+/-9 min , p=0.08). The early and late treatment groups received tirofiban 17+/-3 min and 52+/-10 min after admission, respectively. Procedural success was achieved in all patients. Myocardial risk area were comparable between early and late treatment groups (39.3+/-7.0% vs 37.4+/-4.8%, p=0.6). Scintigraphic outcomes demonstrated a significant reduction in the final infarction size (21.7+/-6.4 % vs 9.6+/-4.8%, p=0.01), and improvement in the salvage index (44.3+/-13.2 % vs 75.4+/-9.4%, p=0.003) in favor of the early treatment group. The 30-day composite end-point of death, recurrent MI or rehospitalization also favored the early treatment group (5 % early, 15 % late, p=0.06).
Conclusion: Early tirofiban administration enhanced the degree of myocardial salvage and clinical outcome in patients with AMI undergoing IRA stenting.

POSTER SESSION

1035 Coronary Disease and Diabetes Risk Factors and Management

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1035-229 Insulin Resistance is an Independent Predictor of Vascular Events in Diabetic Patients with Angiographically Proven Stable Coronary Artery Disease

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Background: Patients with both diabetes and established coronary artery disease are at a high risk of cardiovascular events. Insulin resistance (IR) is a central feature of diabetes mellitus type 2 (DM2). Therefore, the impact of IR on the incidence of vascular events in diabetic patients with established CAD is of particular interest.
Methods: We estimated insulin resistance by the HOMA index in 495 patients with angiographically proven CAD and recorded the incidence of vascular events over a mean follow-up time of 2.3 ± 0.4 years.
Results: The HOMA index was higher in coronary patients with DM2 (n = 127) than in nondiabetic coronary patients (6.5 ± 5.9 vs. 3.0 ± 4.2; p <0.001). Thirty-one (23.8%) patients with DM 2 and 60 nondiabetic patients (14.5%) experienced at least 1 vascular event. In Cox regression analysis adjusting for age, gender, and baseline extent of coronary artery disease (number of angiographic stenoses ≥50%) diabetes was an independent predictor for the incidence of vascular events (OR = 1.725 [1.116 - 2.667]; p = 0.014). Equally, the HOMA index proved independently predictive for the incidence of vascular events in the total study cohort: the standardized OR adjusted for age, gender, and baseline extent of CAD was 1.178 [1.026-1.351]; p = 0.010. In subgroup analyses with respect to diabetes status, the HOMA index was significantly predictive for vascular events in patients with diabetes (OR = 1.354 [1.083 - 1.694; p = 0.008]), but not among nondiabetic patients (OR = 1.022 [0.729 - 1.432]; p = 0.901).
Conclusions: In the setting of secondary prevention, IR is a strong and independent predictor of vascular events among patients with DM2. Thus, the degree of IR significantly contributes to the adverse effects of diabetes on the prognosis in coronary patients.

1035-230 Association of the Metabolic Syndrome with Worse Outcome of Patients with Stable Coronary Disease in the Medicine, Angioplasty or Surgery Study (MASS I I)

Neuza Lopes, Aecio Gois, Alexandre Pereira, Antonio Gagliardi, Jorge Borges, Paulo Soares, Luiz Cesar, Whady Hueb, Heart Institute (InCor) University of Sao Paulo, Sao Paulo, Brazil

Background: In the present study, we examine the association between the metabolic syndrome and its components with the incidence of cardiovascular end-points in a group of coronary artery disease (CAD) multi-vessel individuals prospectively followed-up in the MASS II Study
Methods: We have evaluated individuals enrolled in MASS II for the 5 component conditions of the metabolic syndrome: insulin resistance, obesity, hypertriglyceridemia , low HDL cholesterol , and hypertension , as well as the full syndrome, defined as at least 3 of the 5 conditions. Logistic regression was used to estimate the cross-sectional association of the syndrome and each of its 5 conditions separately with each of the MASS II end-points (death, myocardial infarction, and recurrent ischemia requiring revascularization), as well as the combined end-point.
Results: Among the 611 individuals participating the MASS II Study, there were 52 (8.5%) individuals with refractory angina requiring revascularization; 40 (6.5%) individuals with myocardial infarction; and 43 (7.0%) deaths during the follow-up period of two years. No difference between treatment randomization (medical, surgery or angioplasty) was verified regarding metabolic syndrome status (p = 0.24), nor its components (p = 0.42, for glucose intolerance; p = 0.89, for low HDL-C; p = 0.78, for high triglycerides; p = 0.22, for hypertension). A significant difference regarding treatment allocation was verified for obesity (p = 0.02).
Interestingly, when analyzing mortality as the end-point, both the presence of metabolic syndrome (p=0.05) and glucose intolerance (p=0.04) were associated with an increased mortality in our studied population. Moreover, despite a clear tendency for each of its components to increase the mortality risk, only the presence of the metabolic syndrome significantly increased the risk of mortality among study participants in a multivariate model.(p=0.03, RR 2.5, 95% CI 1.1-6)Conclusion: These results indicate a strong, consistent relationship of the metabolic syndrome with mortality in patients with stable coronary artery disease.

1035-231 Clinical Judgment And Treatment Options In Stable Multivessel Coronary Artery Disease: Results From The 1-Year Follow-Up Of The Mass II Study

Alexandre Costa Pereira, Neuza H. M. Lopes, Paulo R. Soares, Jose E. Krieger, Sergio A. Oliveira, José F. Ramires, Whady Hueb, Heart Institute (INCOR), Sao Paulo, Brazil

Introduction: Despite the progress in coronary artery disease (CAD) risk stratification there is no consensus on the best treatment for patients with stable multi-vessel CAD and preserved left-ventricular function. Here, we examine the predictive power of clinical judgment in the incidence of cardiovascular end-points in a group of CAD multi-vessel individuals prospectively followed in the MASS II Study.
Methods: Preferred treatment allocation was recorded for each of the 611 randomized patients in the MASS II Study prior to randomization. We have divided our sample according to physician-guided decision and randomization result into two categories: concordant or discordant. The incidence of the composite end-point of cardiac death, myocardial infarction and refractory angina was compared between concordant and discordant patients.
Results: The number of concordant individuals (physician-guided x randomization) was 292 (48.2%), and this number was not statistically different between the three studied treatments (p = 0.11). A statistically significant difference (p = 0.02) was disclosed due to an increased incidence of combined end-point events in the group of discordant patients. In a multivariate Cox proportional hazard model, clinical judgment was still a powerful predictor of outcome (p = 0.01) even after adjustment for age, sex, treatment allocation, hypertension, diabetes, smoking status and total cholesterol. The main subgroup explaining this difference was a significant shift towards a worse outcome in the subgroup of discordant patients submitted to PCI (p = 0.003). Angiographic variables were more used in the clinical decision regarding PCI than clinical variables and the only independent predictor of concordance status in the PCI group was the number of diseased vessels (p = 0.01) in a multiple logistic regression model (having three-vessel disease increased the odds of a clinical decision against PCI in 2.1 times).
Conclusions: our data is a reminder that physician judgment remains an important predictor of outcomes.

1035-232 Cost of Care for Patients with Chronic Stable Angina in the United States

Paul A. Heidenreich, Harlan Krumholz, John Spertus, David W. Lee, George A. Goldberg, Jennifer B. Watson, Merle Haberman, David J. Cohen, VA Palo Alto Health Care System, Palo Alto, CA

Background: Nearly 7 million Americans have chronic stable angina, yet little is known about the cost of care for this population.
Methods: We identified angina patients enrolled in one of two U.S. managed care organizations based on the combination of an angina diagnosis and multiple prescriptions for beta-blockers, calcium antagonists or nitrates. We compared the cost of care for patients with angina to the cost for patients with coronary disease but no angina.
Results: There were 23,892 patients that met the criteria for angina. Their mean age was 68 years, 58% were male, 76% had hypertension and 30% had diabetes. Almost all patients (95%) were prescribed at least one anti-anginal medication (beta blocker, calcium antagonist, or long acting nitrate). Emergency visits for coronary related diagnosis during 12 months of follow-up occurred in 9% and revascularization was performed in 23% of patients. Mean total medical claims over 12 months were $28,836 which included $2,224 in drug costs and $26,612 in other medical costs. After adjustment for patient characteristics those with an angina diagnosis had total costs that were 25% higher and drug costs that were double those of patients with coronary disease but not angina (p<0.001). (Table)
Conclusion: When compared to patients with coronary disease and no angina, patients with angina use substantially more medical resources. Further studies are warranted to determine the degree to which improved anginal control may mitigate this burden.

Increase in Cost of Care for Angina Patients

Charges: Angina vs. Non-Angina CAD Patients	All Charges	Medical	Drug
Relative Difference	25%	18%	107%
Absolute Difference	$10,101	$8,384	$3,411

1035-235 Effects of Intensive Versus Moderate Lipid-lowering Therapy on Myocardial Ischemia in Older Patients with Coronary Heart Disease: Results of the Study Assessing Goals in the Elderly (SAGE)

Prakash Deedwania, on behalf of the SAGE steering committee and investigators, UCSF School of Medicine, San Francisco, CA, VACCHCS, Fresno, CA

Background: Few trials have specifically investigated the effects of lipid-lowering therapy with statins in older patients. The Study Assessing Goals in the Elderly (SAGE) investigated statin therapy as a novel approach to the treatment of myocardial ischemia in this patient population.
Methods: SAGE was a prospective, 12-month, double-blind study conducted at 192 sites worldwide. Qualifying patients were men and women with stable CHD (aged 65-85 years; LDL-C between 100 and 250 mg/dL) who had at least 1 episode of myocardial ischemia with total ischemia duration ≥3 mins on baseline 48-hour AECG monitoring. The AECG was performed while patients conducted routine daily activities and continued their usual prescribed anti-anginal medications. In total, 893 patients were randomized to either atorvastatin 80 mg/day (aggressive lipid lowering; A) or pravastatin 40 mg/day (moderate lipid lowering; P). The primary efficacy parameter was the absolute change in the total duration of myocardial ischemia from baseline to Month 12. Secondary efficacy parameters included the proportion of patients who were totally free of ischemia.
Results: A significantly greater reduction in LDL-C from baseline to Month 12 was achieved with A (55% vs. 32% for P; p<0.0001). There was a significant reduction from baseline to Month 12 for both the primary and secondary parameters (p<0.001) within each treatment group. There was, however, no difference between treatment groups in ischemia reduction (absolute change in duration, 48 mins for A vs. 46 mins for P; proportion of patients free of ischemia, 46% for A vs. 45% for P). Although SAGE was neither designed nor powered to assess Major Acute Cardiac Events (MACE), there was a favourable trend for A (HR=0.74, A vs. P; p=0.16). The proportions of patients in the 2

treatment groups having serious adverse events and non-serious adverse events were similar. Withdrawal rates were also similar.
Conclusions: SAGE is the first large, multi-center international trial to demonstrate the efficacy of lipid-lowering therapy on myocardial ischemia in older patients with CHD.

1035-236 **Obesity as a Risk Factor for Major Adverse Cardiovascular Events in Patients with Stable Coronary Disease and Preserved Left Ventricular Function**

Michael Domanski, Kathleen A. Jablonski, Madeline Rice, Sarah Fowler, Marc Pfeffer, Eugene Braunwald, National Heart, Lung, and Blood Institute, Bethesda, MD, The George Washington University Biostatistics Center, Rockville, MD

Background. Obesity is a risk factor for the development of coronary disease (CAD). However, the prognostic impact of obesity on acute events in patients(PTs) with established CAD is less clear.
Methods. The Prevention of Events with Angiotensin Converting Enzyme Inhibition (PEACE) trial randomized 8290 patients with stable CAD & left ventricular ejection fraction $\geq$ 0.40 to trandolapril or placebo & followed them for a mean 4.7 years. In PEACE patients who were non-diabetic at baseline (5693 men & 1170 women), we used proportional hazards analysis to study whether obesity, defined as a body mass index (BMI)$\geq$30 kg/m^2, is an independent risk factor for the composite endpoint of stroke, non-fatal myocardial infarction, revascularization, or cardiovascular death (MACE-1) and for the composite endpoint of stroke, non-fatal myocardial infarction, or cardiovascular death (MACE-2).
Results. A model adjusting for baseline age, gender, current smoking, hypertension, hypercholesterolemia, serum creatinine, & treatment group, showed significant interaction of gender with obesity; 28.5% of men and 29.0% of women were defined as obese. Obesity was an independent risk factor for MACE-1 in men (hazard ratio [HR] 1.34; 95% confidence interval [CI] 1.19 - 1.51; p<0.001), but not in women (HR 0.97; 95% CI 0.73-1.30; p = 0.86). Similarly, BMI-defined obesity was an independent risk factor for MACE-2 in men (HR 1.23; 95% CI 1.02-1.49; p=0.034), but not women (HR 0.89 ; 95% CI 0.55-1.44 ; p =0.63) .
Conclusion. In the presence of established CAD, obesity was independently associated with risk for major adverse cardiovascular events in men.

POSTER SESSION

1036 New Aspects of Cardiopulmonary Resuscitation and/or Defibrillation

Sunday, March 06, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 3:30 p.m.-4:30 p.m.

1036-223 **Ineffectiveness of Precordial Thump for Mechanical Cardioversion of Malignant Ventricular Tachyarrhythmias**

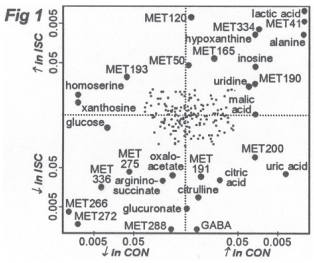
Offer Amir, Jorge E. Schliamser, Neemer Samaniah, Basil S. Lewis, Arie Militianu, Lady Davis Carmel Hospital, Haifa, Israel

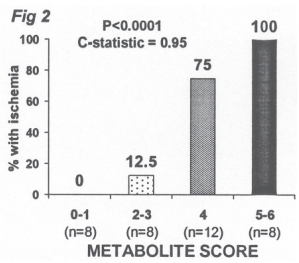
Background: Although mechanical cardioversion with precordial thump (MCPT) is commonly used in patients undergoing cardiopulmonary resuscitation and is recommended in major textbooks and guidelines, there are few studies which scientifically examined the effectiveness of MCPT. We evaluated the ability of MCPT to terminate malignant ventricular tachyarrhythmia which were induced during electrophysiologic testing (EPS) and/or cardioverter defibrillator implantation (ICD).
Methods: The study included 34 patients (mean age 68, range 47-83; 32 males and 2 females). All patients underwent EPS (9 patients) or ICD implantation (25 patients) according to ACC/AHA guidelines and required cardioversion for ventricular tachyarrhythmia during the procedure. 31 patients (91%) had coronary artery disease, 26 patients (76%) were on beta-blockers and 8 (23%) were treated with amiodarone. Mean echocardiographic left ventricular ejection fraction was 29% (range 20-45%).
Malignant ventricular tachyarrhythmia was induced as part of the EPS/ICD implantation procedure protocol; 17 episodes (50%) of ventricular fibrillation, 12 (35%) of polymorphic ventricular tachycardia, and 5 (15%) of sustained monomorphic ventricular tachycardia. MCPT was the first therapeutic treatment in all patients. MCPT was given once, within the first 20 seconds following the tachyarrhythmia, and was delivered by one of four physicians who participated in the study. In the event that the malignant tachyarrhythmia continued after MCPT, external or internal cardioversion was applied.
Results: MCPT was unsuccessful in terminating any of the malignant ventricular tachyarrhythmia episodes, and all the patients required other mode of cardioversion. There were no complications following the precordial thump.
Conclusion: Precordial thump is ineffective in terminating malignant ventricular tachyarrhythmia. We believe that despite its common use, the role of precordial thump in both cardiopulmonary resuscitation and guidelines recommendations, should be revised.

1036-224 **Continuous Oxygen Insufflation is Superior to Intermittent Positive Pressure Ventilation During Cardiopulmonary Resuscitation**

Melinda M. Hayes, Ronald W. Hilwig, Arthur B. Sanders, Robert A. Berg, Nathan Anavy, Karl B. Kern, Gordon A. Ewy, University of Arizona Sarver Heart Center, Tucson, AZ

Background: Professional EMS rescuers providing out-of-hospital CPR have been observed to ventilate more than 30/min! Such hyperventilation was associated with increased intrathoracic pressure (ITP) and decreased survival. This study evaluated the effects of intermittent positive pressure ventilation (IPPV), with and without hyperventilation, compared to continuous oxygen insufflation (COI).
Methods: Thirty swine (25±1 kg) were anesthetized and solid state micromanometer-tipped catheters were placed to measure aortic, right atrial, and ITP. Following 8 min of untreated VF, all animals received manual chest compressions at 100/min and were randomized to one of three ventilation groups. Group 1 (standard) received IPPV at a rate of 10/min; tidal volume (TV) of 20mL/kg. Gp 2 (hyperventilation) received IPPV at a rate of 35/min; TV = 20mL/kg, and Gp 3 received no IPPV but rather COI with a flow rate of 10L/min. Chest compressions, with one of the above methods of oxygenation, were administered for 2 minutes, at which time defibrillation was attempted.
Results: Return of spontaneous circulation was achieved in 30% in each of the three groups. Survival without neurological deficit at 24 Hrs occurred 2/10 in the standard IPPV group, 0/10 in the hyperventilation IPPV group, and 3/10 in the COI group (2 p=.06). Mean neurological deficit score was significantly less in the COI group (1.3±0.3 vs 2.0±0 vs 1.0±0; p<.05). Mean ITP was less with COI then either IPPV group (31±6 vs 33±5 vs 13±4; p<.02). Arterial pH differed among all three groups (7.48±.03 vs 7.65±.02 vs 7.22±.02; p<.0001), but was not related to outcome.
Conclusion: COI resulted in less increase in ITP during CPR, and produced superior neurological outcome to either form of IPPV. COI may be a better choice for ventilation during early resuscitation efforts for prolonged untreated VF.





1036-226 **Survival and Neurologic Damage in out-of-Hospital Cardiac Arrest: Defibrillation or Defibrillation plus CPR?**

Alessandro Capucci, Daniela Aschieri, Simona Bennati, Efrosini Iconomu, Maurizio Arvedi, General Hospital, Piacenza, Italy

The rate of success of cardiac arrest (SCA) mainly depends on the time to defibrillation. Recently the use of automatic external defibrillators (AED)associated with CPR has been demonstrated to improve survival from ventricular fibrillation (VF) compared to cardiopulmonary resuscitation (CPR) alone in a community project. The use of AED alone has not been still investigated.
Methods. 2325 volunteers have been recruited in the of Piacenza Vita Project, including policemen, post-office personnel, sport centers, hotel, public office, railway station personnel, lay ambulance volunteers, and worksite. The volunteers were trained only to use AED without CPR to reduce time and cost of training. Defibrillation (DP) courses last 3-4 hours and began four years ago. After one year all certified lay volunteers undergo a 1-hour review test and a retraining CD-Rom is given to continue home self-training. The volunteers respond to all cases of suspected SCA, simultaneously and in coordination with the EMS. The first who arrives defibrillates the patients (pts).
Results. 1188 SCA were recorded with 143 VF as the first rhythm. The pts were subdivided into two groups: group PV (66 pts), firstly treated by volunteers and group EMS (77 pts), firstly treated by medical staff who perform CPR. They were similar in age (mean: 69.7+12 year), proportion of men (63%), rate of witnessed SCA(73%), and location (74% at home). Time to defibrillation significantly differed between PV and EMS (5.30 min vs 7.30 min; p< 0.01). The survival rate from shockable rhythms was significantly higher for PV vs EMS group: 43% (29/66) vs. 22% (17/77), p=0.003. The neurologically intact survival rate to hospital discharge (level 1 evaluation)was also higher in PV vs EMS treated pts: 93.9% (27/29) vs. 83% (14/17), p=0.008, mainly due to shorter defibrillation time.
Conclusions. Training volunteers to attempt early defibrillation within a structured response system increases the number of survivals to hospital discharge free from neurologic lesion regardless to CPR during resuscitation. Trained layperson can use AED safely and effectively even after many months from a brief training courses of only 3-4 hours duration.

1036-227 **Prognostic Value of Relative Adrenal Insufficiency After Out-of-Hospital Cardiac Arrest**

Frédéric Pène, Hervé Hyvernat, Vincent Mallet, Alice Ohanessian, Alain Cariou, Pierre Carli, Christian Spaulding, Marie-Annick Dugué, Jean-Paul Mira, Cochin Hospital, Paris, France

Background: In survivors of out-of-hospital cardiac arrest (OHCA), post-resuscitation disease shares common hemodynamic features and a similar immunoinflammatory response with septic shock, thus identifying a sepsis-like syndrome. Relative adrenal insufficiency is a poor prognostic factor in patients with septic shock, for whom a replacement treatment reduces mortality and duration of vasopressor therapy. We performed a prospective observational single-center study to assess the prevalence of relative adrenal insufficiency in survivors of OHCA, and its prognostic role in post-resuscitation disease.
Methods: Patients hospitalised after successfully resuscitated OHCA were eligible for the

study. A corticotropin-stimulation test was performed between 12 and 24 hours following admission: serum cortisol level was measured before and 60 minutes after administration of tetracosactide 250µg. Patients with an incremental response < 9µg/dL (non-responders) were considered to have relative adrenal insufficiency.
Results: Between February 2002 and July 2003, 64 patients were included in the study. Thirty three patients (52%) had relative adrenal insufficiency. Baseline cortisol level was higher in non-responders than in responders (41 IQR [27.2-55.5] vs. 22.8 IQR [15.7-35.1] µg/dL respectively, p=0.001). A long interval before initiation of cardiopulmonary resuscitation was associated with relative adrenal insufficiency (5 IQR [3-10] vs. 3 IQR [3-5] min, p=0.03). Thirty eight patients experienced early post-resuscitation shock requiring vasoactive drugs, of whom 13 died of irreversible multiorgan failure. The presence of relative adrenal insufficiency was identified as an independent poor prognostic factor of shock-related mortality in a multivariate logistic regression analysis (Odds ratio 6.77, CI 95% 0.94-48.99, p=0.058).
Conclusion: Relative adrenal insufficiency occurs frequently after successful resuscitation of OHCA, and is associated with a poor prognosis in case of post- resuscitation shock. The role of corticosteroid supplementation should be evaluated in this setting.

1036-228 Adverse Event Reports on Automatic External Defibrillators from 1996 - 2003

Oscar H. Tovar, Beverly Albrecht Gallauresi, Food and Drug Administration, Rockville, MD

Background. The estimated growth rate for automatic external defibrillators (AEDs) in the USA was 8.2% for 2000 and 2001, 11.5% for 2002 and 22.0% for 2003. Despite this growth, there is scarce information about AED-related adverse events.
Methods and Results. We reviewed reports submitted by AED manufacturers to the FDA from 1996 - 2003 for AED-related adverse events (Table 1). Manufacturer conclusions were grouped in categories to assess association of device failure with a patient death (Table 2).

Table 1. Adverse event reports related to AED use

	1996	1997	1998	1999	2000	2001	2002	2003	Total
Deaths	16	45	71	59	65	119	107	108	590
Malfunctions	105	309	537	628	618	1322	1608	1917	7044
Injuries	3	2	1	0	0	3	1	0	10

Table 2. Manufacturers' conclusions

	96-99		00-03	
	n	%	n	%
No conclusion	111	32.3	467	59.9
Unknown if device contributed to death	77	26.7	118	15.1
No device failure	42	22.4	94	12.0
Device failure caused or contributed to death	92	12.2	75	9.6
User error caused or contributed to death	7	2.0	12	1.7
Device maintenance contributed to death	15	4.3	7	0.9
Device not returned or not related to death	0	0	6	0.8
Total	344	100	779	100

Conclusions. 1) Reported deaths associated with AED failure are more frequent than injuries, 2) reported AED malfunctions are increasing, along with increase in AED deployment, and 3) increase of AED-reported deaths over time may be associated with several factors including increased device availability.

POSTER SESSION

1059 Left Ventricular Remodeling After Myocardial Infarction

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1059-203 Lower Risk of Cardiac Rupture in CD39 Null Mice Post Myocardial Infarction

Mika Ogawa, Norihiko Ogawa, Masaharu Nakayama, Eva Csizmadia, Keiichi Enjyoji, Masahiro Kohzuki, Simon C. Robson, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA, Tohoku University Graduate School of Medicine, Sendai, Japan

Background: CD39/NTPDase 1 is an extracellular enzyme expressed on the surface of vascular endothelium, leukocytes and platelets that hydrolyze nucleotides (ATP, ADP, UTP etc.). We have generated cd39/NTPDase 1 null mice (cd39-/- mice) and found the disturbance of macrophage chemotaxis and platelet aggregation in this animal model. In this study, we analyzed cd39-/- mice to examine the role of cd39/NTPDase 1 in acute phase post myocardial infarction (MI).
Methods: Ten-to 13-week-old male wild type mice (wt) and cd39-/- mice underwent left anterior descending coronary artery ligation or sham operation. Mortality post MI was observed. Physiological data were measured. Immunohistochemistry was performed in the excised hearts at day 1 and 3 post MI. Matrix Metalloproteinase (MMP) expression and activity were analyzed by immunoblots and zymography in the ischemic area and non-ischemic area of left ventricle (LV).
Results: CD39-/- mice showed significantly better survival rate than wt by day 8 (38% vs. 88%, P < 0.05). All of the deaths occurring at day 4 to 7 after MI were caused by LV free wall rupture. Systolic blood pressure and LV weight/body weight ratio, however, didn't differ between wt and cd39-/- mice. The ischemic risk area of excised hearts from both groups was similar. CD39/NTPDase 1 expression in wt was downregulated at day 1 and changed to upregulation on vascular endothelium in ischemic border and infiltrated inflammatory cells in ischemic area as well as MMP9 expression. MMP activation of ischemic area in cd39-/- mice was half level as compared to wt (p<0.05).
Conclusion: We demonstrated that cd39-/- mice are protected from the risk of cardiac rupture after MI. CD39 and MMP9 have co-localization in the ischemic area and delayed activation of MMP in cd39-/- mice are observed. These data suggest that CD39/NTPDase 1 may modify MMP activation and cardiac remodeling in acute phase post MI.

1059-204 CD36 Plays an Important Role in LV Remodeling After Acute Myocardial Infarction

Xiaorong Zhou, Maria Febbraio, Arman Askari, Kai Wang, Marc S. Penn, The Cleveland Clinic Foundation, Cleveland, OH

CD36 is a multifunctional membrane-type receptor, mediating the uptake of oxidized LDL and development of atherosclerosis as well as anti-angiogenesis through binding TSP-1. However, its role in left ventricular remodeling after acute myocardial infarction has not been studied. In this study the role of CD36 in LV remodeling was investigated.
Methods and Results. AMI was induced by chronic ligation of LAD in female CD36-/- and wild-type (C57BL/6J). Echocardiography was performed before, 3 and 24 days after AMI to assess the effects of CD36 on LV function and remodeling. At 3 and 24 days after AMI, CD45 and vWF staining were performed to evaluate the effects of CD36 on inflammatory response and angiogenesis. There were no differences of LV size and function before and 3 days after AMI. However, 24 days after AMI, CD36-/- mice showed significantly better LV function, reduced LV end-diastolic size and increased anterior wall thickness (Table) compared to wild-type mice. Along with improved function, we observed significantly decreased leukocyte infiltration (% area) in CD36-/- group 3 days after AMI (25%±8 vs 8%±3%, P=0.016). Vessel density was increased in CD36-/- group at 24 days (14.5 ± 3.7 vs 8.2 ± 5.6 vessels/mm^2, p<0.05) within the infarct border zone.
Conclusion. CD36 play a critical role in the remodeling process following AMI through mediation of the inflammatory and angiogenic responses, and blocking CD36 function may serve as a novel pathway for optimizing LV function after AMI.

Groups	LVEDD (mm)	LVWT(anterior, mm)	FS (%)
CD36 -/-	0.329 ± 0.09 *	0.077 ± 0.024 *	0.292±0.10 *
WT	0.443 ± 0.09	0.047 ± 0.020	0.174±0.09

* P < 0.05 vs WT group

1059-205 Tamoxifen Treatment of Post-Myocardial Infarcted Adult Female Rats Exerted a Nefarious Action on Scar Remodeling

Pedro Geraldes, Hugues Gosselin, Jean-François Tanguay, Robert Clément, Angelino Calderone, Montreal Heart Institute, Montreal, PQ, Canada

The Heart and Estrogen/progesterone Replacement Study (HERS) and the Women's Health Initiative (WHI) recently documented that hormonal replacement therapy (HRT) increased the incidence of non-fatal myocardial infarction (MI) in postmenopausal women with or without coronary artery disease. The partial estrogen receptor agonist Tamoxifen (TAM) may represent an alternative pharmacological approach to HRT. In this regard, the present study examined the effect of TAM on cardiac remodeling post myocardial infarction (MI) in adult female rats. TAM (10 mg kg^{-1} day^{-1}) was administrated 4 hours post-MI and continued for a period of three weeks. In MI rats treated with TAM (n=18), scar surface area (TAM+MI=0.67±0.08 versus MI=0.48±0.07 cm^2) and scar weight (TAM+MI=0.071±0.007 versus MI=0.052±0.006 grams) were significantly greater (p<0.05), as compared to untreated-MI rats (n=25). The nefarious action of TAM on scar remodeling may have been attributed to either predisposing cardiac myocytes to apoptosis and/or compromising angiogenesis. Serine phosphorylation of the anti-apoptotic molecule protein kinase B (PKB) was significantly increased (96±4%, n=11;p<0.05 versus sham) in the non-infarcted left ventricle (NILV) of MI rats, as compared to sham. By contrast, TAM treatment completely abrogated PKB phosphorylation in the NILV (n=11) as compared to untreated-MI rats. In a Matrigel assay, vascular endothelial growth factor (VEGF) (10^{-9} mol/L; n = 3) treatment (48 hr) of rat aortic endothelial cells promoted capillarity-like tubule formation. The co-administration of TAM (n=3) caused a dose-dependent suppression of VEGF-stimulated tubule formation with a maximum effect at 10^{-7} mol/L. These data demonstrate that TAM adversely influenced scar remodeling post-MI and may have occurred by either predisposing cardiac myocytes to apoptosis and/or inhibiting angiogenesis.

1059-206 Alterations In Regional Wall Strain, Enos And Microtubulin Concentrations Signaling Left Ventricular Remodeling Occur Immediately After Acute Myocardial Infarction

Huy Phan, Elizabeth Juneman, Lisa Castellano, Nicholle Johnson, Steven Goldman, Mohamed Gaballa, Hoang M. Thai, Southern Arizona VA Health Care System, Tucson, AZ, Sarver Heart Center at the University of Arizona, Tucson, AZ

Background: Left ventricular (LV) remodeling after myocardial infarction (MI) leads to heart failure (HF). While alterations in LV wall strain are seen in the infarcted regions (IR), it is unclear if this also affects the non-infarcted regions (NIR) of the LV. Additionally, while LV tissue eNOS and constituitive microtubulin (CM) are altered in chronic HF, it is unknown what happens to these biomarkers acutely. We evaluated changes in LV wall strain; myocardial eNOS and CM acutely post MI.
Methods: LV wall motion of Sprague Dawley rats (N = 10) was analyzed by echocardiography at several time points after MI. Hemodynamic measurements were obtained via a Millar catheter. Alterations in myocardial contraction (δ strain) are measured via M-mode echocardiography. CM and eNOS were determined via immunoblot techniques.

Results: Systolic blood pressure decreased (P < 0.05) acutely post MI (127.1 ± 6.1 vs 101.7 ± 10.1 mmHg). LV end diastolic pressure increased (P<0.05) acutely after MI (5.8 ± 0.5 vs. 19.9 ± 2.0 mmHg). These changes were accompanied by a decrease (P< 0.05) in LV dP/dt after MI (7106 ± 520 vs. 4671 ± 350, mmHg/sec). δ strain was decreased in the anterior IR immediately (0.15 ± 0.04 vs 0.1 ± 0.02 mm, P < 0.01); similarly δ strain was also decreased in the posterior NIR starting at 1 minute (0.17 ± 0.02 vs 0.1 ± 0.02 mm, P < 0.01). A decrease in eNOS was seen with both the IR and NIR of the LV (20.8 ± 3.8 intensity unit (IU)/50 µg of tissue vs 11.1 ± 3.3 IU/50 µg, P = 0.04) and (26.7 ± 4.8 vs 8.14 ± 1.6 IU/50 µg, P = 0.002), respectively after MI. Conversely, CM was increased in both IR and NIR of the LV (10.3 ± 2.4 IU/25 µg vs 26.2 ± 4.6 IU/25 µg, P = 0.0005) and (9.3 ± 1.8 vs 18.5 ± 3.7 IU/25 µg, P = 0.003), respectively.
Conclusion: Decreases in δ strain occurred in both IR and NIR of the LV acutely after MI. This is accompanied by alterations in eNOS and CM levels throughout the LV immediately after MI. Our data demonstrate that physical and biomarkers signaling LV remodeling occur immediately after MI, rather than over time.

1059-207 Absence of Infarct Regression one Year After Acute Myocardial Infarction: Serial Measurements by Contrast Hyperenhancement Magnetic Resonance Imaging

Anna KY Chan, Yan Zhang, Gabriel WK Yip, Wynnie Lam, C.M. Yu, John E Sanderson, The Chinese University of Hong Kong, Hong Kong SAR., Hong Kong

Background: Late myocardial infarct regression causing a decrease in the proportion of the left ventricle occupied by non-viable myocardium has been postulated due to scar contraction. Temporal change of infarct size by contrast hyperenhancement magnetic resonance imaging (Ce-MRI), in relation to left ventricular (LV) remodeling at 1 year after myocardial infarction (MI) is not clear.
Methods: Total 47 consecutive patients with first documented MI were evaluated by serial Ce-MRI at the following interval: within 7 days, and after 3 and 12 months. MRI infarct size was expressed as a percentage of total hyperenhanced regions over left ventricular (LV) mass from a stack of short axis views covering the whole LV. Echocardiographic LV end-systolic, end-diastolic volumes and LV ejection fraction (LVEF) were measured.
Results: Patients were classified into 2 groups according to the change in LVEF between baseline and 1 year. Twenty-seven patients with unchanged or improved LVEF and 20 patients had LV remodeling with a decline in LVEF ≥ 10%. Patients with LV remodeling had significantly larger MRI infarct size by Ce-MRI compared to those without remodeling (24.6 %±3.3 vs 12.6±6.1, p=0.001). There was no temporal change in infarct size at baseline, 3 and 12 months after index infarction, both in the groups with or without remodeling, irrespective of baseline infarct size (Table).
Conclusion: Infarct regression is not evidenced during 1 year follow up in patients with or without left ventricular remodeling after MI.

Temporal changes of infarct size by Ce-MRI

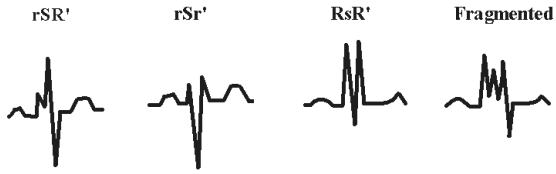
Ce-MRI Infarct Size (%)	Without Remodeling (n=27)	With Remodeling (n=20)
Baseline	12.6 ± 6.1*	24.6 ±13.3
3 Months	12.5 ± 7.2*	25.3 ± 10.6
12 Months	12.3 ± 8.9*	25.9±13.7

1059-208 Quest for a Sensitive ECG Sign Of Myocardial Infarction Scar: Beyond Q wave

Bilal Khan, Mithilesh K. Das, Sony Jacob, Avaneesh Kumar, Jo Mahenthiran, Krannert Institute of Cardiology, Indianapolis, IN

Background: Pathological Q wave on EKG is a specific marker with limited sensitivity (20-30%) for myocardial scar. Myocardial scar is shown to alter ventricular depolarization resulting in terminal QRS conduction delay (RSR' pattern). We postulate that an abnormal fragmented QRS (fQRS) pattern including RSR' and its variants (figure), not related to bundle branch block (BBB) is highly predictive of a myocardial scar.
Methods: Of 250 patients (pts), baseline ECG and myocardial perfusion imaging (MPI) of 239 pts (138 [55%] males, mean age: 58 ±12 years) were studied (11 excluded due to BBB or a pacemaker rhythm).The fQRS was defined as QRS with more than one R' (duration <120 ms) on ≥ 2 leads corresponding to individual coronary artery territory. MPI scar was defined by a single segment and sum rest score ≥ 3 and a sum difference score of stress and rest ≤ 3 using a standard 17-segment, 5-point scale, corresponding to a coronary artery territory.
Results: MPI was consistent with scar in 112 (47%) pts. The LAD scar (n=38) had Q in 6, fQRS in 35 and Q + fQRS in 3 pts. LCx scar (n=19) had Q in 3, fQRS in 13 and Q + fQRS in 1 pts. RCA scar (n=100) had Q in 39, fQRS in 101 and Q + fQRS in 29 pts. The sensitivity for MPI scar with Q wave increased significantly from 28.6% to 82.8% when combined with fQRS and specificity decreased from 99.4% to 92.3% (see table).
Conclusion: The fQRS not related to BBB significantly increases the sensitivity of a myocardial infarction scar as compared to the presence of Q wave alone on EKG.

Fragmented QRS including RSR' morphology and its variants



Tests	Q wave only	fQRS	Q wave and/or fQRS	Q +fQRS
Sensitivity (%)	28.6	74.5	82.8	35.6
Specificity (%)	99.4	94.6	92.3	98.4

POSTER SESSION

1060 Plaque Morphology in Acute Ischemic Syndrome

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1060-195 The Presence of Coronary Artery Soft Plaques is Associated with Insulin Resistance in Patients with Coronary Artery Disease: Assessment by Multislice Computed Tomography

Taeko Kunimasa, Masao Moroi, Tatsuhiko Furuhashi, Hiroshi Fukuda, Kaoru Sugi, Toho University School of Medicine, Ohashi Hospital, Tokyo, Japan

Disruption of the vulnerable plaque (soft plaque) is thought to be the primary cause of acute coronary syndrome. We evaluated the relationship between metabolic syndrome and the presence of coronary artery soft plaques detected by multislice computed tomography (MSCT).
Methods: MSCT (Aquillion 16, Toshiba Medical, Tokyo, Japan) was performed in 58 patients (mean age =63, male/female=50/8) with known or suspected coronary artery disease (CAD). On an axial image of MSCT, at least four randomly selected regions of interest (1.0mm^2) were positioned on the plaque and the density was measured. Plaques with the CT density less than 50 Hounsfield Units were defined as soft plaques. We assessed the relationship among the presence of coronary soft plaques, metabolic syndrome (NCEP ATP III) and the homeostasis model assessment-insulin resistance index (HOMA-IR=fasting blood glucose level × fasting serum insulin level /405).
Results: Coronary artery soft plaques were detected in 29 of 58 patients. The logistic regression analysis revealed that HOMA-IR greater than 1.7 was the most important risk factor for the development of coronary soft plaques as shown in Table.
Conclusion: Insulin resistance may be an important risk factor for the development of vulnerable plaques in CAD patients.

Logistic Regression Analysis

	Odds ratio	95%CI	P value
HOMA-IR>1.7	3.2	1.08-9.66	0.04
HDL-Cholesterol<40mg/dl	3.5	0.65-19.2	0.15
Metabolic syndrome	1.9	0.66-5.51	0.24
Body Mass Index>24	1.9	0.60-5.85	0.28
Triglyceride>150mg/dl	1.6	0.53-4.85	0.40
Hypertension	1.2	0.38-3.67	0.77

1060-196 Intravascular Ultrasound Characteristics of Ruptured Plaques in the Left Main Coronary Artery.

Jerzy Pregowski, Pawel Tyczynski, Gary Mintz, Mariusz Kruk, Adam Witkowski, Sang-Wook Kim, Akiko Maehara, Kenneth Kent, Augusto Pichard, Szymon Bieganski, Neil Weissman, Washington Hospital Center, Washington, DC, Cardiovascular Research Foundatio, New York, NY

Acute coronary syndromes with culprit lesion located in the left main coronary artery (LMCA) may be especially life-threatening. Methods We identified 17 LMCA ruptured plaques (RPs) in 16 patients (14 males, ages 69.1±9.7yrs). If the plaque cavity was also seen at LMCA bifurcation the rupture was classified as bifurcated RP. Standard IVUS measurements were performed within LMCA at minimal lumen area (MLA), maximal plaque cavity (MPC), and proximal reference sites. Results There were 2 patients with recent myocardial infarction, 13 with unstable angina, and 1 with stable angina. Thrombus was identified in 4 lesions. Six RPs involved the bifurcation (3 into the LAD and 3 into the LCX); 11 RPs were confined to LMCA. The angle between the MPC and the LAD/LCX flow divider was 162.3±15.6 º in bifurcation RPs vs 71.3±41.6 º in non-bifurcation RPs,

p=0.004. Mean LMCA RP length was 2.4±1.3mm; cavity area was 3.2±1.8mm2. There was no difference between bifurcation and non-bifurcation RPs. LMCA length measured 11.6±5.6mm; but the distance between MPC and the aortic ostium measured 9.7±5.7mm. In bifurcation RPs the MPC tended to be located father from aortic ostium (12.3±5.5mm vs 7.9±5.0mm, p=0.12). The MLA (6.5±3.8mm2 overall) was within the MPC site in 11 lesions and distal to the MPC in 6 lesions. Nine lesions had an MLA <6mm2 - the threshold that has been correlated with LMCA-associated ischemia. There was a tendency for a smaller LMCA MLA in non-bifurcation lesions: 6.0±3.3mm2 vs 7.4±4.7mm2 (p=0.3), but there was no difference in daughter vessel MLA (6.7 ±3.0mm2 vs 6.6 ±3.5mm2, p=0.9). Conclusions RPs involving LMCA may occur with various clinical presentations, almost exclusively involve the distal LMCA and/or its bifurcation, and are rarely lumen compromising.

1060-197 Long-Term Prognosis of Nonobstructive Coronary Artery Disease in the Setting of Acute Coronary Syndrome: A TIMI 22 Substudy

Raffaele Bugiardini, Olivia Manfrini, Sabina A. Murphy, Gaetano M. De Ferrari, Christopher P. Cannon, TIMI 22 investigators, Brigham and Women's Hospital, Boston, MA, University Alma Mater, Bologna, Italy

Background. The long-term prognostic implication of normal coronary arteries (0% stenosis) or mild (>0 to<50% stenosis) coronary artery disease (CAD) at angiography is assumed to be benign. Consequently, recurrence of chest pain symptoms in non-obstructive (<50% stenosis) CAD is often disregarded and, more importantly, there is a tendency to not recommend preventive therapy for these patients.
Methods. The TIMI 22 trial enrolled 3580 patients (2788 men and 792 women) who had been hospitalized for an acute coronary syndrome within the preceding 10 days and had cardiac catheterization. There were 178 (5%) patients with non-obstructive CAD that were used for this analysis. The primary end-point was the composite of death, myocardial infarction, unstable angina requiring re-hospitalization, revascularization, and stroke at 2-year follow-up.
Results. Patients with non-obstructive CAD included 109 men and 69 women (3.9% and 8.7%, respectively, of the overall TIMI 22 population). Women were older than men (58.3 ± 11.8 versus 52.9 ± 10.8 years; p = 0.0019). There were 55/178 patients (31%) with normal coronary arteries and 124/178 patients (69%) with mild-CAD. Patients with normal coronary arteries and those with mild-CAD matched well with regard to the qualifying event, gender and baseline characteristics. There was no difference in angiographic group by treatment. Kaplan-Meier estimates of the rates of the primary end point at two years were 8.3% in the normal angiography group and 10.2% in the mild-CAD group. The combined hard end point of cardiac death, myocardial infarction, stroke or revascularization was 6.1 % and 9.4 %, respectively. Revascularization was the most frequent endpoint (50% of events) in non-obstructive CAD.
Conclusion. Patients presenting with a clear acute coronary syndrome, but who had non-obstructive CAD have a prognosis that is not as benign as previously thought. Normal angiography and mild-CAD did not differentiate patients with regard to their prognosis. Adverse event rate was driven by revascularization that implies acceleration of the underling atherosclerotic process. Aggressive treatment for this "hidden" CAD is timely.

1060-198 Troponin Positive and Creatine-Kinase Negative Acute Myocardial Infarction: A Clinical, Electrocardiographic and Quantitative Coronary Angiography Analysis

Luis Gruberg, Haim Hammerman, Michael Kapeliovich, Walter Markewicz, Rafael Beyar, Rambam Medical Center, Haifa, Israel

Background: Cardiac troponins are part of the new definition of acute myocardial infarction (AMI) by the European Society of Cardiology and the ACC. There is scarce data regarding the angiographic characteristics of troponin I (cTnI) positive, creatine kinase (CK) negative AMI patients. We assessed the clinical, electrocardiographic and angiographic characteristics of these patients.

Methods: Between 1/2002 and 7/2004, a total of 44 consecutive cTnI positive, CK negative AMI patients were admitted to the ICCU and underwent coronary angiography.
Results: The mean age was 61±12 years, 40% were diabetics, 37% smokers and 44% had hyperlipidemia. Mean cTnI was 11.6±14.1 ug/L and mean CK was 91±40 U/L. All patients had normal renal function (serum creatinine: 0.85±0.2 mg/dL). Admission electrocardiogram showed inverted T waves in 42%, ST elevation in 35%, ST depression in 19% and was normal in 19%. Only six patients (14%) had a totally occluded infarct related artery and 37% had one-vessel disease. A total of 129 lesions were analyzed by QCA (CAAS II, Pie Medical), as shown in the Table.

	n=129
Percent diameter stenosis (%)	63.3±21.4
Minimal lumen diameter (mm)	0.95±0.72
Reference vessel diameter (mm)	2.52±0.84
Lesion length (mm)	8.05±4.7
Plaque area (mm2)	7.0±7.3
Plaque volume (mm3)	19.4±29.2

Conclusions: This is the first detailed QCA analysis of cTnI positive, CK negative AMI patients. Contrary to cTnI positive, CK positive patients, a minority of cTnI positive, CK negative AMI patients have a totally occluded infarct related artery. Nevertheless, there is a high prevalence of significant coronary artery disease in these patients, with 63% having multiple lesions in at least two coronary arteries.

1060-199 Slow Flow Phenomenon Is Associated With Type of Plaque Disruption

Yasunori Ueda, Atsushi Hirayama, Kazuhisa Kodama, Osaka Police Hospital, Osaka, Japan

Background: Distal embolization of thrombus and plaque contents from the culprit lesion is supposed to cause slow flow phenomenon and deteriorate left ventricular function but can be prevented by distal protection device. Therefore, we examined the predictive factors of slow flow phenomenon.
Methods: A series of 202 patients with ischemic heart diseases who received PCI and angioscopic examination were analyzed. The effect of patients characteristics, technical data of PCI, and angiographic and angioscopic findings on the occurrence of slow flow phenomenon was examined.
Results: Diagnosis of the study patients was acute myocardial infarction, unstable angina, stable effort angina, and silent myocardial ischemia in 105, 51, 18, and 28 patients, respectively. Slow flow phenomenon was detected in 8.4%. Slow flow phenomenon was significantly associated with acute myocardial infarction, high fasting blood glucose, not taking antiplatele medications, long lesion length, TIMI flow grade=0 before PCI, angioscopic detection of massive thrombus, and angioscopic detection of ruptured plaque. The incidence of slow flow phenomenon (19% vs. 6%, p=0.008) was higher when ruptured plaque was detected by angioscopy than when erosive plaque was detected.
Conclusions: Multiple factors including angioscopic findings were significantly associated with slow flow phenomenon. We may be able to know the risk of slow flow phenomenon by evaluating these factors.

1060-200 Vulnerability of Coronary Plaques Associates with Elevated Cardiac Troponin T in Patients with non-ST Elevation Acute Coronary Syndrome: Analysis by Using Coronary Angioscopy and Intravascular Ultrasound

Taku Sakai, Yasunori Ueda, Yuji Okuyama, Yuzuru Takano, Atsushi Hirayama, Kazuhisa Kodama, Osaka Police Hospital, Osaka, Japan

Background: Elevated troponin T (TnT) predicts adverse outcome in non-ST elevation-acute coronary syndrome (NSTE-ACS). But the relation between the culprit lesion morphology and elevated TnT level are poorly understood.
Objectives: In this study, we analyzed the culprit lesion morphology by using coronary angioscopy and intravasclar ultrasound (IVUS) in relation to different TnT levels in patients with NSTE-ACS.
Methods: A series of 57 patients with NSTE-ACS who underwent angioscopic and IVUS examinations were enrolled. Patients were divided into three groups based on TnT levels on admission. (<0.01μg/l, n=31; 0.01 to 0.1μg/l, n=15; >0.1μg/l; n=11). In angioscopic analysis, we assessed the number of yellow plaques, the color grade of yellow plaques (Grade 1: slight yellow, 2:yellow, 3:intensive yellow), and the prevalence of thrombus. Quantitative IVUS analysis was also performed to evaluate the plaque area. The percentage of plaque area was calculated as (external elastic membrane cross sectional area-lumen cross sectional area / external elastic membrane cross sectional area)×100(%).
Results: Among those patients with TnT<0.01μg/l, 0.01 to 0.1μg/l, >0.1μg/l, the number of yellow plaques were 2.0±0.3, 2.4±0.3, 2.1±0.4, respectively (p=ns). The corresponding figures for the plaque color grades were 2.0±0.4, 1.6±0.2, 2.36±0.3 (P<0.05), and for the occurrence of thrombus 53%, 61%, 91% (p<0.05). The prevalence of thrombus at culprit lesions increased in proportion to the levels of TnT. The percentage of plaque area evaluated by IVUS were 57.7±9.9%, 60.2±11.5%, 64.2±8.9% (p=ns), respectively.
Conclusion: In patients with NSTE-ACS, the elevated TnT levels did not associate with the plaque burden, but related with the plaque color intensity and the presence of intracoronary thrombus. These results may indicate the plaque vulnerability and likelihood of thrombus in NSTE-ACS patients with positive TnT.

1060-201 Presence of Soft Plaques in Nonculprit Coronary Arteries in Patients With Acute Coronary Syndromes : Evaluation by Multislice Computed Tomography

Taeko Kunimasa, Masao Moroi, Tatsuhiko Furuhashi, Hiroshi Fukuda, Kaoru Sugi, Toho University School of Medicine, Ohashi Hospital, Tokyo, Japan

Recent clinical observations have suggested that the disruption of the vulnerable plaque is the primary cause of acute coronary syndromes (ACS). We hypothesized that ACS patients may often have soft plaques in non-culprit coronary arteries compared with non-ACS patients.
Methods: MSCT (Aquillion 16, Toshiba Medical, Tokyo, Japan) was performed in 22 patients with ACS (acute myocardial infarction:16, unstable angina:6) and 40 patients with non-ACS (stable angina:33, old myocardial infarction:7). On an axial image of MSCT, at least four randomly selected regions of interest (1.0mm^2) were positioned on the plaque and the density was measured. Plaques with the CT density less than 50 Hounsfield Units were defined as soft plaques.
Results: Sixteen of 22 patients (73%) with ACS had plaques in the non-culprit coronary arteries whereas 17 of 40 patients with non-ACS (58%) had plaques. There was no statistical difference in the number of plaques between ACS and non-ACS patients. Among patients with plaques in non-culprit coronary arteries, the incidence of soft plaques was significantly higher in patients with ACS (13 of the 22 patients, 59%) than those with non-ACS (7 of the 40 patients, 18%, P=0.002).
Conclusion: ACS patients often have soft plaques in non-culprit coronary arteries compared with non-ACS patients. This supports the concept of a vulnerable patient but not a vulnerable plaque in a patient.

1060-202 **Culprit Coronary Levels of Angiotensin II and Impaired Microvascular Reperfusion in Patients With ST-Segment Elevation Myocardial Infarction**

Makoto Suzuki, Masamichi Tanaka, Eiki Hirose, Hideyuki Saeki, Tsuyoshi Matsunaka, Shinichi Hiramatsu, Yukio Kazatani, Ehime Prefectural Central Hospital, Ehime, Japan

Background We investigated the association between culprit coronary levels of angiotensin II (AII) and microvascular reperfusion in patients who underwent coronary angioplasty for ST-segment elevation myocardial infarction (STEMI).
Methods A total of 30 patients (62±10 years) with an early phase of STEMI due to proximal left anterior descending coronary artery obstruction were enrolled. Aspirated coronary blood was sampled to measure culprit levels of AII and inflammatory markers such as high sensitive C-reactive protein (hs-CRP), interleukin (IL)-6, and matrix metalloproteinase (MMP)-9. Complete microvascular reperfusion was defined as both the angiographic myocardial blush (MB) grade 3 and >50% ST-segment resolution in lead I, aVL, and V1 through V6 after coronary angioplasty. Enzymatic infarct size was calculated by serial measurements of creatine kinase-MB.
Results Despite successful coronary angioplasty in all patients, complete microvascular reperfusion was obtained in 17 patients (57%). Enzymatic infarct size was large in patients with incomplete microvascular reperfusion as compared with complete microvascular reperfusion (9916±4318 vs. 6390±4341 IU/L, p=0.041). Culprit levels of AII were significantly higher in patients with incomplete microvascular reperfusion than with complete microvascular reperfusion (19±9 vs. 7±4 pg/mL, p=0.001). Levels of hs-CRP and IL-6 but not MMP-9 were also elevated in patients with incomplete microvascular reperfusion than with complete microvascular reperfusion (hs-CRP, 4.5±3.6 vs. 1.4±1.7 mg/L, p=0.004, IL-6, 88±102 vs. 23±34 pg/mL, p=0.021, MMP-9, 134±66 vs. 198±194 ng/mL, p=0.278). A multivariate regression analysis showed the most association of AII with incomplete microvascular reperfusion (r=0.78, p=0.0001).
Conclusions These results may provide in vivo evidence regarding the culprit link between AII and impaired microvascular reperfusion in patients with STEMI.

POSTER SESSION

1061 Assessing Risk in Acute Myocardial Infarction

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1061-215 **Predictors of Infarct Size by Technetium-99m Sestamibi Imaging After Angioplasty in Acute Myocardial Infarction: Meta-analysis From Four Contemporary Randomized Trials**

Gregg W. Stone, William W. O'Neill, Simon Dixon, David A. Cox, John G. Webb, Bruce Brodie, John J. Griffin, Jack Martin, Raymond Gibbons, Martin Fahy, Roxana Mehran, Cindy Grines, Columbia University Medical Center, New York, NY, Cardiovascular Research Foundation, New York, NY

Background. Radionuclide imaging with Tc-99m sestamibi is frequently used in reperfusion therapy trials to assess infarct size. Prior studies have been inadequately powered to fully describe all the determinates of infarct size using this technique after angioplasty in AMI.
Methods. We pooled patient level data from 4 contemporary randomized controlled trials of PCI in AMI: EMERALD (n=501), COOLMI (n=357), AMIHOT (n=269) and ICE-IT (n=228). Of 1,355 total pts, infarct size was determined by Tc-99m sestamibi in 1,234 pts (91.1%) at mean time 23 ± 15 days.

Results. The pt population was characterized as follows: Mean age 59.3 years, 76.3% male, prior MI 9.6%, 84.6% primary PCI and 15.4% rescue PCI, 42.9% anterior MI, mean symptom to balloon time 139 mins and door to balloon 105 mins, TIMI 0/1 pre 73.4%, TIMI 3 post 91.5%. Mean infarct size was 16.3 ± 18.0% of the left ventricle. The independent baseline predictors of infarct size by multivariate linear regression appear in the table; factors unrelated to infarct size were investigational device, diabetes, smoking, creatinine, stent or GPIIb/IIIa use, discharge use of beta blockers, and time to sestamibi.
Conclusions. Anterior infarction, baseline and final TIMI flow, rescue PCI, male gender, prior MI and time to reperfusion are important predictors of infarct size after PCI in AMI. These variables should be considered when planning future trials of investigational drugs or devices designed to enhance myocardial salvage.

	Infarct size with variable (%LV)	Infarct size without variable (%LV)	Multivariate P value
Pain to door time >median (97 min)	17.2 ± 17.9	15.7 ± 18.1	0.02
Door to balloon time >median (100 min)	17.7 ± 18.9	14.3 ± 15.8	<0.0001
Male	17.4 ± 17.6	12.9 ± 19.1	<0.0001
Hypertension	17.3 ± 18.5	15.6 ± 17.6	0.04
Prior MI	20.6 ± 19.0	16.0 ± 17.9	0.003
Rescue PCI	17.0 ± 17.8	16.2 ± 18.1	0.03
LAD infarct artery	23.6 ± 20.1	10.1 ± 12.0	<0.0001
Pre TIMI 0/1	18.0 ± 18.0	11.4 ± 16.4	<0.0001
Post TIMI 0-2	27.3 ± 20.2	15.1 ± 17.1	0.0008

1061-216 **Continuous 12-lead ST-Segment Recovery Predicts Ejection Fraction, Clinical Outcome and Death After PCI for Acute ST-elevation MI: Results from the EMERALD Study**

Mitchell W. Krucoff, Per Johanson, Ricardo Baeza, Bruce R. Brodie, John Webb, David A. Cox, Mansoor Qureshi, Daniel Dulas, Anna Kalynych, Turco Mark, Heinz P. Schultheiss, Barry Rutherford, Alexandra Lansky, Manuela Negoita, Yingbo Na, Roxanna Mehran, Gregg W. Stone, for the EMERALD Investigators, Duke University Medical Center/Duke Clinical Research Institute, Durham, NC

Background: After infarct artery recanalization, biomarkers of microvascular reperfusion such as ST-segment recovery have been correlated with additional predictive information about outcome. In the EMERALD study 591 pts.with acute ST elevation MI (STEMI) underwent direct PCI, randomized equally to use of distal protection, with TIMI 3 epicardial flow achieved in 89.6%.
Methods: Acute 24 hours continuous digital 12-lead ECG monitoring (NEMON 180+) was performed in all pts. In a blinded core laboratory the most abnormal (peak) ST levels (J+60ms) prior to PCI were compared to ST levels 30 min. after the last contrast injection to determine ST recovery of <30%, 30-70%, or >70%. Acute ejection fraction and independently adjudicated 6 month death and combined death, new heart failure, shock or urgent revascularization (MACE) were correlated with ST recovery categories using log rank test for trends across ST recovery categories.
Results: There were no differences in clinical descriptors, use of distal protection or use of IIbIIIa inhibitors between ST recovery groups. Outcomes correlations were: TABLE
Conclusion: Continuous 12-lead ST-segment recovery reflects the cellular response to reperfusion in the setting of acute STEMI. In the largest data set ever reported with direct PCI in acute STEMI, the EMERALD study results confirm that ST-segment recovery provides highly significant information about outcome even in the setting of epicardial recanalization.

ST Recovery vs. EFx & Outcomes Correlations

Parameter	<30%	30-70%	>70%	P value
# Pts	42	118	431	
EFx (%)	56.00 (49.00, 65.00)	60.00 (51.00, 68.00)	65.50 (57.00, 73.00)	<.0001
6 mo MACE (% of pts)	17.70	9.70	5.50	<.006
6 mo Death (% of pts)	9.10	7.10	0.00	<.0001

1061-217 **Initial Cumulative ST Segment Deviation Predicts Left Ventricular Function and One Year Mortality Strongly in Patients With an Anterior Myocardial Infarction, but to a Lesser Extent in Patients With a Non-Anterior Myocardial Infarction**

Peter Elsman, Arthur CP Maas, Jan Paul Ottervanger, Jan-Henk E. Dambrink, Menko-Jan de Boer, Marcel Gosselink, Jan CA Hoorntje, Felix Zijlstra, Harry Suryapranata, Arnoud WJ van 't Hof, Isala Klinieken, locatie Weezenlanden, Zwolle, The Netherlands

Background: The initial extent of ST segment deviation (ST dev) is often used for risk stratification in patients (pts) with acute myocardial infarction (AMI). However, only few data exist on the effect of infarct location on the predictive value of ST dev.
Methods: During a 4 year period all consecutive pts who underwent primary angioplasty for AMI at our institution were eligible for inclusion in the study. The cumulative extent of ST segment deviation was measured on the initial diagnostic ECG's by an independent core-lab technician. Successful PCI was defined as TIMI 3 flow and DS<50%. Left ventricular ejection fraction (LVEF) was measured using Technetium labelling nuclear technique. The cut-off value for pts at high risk was set at 15 mm ST dev.
Results: ECG data were available in 1,163 pts, 566 (49%) had an anterior MI. . ST dev > 15 mm was present in 411 pts (35%). Pts with ST dev >15 mm had a lower ejection fraction (41 ± 12 % vs 45 ± 11 %, p<0.001) and a higher 1 yr mortality (8.5% vs 3.4%, p<0.001), as compared to pts with ST dev < 15 mm. For further results see table (numbers are percentages or p-values).
Conclusion: Although cumulative ST dev predicts left ventricular function and outcome in all pts undergoing primary angioplasty for AMI, the predictive value is stronger in pts with an anterior MI. The combined information of infarct location and extent of ST dev better predicts LVEF and clinical outcome as compared to ST dev alone.

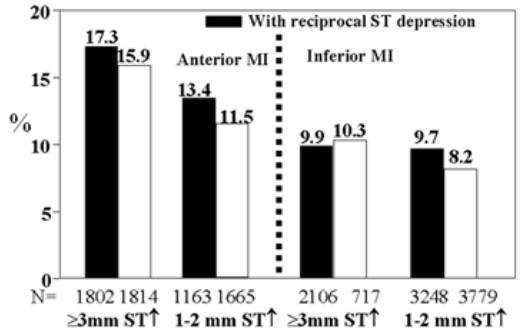
MI location	Anterior		P	Non-anterior		P
ST-dev (mm)	< 15	> 15		< 15	>15	
N	349 (62%)	217 (38%)		403(68%)	194(33%)	
Success PCI	88%	89%	ns	91%	90%	ns
EF	40±11	35±10	<0.001	49±8	48±9	ns
1 yr mortality(%)	5	12	0.003	2	5	0.04

1061-218 **The Baseline ECG in ST Elevation Myocardial Infarction Provides Powerful Prognostic Insight: Observations from ASSENT 2**

Saleh Alghamdi, Yuling Fu, Shaun G. Goodman, Weiching Chang, Frans Van de Werf, Christopher B. Granger, Paul W. Armstrong, University of Alberta, Edmonton, AB, Canada, Duke Clinical Research Institute, Durham, NC

Background: The extent of ST segment elevation and anterior infarct location on admission ECG are associated with worse clinical outcomes in patients with ST elevation myocardial infarction (STEMI). The prognostic value of reciprocal ST depression has also been demonstrated in such pts. To date, little information exists regarding the utility of combining these 3 ECG variables beyond their individual prognostic value in predicting

adverse event. Accordingly, we undertook a study of 16,949 patients (ASSENT-2 trial) to examine this issue.
Methods: The baseline ECGs were evaluated centrally without knowledge of clinical outcome at the ECG core lab. Patients were classified into 8 groups based on the infarct location, the presence or absence of reciprocal ST depression, and the extent of ST elevation of 3mm or more, 1-2 mm in at least two limb leads or two contiguous precordial leads, respectively. **Results:** composite of outcome (30-day death, in-hospital shock/ CHF) of these groups are depicted in the figure.
Conclusion: This risk stratification tool is simple and easy to use at the bedside, can help clinicians identify higher risk populations which will benefit from more aggressive management strategies. Furthermore these data permit refinement of pt selection that facilitates clinical trial planning in order to better evaluate sample size/ event ratios.



1061-219 **Correlations of Infarct Size Assessed by Delayed Contrast Enhanced MRI After Primary PCI With Peak Levels of Plasma Creatine-Kinase, C-Reactive Protein and Time to Intervention**

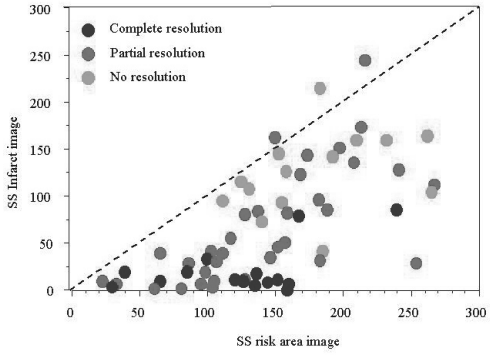
Juergen Haase, Torsten Sommer, Rusen Bayar, Matthias Hackenbroch, Claudia Piancatelli, Jule Thomas, Hans Störger, Franz Schwarz, Red Cross Hospital, Frankfurt, Germany, University of Bonn, Bonn, Germany

Background: We investigated the relationship between size of myocardial infarctions assessed by delayed contrast-enhanced MRI after primary PCI, elevation of plasma creatine-kinase (CK), c-reactive protein (CRP), and the time from onset of symptoms to intervention.
Methods: Four to 10 days after immediate PCI in 45 acute STEMI patients (<24h) with stenting of the infarct-related artery and treatment with abciximab (i.c. bolus injection of 0.25mg/kg), we performed gadolinium contrast-enhanced 3D inversion recovery gradient-echo MR sequences with complete coverage of the LV-myocardium in short axis slices. The mass of infarcted tissue based on the volume of hyperenhanced myocardium was calculated and linear regression analysis was performed to assess the correlation between absolute size of infarctions (g) as well as relative size (LV%) with peak values of CK (U/l), CRP (U/l), and time to PCI (h).
Results: There was a significant correlation between absolute size of infarctions (g) and peak CK-values (r=0.72; p<0.001) as well as the relative size (LV%) and peak CK (r=0.77; p<0.001). No correlations were found between absolute size (r=0.33) as well as relative size (r=0.27) of infarctions and peak CRP. There was also no correlation between absolute (r=0.29) as well as relative size of infarctions (r=0.27) and the time from onset of symptoms to PCI.
Conclusions: In patients with acute STEMI (<24h) undergoing immediate PCI with stenting and treatment with abciximab, peak CK values correlated well with infarct size as assessed by delayed contrast-enhanced MRI. There were no correlations between infarct size and peak CRP as well as the time to intervention.

1061-220 **ST Resolution after Mechanical Reperfusion Closely Correlates With Myocardial Salvage And Depends on The Severity of Area at Risk Assessed By ^{99m}Tc Tetrofosmin Imaging**

Takeru Shiraki, Hitoshi Matsuo, Takatomo Watanabe, Shun-ichiro Warita, Tai Kojima, Takeshi Hirose, Makoto Iwama, Koji Ono, Haruki Takahashi, Tomonori Segawa, Yukihiko Matsuno, Sachiro Watanabe, Gifu Prefectural Gifu Hospital, Gifu, Japan

Background: Early resolution of ST-segment elevation is an indicator of final infarct size and clinical outcomes. However, the relationship between the degree of ST resolution and the indexes derived from perfusion scintigraphy such as area at risk(AAR), infarct size(IR), and salvaged myocardium(SI) is unclear.
Methods : Consecutive 65 patients with anteroseptal myocardial infarction with successful mechanical reperfusion, whose AAR, IS, and SI could be assessed by myocardial perfusion imaging, were studied. Serial 12 leads electrocardiograms were performed at baseline, 90 minutes after reperfusion. ST resolution was defined as complete (≥70%, n=16), partial (<70% to 30%, n=36), or no resolution(<30%, n=13).
Results : Patients with no resolution group tended to be longer time to reperfusion (complete: 4.0±7.5 partial: 6.5±8.2 No: 7.4±6.6). Peak CPK inversely correlated with level of ST resolution(complete:1689±1395 partial:3078±2577 No:5252±2537 p<0.01).. As for the scintigraphical indexes such as AAR, IR, and SI, all these indexes had significant association with the level of ST resolution(AAR: complete 114±54 partial 145±58 no 178±51 p<0.05, IS:complete 21±26 partial 66±60 no 131±31 p<0.001, SI: complete 81.9±16.2 partial 57.6±29.4 no 27.7±23.9 p<0.001)
Conclusion : Early resolution of ST-segment elevation closely correlated with AAR, IS, and SI as assessed by scintigraphy. These data validates the use of ST resolution as assessment of efficacy of reperfusion therapy.



1061-221 **New Left Bundle Branch Block (LBBB) in Acute Myocardial Infarction (AMI) - A Strong Predictor of Death Both In-Hospital and in Early Follow-Up**

Mircea Petrina, Jianming Fang, Fadi Saab, Richard Otten, Amisha Patel, David F. Armstrong, Kim A. Eagle, University of Michigan Cardiovascular Center, Ann Arbor, MI

Background: Much of the recent literature on LBBB complicating AMI has come from clinical trials testing reperfusion strategies in ST elevation AMI and has primarily examined in-hospital outcomes.
Methods: We studied 1,154 consecutive patients admitted to the University of Michigan Cardiovascular Center between January 1999 and August 2003 to asses the incidence of LBBB in all forms of AMI and their correlation with comorbid conditions, treatment and outcomes, in-hospital and at six months follow-up. Patients with and without new LBBB on the index ECG were compared using chi-square test for binary and Students' t-test for continuous variables.
Results (see table): 84 (7.3%) patients had new LBBB; they were older and had higher frequencies of DM, HTN, prior AMI, prior CHF and renal insufficiency, but received similar rates of coronary revascularization and evidence-based medicine as non-new LBBB patients. Patients with LBBB were three times more likely to die in the hospital and at six months, with an overall admission to six-month mortality of 31/84 (37%).
Conclusion: Patients who develop LBBB in the setting of AMI have worse comorbidities and in-patient and six-month outcomes compared to non-new LBBB patients. The striking mortality after discharge argues for a careful look to see if such patients may benefit from more intensive treatments including revascularization and/or implantable defibrillator or biventricular pacemaker in addition to maximized evidence-based therapies and rehabilitation.

Table

Variable	LBBB (n=84)	No-LBBB (n=1,070)	P value
Mean Age	72±12	65±14	<0.0001
Prior AMI	49 (59%)	401 (37%)	0.0001
Prior CHF	41 (49%)	208 (20%)	<0.0001
Diabetes Mellitus	37 (44%)	332 (31%)	0.0147
STEMI	35 (42%)	195 (18%)	<0.0001
Killip Class (2-4)	23 (27%)	155 (14%)	0.0018
PCI/CABG	38 (45%)	486 (45%)	NS
Death (in-hospital)	11 (13%)	48 (4%)	0.0006
Death (6-months)	20 (29%)	82 (9%)	<0.0001

1061-222 **Decreased D-dimer Levels Indicate Reduced Risk of New Ischemic Events After a Myocardial Infarction - Beneficial Effects of Ximelagatran**

Christina Christersson, Jonas Oldgren, Anders Bylock, Agneta Siegbahn, Lars Wallentin, Uppsala University, Uppsala, Sweden

Background: The ESTEEM trial demonstrated that long-term treatment with the first oral direct thrombin inhibitor ximelagatran reduced the risk of new ischemic events after a myocardial infarction, but without any differences between the four evaluated doses. We related the change in D-dimer levels, a marker for fibrin turnover, to the risk of new ischemic events.
Methods and Results: Patients were randomized, at 6 days (mean) after a myocardial infarction, to one of four doses of ximelagatran (n=294) or placebo (n=153) together with aspirin 160 mg for six months. D-dimer was measured at randomization and after 1 week on treatment. In the placebo group 49% of the patients had reduced D-dimer levels after 1 week compared to 80% in the ximelagatran group (p<0.001). The cumulative rate of myocardial infarction, severe recurrent ischemia, ischemic stroke or death at six months was 19.7 % in patients with unchanged/increased and 11.5 % in patients with decreased D-dimer levels (p=0.01).
Conclusion: Ximelagatran proved to be highly effective in reducing the D-dimer levels in patients with a recent myocardial infarction. Early reduced D-dimer levels were related to decreased risk of new ischemic events.

1061-224 **Use of Reperfusion Therapy in Elderly Patients with Acute Myocardial Infarction**

Jeptha P. Curtis, Saif S. Rathore, Yongfei Wang, Mikhail Kosiborod, Joanne M. Foody, Frederick A. Masoudi, Harlan M. Krumholz, Yale University School of Medicine, New haven, CT, University of Colorado Health Sciences Center, Denver, CO

Background: Although both fibrinolytic therapy and primary PCI improve survival of patients with ST-elevation myocardial infarction (STEMI), potential bleeding complications limit the number of patients who can safely receive fibrinolytic therapy. Whether the availability of primary PCI increases the proportion of STEMI patients who receive reperfusion therapy is not known.
Methods: In two national cohorts of 31,339 and 31,759 elderly patients hospitalized between 1998-9 and 2000-1 with confirmed AMI, we identified STEMI patients (n=7,777) who presented within 12 hours of symptom onset. To investigate how the availability of primary PCI expands the pool of patients receiving reperfusion therapy, we included patients who were not ideal candidates for reperfusion therapy. Patients were divided into those who presented to hospitals with PCI capability (n=3,317), hospitals with a cath lab but not PCI capable (n=2,599), and hospitals with no cath laboratory (n=1,861). We determined rates of reperfusion within 12 hours of admission and compared use of reperfusion therapy across hospital type.
Results: Overall, only 2,687 (35.6%) patients received reperfusion therapy, with 1,561 (20.1%) receiving fibrinolysis and 1,206 (15.5%) undergoing primary PCI. A higher proportion of patients received reperfusion therapy at PCI capable hospitals compared with patients treated at cath lab only hospitals or hospitals without cath capability (48.2%, 24.5%, and 24.2% respectively, p<0.01).
Conclusions: The proportion of elderly patients with STEMI who receive reperfusion therapy is low. The availability of primary PCI is associated with increased use of reperfusion therapy.

1061-225 **The Influence of Gender on Survival Following Angioplasty for Acute Myocardial Infarction: A Report From the New York State Coronary Angioplasty Reporting System Database**

Jeffrey S. Berger, David L. Brown, Beth Israel Medical Center, New York City, NY

Background: Previous studies have shown that women treated with primary angioplasty for acute myocardial infarction (AMI) have a greater morbidity and mortality than men. However, it is not clear if the survival disadvantage for women has persisted into a more contemporary era of percutaneous revascularization characterized by widespread use of stents deployed at high pressures and potent anti-platelet therapies. We therefore sought to determine whether gender influenced short-term outcomes in a cohort of AMI patients, all of whom underwent angioplasty.
Methods: We conducted a retrospective cohort study of all patients undergoing angioplasty within 24 hours of an AMI in New York State between 1997 and 1999. No patients were excluded. The primary end point was in-hospital mortality.
Results: A total of 9,015 patients, 2,619 women and 6,396 men, were identified. Women were significantly older than men (66±13 years vs. 59±12 years, P<0.01) and had a higher prevalence of hypertension (64% vs. 52%, P<0.01), diabetes (23% vs. 15%, P<0.01) and peripheral vascular disease (8.1% vs. 5.0%, *P*<0.01). Women presented more frequently with heart failure (15% vs. 9%, P<0.01), pre-shock (6.3% vs. 5.1%, *P*<0.01) and shock (5.8% vs. 3.1%, P=0.02) than men. Ejection fraction was 46% in women and 47% in men (P=NS). Stent use was less common in women than men (76% vs. 79%, P=0.001). There was no difference in glycoprotein IIb/IIIa inhibitor use between groups. The unadjusted in-hospital mortality rate was 6.7% in women and 3.4% in men (P<0.01). After multivariate logistic regression analysis, female gender was not a significant predictor of in-hospital death (Odds Ratio 0.629, 95% confidence interval 0.249-1.589, P=0.327).
Conclusion: Women have a higher unadjusted mortality following angioplasty for AMI than men. However, after adjustment for their higher risk characteristics, female gender is not an independent predictor of in-hospital mortality among women undergoing angioplasty following for AMI in the contemporary era.

POSTER SESSION

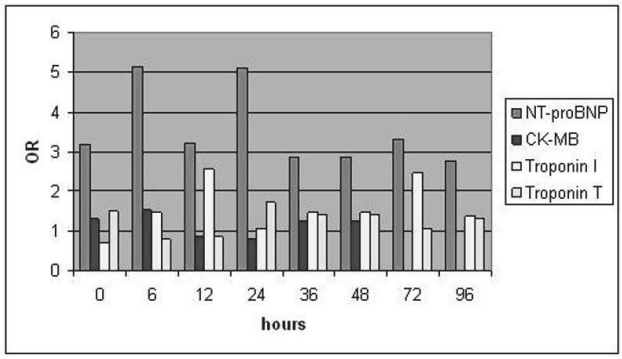
1062 Assessing Short- and Long-Term Outcome After Acute Coronary Syndrome I

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1062-223 **Sustained Prognostic Power of NT-proBNP during Hospitalization for Acute Coronary Syndromes.**

Mads Riiskjær, Kristian Thygesen, Bjarne Nørgaard, Jens Refsgaard, Lene Heickendorff, Aarhus University Hospital, Aarhus, Denmark

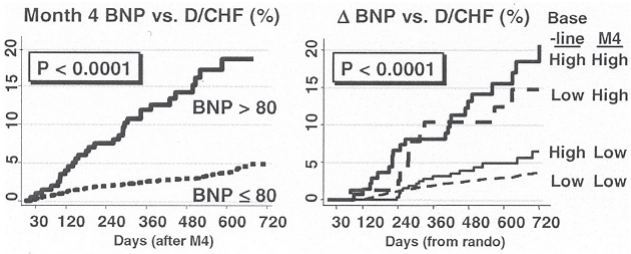
Background: An elevated level of N-terminal proBNP (NT-proBNP) indicates increased risk in patients with acute coronary syndrome (ACS). However, the optimal timing for determination of NT-proBNP during hospitalization as regards risk prediction has not been well established.
Methods: This investigation included 494 patients with unstable angina or non-STEMI. Study inclusion was within 24 hours of the latest episode of angina. NT-proBNP and CK-MB mass (cutoff: 10 µg/L), TnT (0.10 µg/L) and TnI (2.0 µg/L) were measured on blood samples drawn at 0, 6, 12, 24, 36, 48, 72, and 96 hours after admission. All events regarding the composite endpoint (death and acute myocardial infarction) during the follow-up of 30 days, were adjudicated by an independent Endpoint Committee.
Results: The study shows that patients in the upper quartile (n=124), based on the admission NT-proBNP values, had an absolute risk of the composite endpoint of 23.4% (15.9-30.8%). That is a 7.8-fold increase as compared to patients with NT-proBNP values in the first, second and third quartiles (n=370). Furthermore, when comparing simultaneously drawn samples of NT-proBNP, CK-MB mass, TnT and TnI by multivariate analysis, NT-proBNP was consistently the most powerful risk predictor within 96 hours after admission for ACS (Figure).
Conclusions: NT-proBNP has sustained prognostic power within 96 hours after admission for ACS, and when compared to specific, cardiac, necrosis markers, NT-proBNP is consistently the most powerful risk predictor.



1062-226 **Value of Serial Measurement of B-type Natriuretic Peptide in Patients with Acute Coronary Syndrome: An AtoZ Substudy**

David A. Morrow, James A. de Lemos, Michael A. Blazing, Petr Jarolim, Marc S. Sabatine, Sabina A. Murphy, Joanne Palmisano, Harvey D. White, Keith A. A. Fox, Robert M. Califf, Eugene Braunwald, Brigham & Women's Hospital, Boston, MA, Duke University Medical Center, Durham, NC

Measured early after presentation with an acute coronary syndrome (ACS), B-type natriuretic peptide (BNP) is a potent indicator of the risk for death or development of heart failure (CHF). However, few data are available with respect to the value of serial measurements for incremental assessment of risk and the response to therapy. **METHODS**: We measured the plasma concentration of BNP (Bayer Centaur) after initial stabilization of ACS (median 3.5 days), and at 4 months in 4273 patients with UA/NSTEMI or STEMI enrolled in the Aggrastat to Zocor Trial. A decision-limit of 80 pg/mL was pre-specified based on prior work. Outcomes were followed through end-of-study (median 2 yrs). **RESULTS**: Patients with baseline BNP >80 pg/ml ("High", n = 609, 14%) were at significantly higher 2-year risk of death (HR 2.8; 95% CI 2.1 - 3.7) and death or CHF (HR 3.2; 95% CI 2.5 - 4.0). Similarly, BNP measured at 4 months was strongly associated with subsequent risk of death (HR 4.3; 95% CI 2.6-7.1) and death or CHF (Figure Left, HR 5.1; 95% CI 3.4-7.6) in patients who were free of events up to four months. Categorized by change in BNP (baseline to 4 mo), patients with persistent or new elevation in BNP were at significantly higher risk than those with persistently low or falling BNP (Figure, Right).
CONCLUSIONS: Re-assessment of BNP 4 months after presentation with ACS may be used to enhance risk assessment for secondary prevention and may provide a basis for monitoring the response to therapies effective in modifying the risk of death and CHF.



1062-227 **One-Year Rehospitalization and Mortality Rates After Hospitalization for Acute Coronary Syndrome.**

Stephen Sidney, Michael Sorel, Charles P. Quesenberry, Jr., Patrick L. McCollam, Kaiser Permanente Medical Care Program, Oakland, CA, Global Health Outcomes, Eli Lilly and Company, Indianapolis, IN

Background: Prevalence estimates of acute coronary syndrome (ACS) vary considerably and few data are available on longer-term (e.g., 1-year) outcomes of persons hospitalized for ACS.
Methods: We included patients age ≥ 40 years of the Kaiser Permanente Medical Care Program, an integrated health care program, who were hospitalized with an ACS diagnosis from 1/1/99-12/31/00. Co-morbidities (hypertension (HTN), hyperlipidemia, diabetes mellitus (DM)) were assessed for 6 months prior to hospitalization, and re-hospitalizations and mortality were assessed for 1-year after the index event.
Results: There were 14,852 patients hospitalized for ACS (7,919 for myocardial infarction (MI), 6,933 for unstable angina (UA)) representing an incidence of 5.7 cases/1,000 person-years. During the first year after the index event, re-hospitalization occurred in 13.5% of patients for MI, 17.2% for UA, and 38.5% for all coronary heart disease; revascularization was performed

in 16.8%. One-year all-cause mortality was 17.2%. Male gender, HTN and DM were associated with ACS re-hospitalization (see table). However, acute MI and UA had different associations most notable for age and hyperlipidemia. HTN was associated with re-hospitalization for UA only.
Conclusions: Hospitalization for ACS was associated with substantial 1-year re-hospitalization and mortality. Risk factors for re-hospitalization for MI and UA differ, possibly reflecting differences in disease severity or pharmacological treatment.

Relative risk of re-hospitalization in the 12 months after an ACS event, multivariable analysis

Demographics & prevalence of risk factors	Referent group	ACS	MI	Unstable angina
		RR (95% CI)	RR (95% CI)	RR (95% CI)
Age mean 67.2 ± 12.0 yrs	<65 years old	0.98 (0.92, 1.04)	1.16 (1.06, 1.27)	0.88 (0.82, 0.96)
Gender 63.9% male	female	1.10 (1.03, 1.17)	1.01 (0.92, 1.11)	1.14 (1.05, 1.24)
Hypertension 31.0%	without hypertension	1.07 (1.00, 1.14)	1.03 (0.94, 1.14)	1.13 (1.04, 1.23)
Hyperlipidemia 28.2%	without hyperlipidemia	1.04 (0.98, 1.12)	0.68 (0.61, 0.76)	1.40 (1.29, 1.52)
Diabetes mellitus 34.9%	without diabetes	1.15 (1.08, 1.23)	1.26 (1.15, 1.38)	1.14 (1.05, 1.23)

1062-228 **Early Aggressive Versus Conservative Managment On One Year Outcome In Octogenarians Patients With Unstable Angina And Non-St-Elevation Myocardial Infarction.**

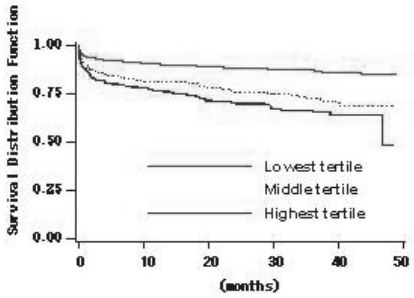
Fabio Alfredo Sgura, Elisa Guerri, Roberto D'amico, Emilio Chiurlia, Rosario Rossi, Chiara Leuzzi, Maria Grazia Modena, Institute of Cadiology of Modena and Reggio Emilia, Modena, Italy

BACKGROUND: Although increasing age is an important risk factor for adverse outcome among patients with acute coronary syndromes, elderly patients are more often managed conservatively. The goal of our study was to examine, at one year, the outcome in patients over 80 years old treated with aggressive management (AM) compared with the conservative management (CM).
METHODS: At our institution from January 2000 to April 2003, a total of 396 consecutive octogenarians patients were admitted to coronary care unit for Unstable Angina and Non-ST-Segment Elevation (UA/NSTEMI). Aggressive therapy at 4 to 48 hours vs. conservative therapy was analyzed to identify the prognostic factors of mortality. Multivariate analysis was performed to evaluated prognostic factors of 1 year survival.
RESULTS: 128 (32%) our patients underwent AM and 268 (68%) received CM. CM had higher heart rate at admission (80.2±20.3 vs. 74.5±18.3, p=0.007), lower systolic blood pressure (130.5±22.7 vs. 138.2±23.6, p=0.0019), lower creatinine clearance (47.2±22.2 vs. 55.4±20.6, p= 0.005), creatinine greater than 1.5 mg/dl (31% vs.15% p<0.0001), and less anemia (54% vs. 41%, p= 0.015). Gender female, diabetes, hypertension, previous MI and TIMI risk score were similar in both groups. After one year of follow up, cardiac mortality was 2% in AM and 22% in CM, respectively (p<0.001). Multivariate analysis identified the aggressive treatment as a factor that reduced the odds of mortality of than 56% (95% CI from 19% to 93%, OR=42%,).
CONCLUSION: This study demonstrated a significant difference in mortality regarding octogenarians patients treated with aggressive versus conservative therapy. The early invasive strategy may significantly improve outcome and survival in very old patients with NSTEMI Acute Coronary Syndrome.

1062-231 **C-reactive Protein Level on Presentation Predicts In-hospital and Long-Term Mortality in Patients with ST elevation Acute Myocardial Infarction in Reperfusion Era - From the Heart Institute of Japan Acute Myocardial Infarction (HIJAMI) Registry -**

Haruki Sekiguchi, Junichi Yamaguchi, Kentaro JuJo, Michitaka Nagashima, Tomohiro Kurihara, Yasuhiro Ishii, Atsushi Takagi, Yukio Tsurumi, Hiroshi Ogawa, Hiroshi Kasanuki, *for the HIJC Investigators, Tokyo Women's Medical University, Tokyo, Japan

Backgroud: The influence of CRP elevation on prognosis in patients with ST elevation acute myocardial infarction (STEMI) in recent reperfusion era remains to determine. The purpose of this study was to evaluate the impact of the CRP elevation on in-hospital and long-term mortality in patients with STEMI. **METHODS:** From 1999 to 2001, 2363 consecutive STEMI patients were prospectively registered in Heart Institute of Japan Acute Myocardial Infarction (HIJAMI) registry, multi-center, observational cohort study investigating real-world treatment practice for AMI in reperfusion era in Japan. We analyzed in-hospital and long-term mortality in these patients on the basis of CRP level on presentation. The study population was divided into three groups (lowest tertile: <1.0mg/dl, middle tertile: 1.0 ≤, < 3.0mg/dl, highest tertile: 3.0mg ≤). **RESULTS:** The lowest tertile included 1817 patients (76.9%), the middle and highest tertile included 287 patients (12.1%) and 259 patients (11.0%), respectively. Unvariate analyses showed statistical differences among three groups in age, hyperlidemia, peak creatine kinase, time from onset to admission, reperfusion therapy and Killip class. The results of multivariate analysis is shown below. During mean follow-up periods of 29 months, the event free survival rate was lower in the highest and middle tertile than the lowest tertile (p<0.0001).
CONCLUSIONS: The CRP level is an independent predictor of in-hospital and long-term mortality in patients with STEMI.



1062-232 **Primary Percutaneous Coronary Interventions: Predictors of One-year Mortality Among Patients Surviving 30 days.**

Rajendra H. Mehta, William O'Neill, Kishore J. Harjai, Judy Boura, David Fox, Bruce Brodie, Gregg Stone, Cindy L. Grines, On Behalf of the STENT-PAMI and CADILLAC Investigators, Duke Clinical Research Institute, Durham, NC, William Beaumont Hospital, Royal Oak, MI

Background: Little information exists on factors influencing the long-term prognosis of patients (pts) with ST elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI) who survive the acute phase.
Methods: Accordingly, we examined 3280 pts with STEMI enrolled in Stent-PAMI and CADILLAC trials treated with primary PCI and who survived beyond 30-days of their STEMI.
Results: Death at 1-year occurred among 74 pts (2.3%) who survived beyond 30-days of their index STEMI. Univariate associations of the risk of death are shown in Table. Cox Proportional Hazard Model identified: Age ≥70 years (odds ratio [OR] 3.3 95% confidence interval [CI] 1.7-5.7); weight <80 Kg (OR 1.9, 95% CI 1.1-3.6); any tachyarrhythmia during index hospitalization (defined as ventricular tachycardia/fibrillation or supraventricular tachycardia requiring treatment, OR 2.4, 95% CI 1.2-4.8); number of diseased coronary arteries (OR 1.5, 95% CI 1.1-2.1); and left ventricular ejection fraction (each 10% increase, OR 0.68, 95% CI 0.55-0.86) as factors independently associated with risk of 1-year death among 30-day survivors (Model C-statistic=0.77, Hosmer Lemeshow Chisquare=13, degrees of freedom=8, p=0.12).
Conclusions: Our study provides a method for clinicians to advice patients treated with primary PCI surviving the acute phase of their STEMI regarding their long-term prognosis, thereby enhancing planning and setting up of realistic expectations.

Table

Clinical factors	Alive-1 year, N=3206	Dead-1 year, N=74	P value	*Angiographic factors*	Alive-1 year, N=3206	Dead-1 year, N=74	P value
Age≥70	682 (21%)	41 (55%)	<0.0001	Ejection fraction	49±12	42±14	<0.0001
Weight (Kg)	82±16	76±19	<0.0001	Final TIMI flow <3	179 (5.6%)	9 (12.2%)	0.022
Females	818 (26%)	28 (38%)	0.017	***In-hospital events***			
Prior stroke	111 (3.5%)	6 (8.1%)	0.047	Stroke	12 (0.4%)	2 (2.7%)	0.038
Sum ST elevation (mm)	4.2±2.0	5.2±1.9	0.020	Intubation	8 (0.3%)	2 (2.7%)	0.020
Angiographic factors				Pulmonary complications	11 (1.4%)	2 (15%)	0.016
3 vessel disease	506 (15.8%)	26 (35.1%)	<0.0001	Vasopressor support	73 (2.6%)	5 (8.3%)	0.022
LAD Infarct	1211 (38%)	41 (55%)	0.0020	Tachyarrhythmia	247 (9%)	13 (22%)	0.0005

POSTER SESSION

1063 Chronic Ischemic Heart Disease: Stress Testing

Monday, March 07, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 10:00 a.m.-11:00 a.m.

1063-229 **Does a Gradual Exercise Test (Ramp) Attenuate Myocardial Ischemia?**

Martin Noël, Jean Jobin, Paul Poirier, Gilles R. Dagenais, Peter Bogaty, Institut Universitaire de Cardiologie et de Pneumologie de l'Hôpital Laval, Ste-Foy, PQ, Canada

Background: In patients with ischemic heart disease (IHD), it is accepted that the heart rate x systolic blood pressure product (RPP) at 1 mm ST depression [ischemic threshold] is relatively reproducible on the Bruce protocol treadmill. Would ischemic threshold (IT) be higher because of a warm-up effect on a more progressive exercise protocol?
Methods: We compared ischemic parameters on the Bruce protocol treadmill with a ramp protocol ergocycle in 18 patients with documented IHD (≥ 70% stenosis) and a previous ischemic exercise test. These 2 symptom-limited tests were performed in random order 2 weeks apart. Respiratory gases, ECG and blood pressure were monitored. The IT and maximum ST depression corresponding to the highest RPP common to the 2 tests (Max STD) were determined.
Results: While all subjects showed ischemia on the treadmill, 6/18 did not on the ergocycle. Despite greater peak RPP and comparable exercise intensity (VO_2) at 1 mm ST depression and peak exercise, IT was higher and max STD was lower on the ergocycle.

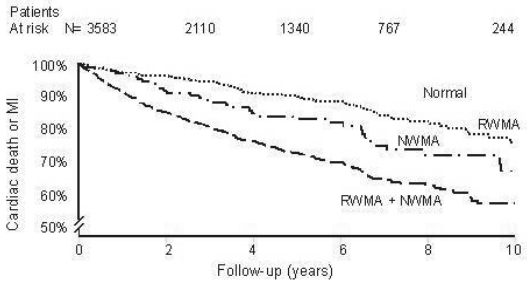
	Treadmill	Ergocycle	
IT*	20155 ± 3560	23491 ± 5670	P<0.005
VO_2 at IT (mlO_2* min^{-1} * kg^{-1})	20.77 ± 4.50	20.28 ± 6.41	P=0.7
Peak VO_2 (mlO_2* min^{-1} * kg^{-1})	26.76 ± 4.54	25.67 ± 5.43	P<0.05
Peak RPP	25781 ± 6385	28015 ± 6731	P=0.02
Max STD (mm)	1.8 ± 0.9	1.1 ± 0.9	P=0.003
* Peak RPP substituted for IT in the 6 patients with no ischemia on the ergocycle.			

Conclusion: Exercise-induced myocardial ischemia is markedly attenuated on the ramp ergocycle compared to the Bruce protocol treadmill, an effect unexplained by exercise intensity (VO_2) or cardiac work (RPP). The more gradually increasing workload of the ramp ergocycle protocol may have favoured a "warm-up" ischemic effect despite achieving higher RPP than the Bruce protocol treadmill suggesting it may be physiologically preferable for exercise prescription in patients with IHD.

1063-230 Long-term Prognostic Value of Dobutamine-atropine Stress Echocardiography in 3800 Patients

Boudewijn J. Krenning, Jeroen J. Bax, Elena Biagini, Vittoria Rizzello, Arend F.L. Schinkel, Miklos D. Kertai, Olaf Schouten, Ron T. van Domburg, Maarten L. Simoons, Don Poldermans, Thoraxcenter, Rotterdam, The Netherlands

Background: Dobutamine-atropine stress echocardiography (DSE) is increasingly used to assess the long-term prognosis in patients with proven or suspected coronary artery disease. The aim of this prospective study was to investigate the incremental prognostic value of DSE for assessment of long-term prognosis.
Methods: Clinical data and DSE results were evaluated in 3,800 patients undergoing DSE between 1989 and 2002. Patients were followed for a mean of 6±4 years (range 0.5-14 year); those who underwent revascularization within 3 months (n= 217) were excluded, 50 patients were lost-to follow-up. The value of DSE in predicting cardiac events (cardiac death and MI), clinical and DSE data were analyzed using a multivariable Cox proportional-hazards model.
Results: In 1255 patients with a normal DSE, cardiac events occurred in 17% during 10 year follow-up (Figure). 406 of 1691 patients (24%) with stress-induced ischemia suffered an cardiac event. However, extensive ischemia was associated with an increased risk of 5% for every ischemic segment. Both rest and new wall motion abnormalities were present in 1513 (42%). A rest wall motion score > 1.7 is associated with a 2-fold increased risk of late cardiac events.
Conclusion: A normal DSE has a relatively good cardiac prognosis. DSE results, such as rest wall motion score and number of ischemic segments provide important information for predicting subsequent cardiac events.



1063-233 The Incidence of Gastro-Esophageal Disease in the Patients with Normal or Minimal Coronary Artery Disease

Chang-Wook Nam, Kee-Sik Kim, Seung-Ho Seung-Ho Hur, Seong-Wook Han, Yoon-Nyun Kim, Young-Soo Lee, Sang-Hoon Lee, Young-Soo Lee, College of Medicine, Keimyung University, Daegu, South Korea

BACKGROUND The stomach and esophagus may be the origin of chest pain clinically indistinguishable from that of myocardial ischemia. When the coronary angiogram shows normal or minimal lesion, motility studies are important for adequate diagnosis.
OBJECTIVES This study investigated the identification of gastro-esophageal disease in patients with chest pain and showing negative coronary angiogram.
METHODS 126 patients (male 42, 33.3%) who showed negative coronary angiogram with typical chest pain were included. All patients underwent UGI endoscopy, and most of them were performed Berstein test and esophageal manometry.
RESULTS Among the 126 patients, clinically stable angina was in 109 (86.5%). Stress teat was done in 84 (66.7%; positive 53, 63.1%). Endoscopical finding was normal or nonspecific gastritis in 78 patients (62.5%), erosive gastritis in 18 (14.3%), gastric ulcer in 5 (4.0%), duodenal ulcer in 7 (5.6%), reflux esophagitis in 17 (13.5%). One case of stomach cancer was detected during endoscopy. Berstein test was done in 122 patients. Positive result was 68 patients (55.7%). 59 (48.4%) of them was non-erosive reflux disease. Esophageal manometry was done 121 patients. 35 patients (28.9%) of them had motility disorders. Nutcracker esophagus was in 24 patients (19.8), nonspecific esophageal motility disorder in 5 (4.1%), hypertensive lower esophageal sphincter in 3 (2.5%). Among the 53 patients of positive cardiac stress test with negative coronary angiogram (clinically corresponded to microvascular angina), 46 patients (86.8%) showed abnormal findings in gastro-esophageal studies.
CONCLUSIONS In our study, 107 (84.9%) of patients with chest pain and showing negative coronary angiogram revealed positive result of gastric or esophageal disease. In spite of existing microvascular anginal evidence, it will be more advisable to perform gastro-esophageal studies.

1063-234 Stress Myocardial Scintigraphy and Dobutamine Echocardiography in the Detection of Coronary Disease in Asymptomatic Patients with type 2 Diabetes.

Claude Le Feuvre, Olivier Barthélémy, Danielle Dubois, Christophe Maunoury, Agnès Mogenet, Gérard Helft, José Timsit, Jean Philippe Metzger, AP-HP, Paris, France

The most appropriate test to detect silent myocardial ischemia (SMI) in diabetic patients unable to perform an exercise test is unknown, and few data are available on the long-term outcome after aggressive therapy of SMI. This prospective study aimed: (1) to compare stress thallium-201 single photon emission computed tomography (SPECT) and dobutamine echocardiography (DE) in the detection of SMI in asymptomatic high risk diabetic patients; (2) to analyse long-term outcome after intensive care of SMI in these patients.
SPECT was performed in 100 high risk diabetic patients and DE in the first 75 patients. Coronary angiography was realized in patients with SMI, with systematic revascularization for suitable lesions. Intensive treatment of atherosclerosis risk factors was performed in all patients. Patients were followed 2+/-0.5 years for the subsequent occurrence of cardiac death, myocardial infarction and revascularization.
SMI was detected by SPECT in 62% and by DE in 10% of the patients ($p < 0.0001$), whereas significant coronary stenosis at angiography was detected by SPECT in 26% and by DE in 5% of the patients ($p < 0.02$). Independent predictive factors of significant coronary stenosis were male gender ($p < 0.03$) and peripheral arterial disease ($p < 0.007$). Nonfatal myocardial infarction occurred during follow-up in 2 patients (2%). Subsequent revascularization procedure was needed in 9 patients. Baseline patients' characteristics, as well as stress test results, were not predictive of cardiac event during follow up.
Conclusions: SPECT seems more accurate than DE to detect significant coronary stenosis in high risk asymptomatic diabetic patients. In this population, aggressive treatment of SMI with systematic revascularization combined with intensive care of risk factors is associated with a favourable long-term prognosis.

1063-235 Prognostic Value Of hsCRP In Patients With Stable Coronary Disease And Angina Of Effort, Univariately And In The Presence Of N-terminal BNP And Other Risk Factors

Ian Ford, Michele Robertson, David Gaze, Henry J. Dargie, Lisa Garrison, Paul Collinson, University of Glasgow, Robertson Centre for Biostatistics, Glasgow, United Kingdom

Background: The independence of the relationship between hsCRP and outcome in coronary heart disease has recently been questioned.
Methods: We investigated the association between hsCRP and occurrence of coronary events or all-cause mortality in the IONA clinical trial Biobank sub-study (BIONA) of nicorandil versus placebo in patients with stable coronary disease and angina of effort. 1505 patients were included in the sub-study of whom 90 had a non-fatal MI or died from CHD causes and 90 died from any cause after an average follow-up of 1.6 years. The associations between prognostic factors and outcomes were investigated using Cox proportional hazards models, first for the logarithm of hsCRP levels (log mg/L) and then after adjusting for other cardiovascular risk factors and for the logarithm of N-terminal pro BNP levels (log pg/mL). Models were adjusted for randomised treatment allocation.
Results: Estimated hazard ratios and 95% confidence intervals are given below.

Endpoint	Variables in the model	Variable	Hazard ratio (95%CI)	P-value
CHD death/non-fatal MI	LogCRP/randomized treatment	logCRP (1 unit)	1.23(1.02,1.48)	0.032
CHD death/non-fatal MI	LogCRP/ log NT proBNP/randomized treatment	logCRP (1 unit) logBNP (1 unit)	1.15(0.95,1.39) 2.26(1.91,2.69)	0.16 <0.0001
CHD death/non-fatal MI	LogCRP/randomized treatment/other CHD risk factors	logCRP (1 unit)	1.14(0.94,1.39)	0.189
All cause mortality	LogCRP/randomized treatment	logCRP (1 unit)	1.42(1.18,1.71)	0.0002
All cause mortality	LogCRP/ log NT proBNP/randomized treatment	logCRP (1 unit) logBNP (1 unit)	1.33(1.11,1.61) 2.20(1.85,2.61)	0.003 <0.0001
All cause mortality	LogCRP/randomized treatment/other CHD risk factors	logCRP (1 unit)	1.33(1.09,1.63)	0.005

Conclusions: hsCRP levels were significantly univariately associated with both coronary outcomes and all-cause mortality. The strength of the association was attenuated after adjusting for traditional risk factors and for NT proBNP, becoming non-significant for coronary events but not all-cause mortality. This study confirms the importance of NT proBNP as an important independent risk factor for coronary events and for all cause mortality and suggests that hsCRP carries additional prognostic value, at least for the mortality outcome.

1063-236 Serum Level of SAA/LDL Complex in Stable and Unstable Coronary Artery Disease

Ayumi Goda, Ken Ogasawara, Shinichi Mashiba, Hideki Hashimoto, Kazuo Uchida, Tadanori Aizawa, Long-Tai Fu, The Cardiovascular Institute, Tokyo, Japan, Teikyo University School of Medicine, Tokyo, Japan

OBJECTIVE: Previously we reported that a serum amyloid A (SAA) and LDL complex (SAA/LDL) which is derived by oxidative interaction between SAA and lipoproteins at the vascular site in atherosclerotic process can be a novel prognostic marker in patients with stable coronary artery disease (CAD). In the present cross-sectional study we attempted to determine the relationship between the serum level of SAA/LDL and stable/unstable angina.
METHODS: Consecutive 428 patients who underwent coronary angiography were enrolled. Serum levels of lipoproteins, CRP, SAA and SAA/LDL were measured in each subject. SAA/LDL was assayed by newly developed ELISA method.

RESULTS: The patients consisted of 36 with unstable angina (UA), 252 with stable CAD (ST) and 140 without CAD (CON). The values of inflammatory markers expressed as median (25th, 75th percentile) in each group are shown below.

	UA(n=36)	ST(n=252)	CON(n=140)
CRP(mg/dl)	0.21 (0.11, 0.31)	0.09 (0.06, 0.15)	0.08 (0.06, 0.12)
SAA(μg/ml)	12.4 (6.1, 12.6)	4.2 (2.5, 7.1)	4.4 (2.7, 6.4)
SAA/LDL(μg/ml)	52.0 (36.8, 81.9)	20.5 (14.0, 30.4)	17.9 (11.8, 27.6)

By logistic regression analysis, SAA/LDL and CRP were independent and statistically significant to predict CAD and to discriminate unstable angina (p=0,001~0.008) even after controlling for classical risk factors, while SAA was only marginal (p=0.047~0,076). ROC analysis showed that SAA/LDL was equivalent with CRP for the diagnosis of CAD (AUC=0.613,0.593, respectively. p>0.20), and that SAA/LDL was superior to CRP in discriminating unstable angina (AUC=0.838, 0.733, respectively, p=0.013).
CONCLUSION: The serum level of SAA/LDL can predict the existence of both CAD and unstable angina more accurately than CRP.

ORAL CONTRIBUTIONS

803 Stable Cardiac Ischemic Syndromes: Impact of Diabetes Mellitus

Monday, March 07, 2005, 9:15 a.m.-10:30 a.m.
Orange County Convention Center, Room 414A

9:15 a.m.

803-3 Insulin Improves Myocardial Blood Flow in Patients With Type 2 Diabetes and Coronary Artery Disease

Riikka Lautamäki, K.E.Juhani Airaksinen, Marko Seppänen, Jyri Toikka, Matti Luotolahti, Ronald Borra, Jan Sundell, Juhani Knuuti, Pirjo Nuutila, University of Turku, Turku, Finland, Turku University Central Hospital, Turku, Finland

Background: Intense insulin therapy improves prognosis for type 2 diabetic patients (T2DM) with myocardial ischemia. Insulin infusion enhances myocardial blood flow in healthy subjects. In this study, the effects of insulin on myocardial perfusion were studied in T2DM patients with coronary artery disease (CAD).
Methods: We studied the effects of insulin on myocardial blood flow in regions of exercise-induced ischemia evaluated by SPECT and coronary artery stenosis confirmed by coronary angiography, and in non-ischemic regions in 43 patients (age 63 +/- 7yrs) with T2DM (HbA1c 7.1 +/- 0.9%). Myocardial blood flow was measured in the fasting state and during euglycemic hyperinsulinemic clamp at rest (n=43) and during adenosine-induced (140 μg/kg/min for 5min) hyperemia (n=26) using positron emission tomography (PET) and 15O-labelled water.
Results: In general, myocardial blood flow was significantly (P<0.05) attenuated in ischemic regions as compared to non-ischemic regions. At rest, insulin infusion increased myocardial blood flow by 13% in ischemic regions (P=0.043) and by 22% in non-ischemic regions (P=0.003). During adenosine infusion, insulin enhanced myocardial blood flow by 20% (P=0.018) in ischemic regions, and by 18% (P=0.045) in non-ischemic regions.
Conclusions: Insulin infusion improves myocardial blood flow similarly both in ischemic and non-ischemic regions in T2DM patients with CAD. Thus, the acute beneficial effects of aggressive insulin therapy in these patients may be partly related to the improvement of blood flow in ischemic regions of the myocardium.

9:30 a.m.

803-4 Comparison of Diabetics and Non-Diabetics with Chronotropic Incompetence During Dobutamine Stress Echocardiogram.

Shrikanth P. Upadya, Sheikh Mahfuzul Hoq, Siu-Sun Yao, Farooq A. Chaudhry, St. Luke's-Roosevelt Hospital, New York, NY, Yale University School of Medicine, Bridgeport, CT

Background: When patients do not reach 85% of the maximum predicted heart rate (MPHR) for the age during a dobutamine stress echocardiogram (DSE), frequently it is reported as a non-diagnostic test due to chronotropic incompetence (CI). In this study, we examined the role of DSE between diabetics (DM) and non-diabetics with CI.
Methods: We compared 329 DM to 708 non-DM patients referred for DSE. CI was defined as an inability in attaining 85% of the maximum predicted heart rate for the age during DSE. Wall motion analysis was performed using a standard 16-segment model. Ischemia was defined as new reversible wall motion abnormality and/or biphasic response. Five-year follow up was obtained for MI and cardiac death and annual event rate calculated.
Results: CI was seen in 340 patients, 212 (29.9 %) non-DM and 128(38.9%) DM patients. Results of univariate analysis are as shown in the Table. By multivariate logistic regression, BSA (p=0.005), hyperlipidemia (p=0.01) and ischemia on DSE (odds ratio=2.3, p=0.01) were predictive of hard events. Annual hard events in non- DM and. DM were 2.7% vs. 5.6% (P= 0.028).
Conclusions: Diabetics with CI have worse outcomes when compared to non-diabetics with CI. Ischemia on DSE in patients with CI was predictive of worse outcomes and associated with a 2.3 times increase in adverse outcomes.

	Non- Diabetic (N=212)	Diabetic (N= 128)	P value
Age (yrs)	59 ± 13	60 ± 11	NS
Males (%)	61.8	62.5	NS
Peak heart rate	116 ± 21	113 ± 22	NS
Hypertension (%)	66	78.9	0.23
Smoking history (%)	36.5	28.5	NS
Hyperlipidemia(%)	37.4	57	0.001
BSA (m^2)	1.9 ± 0.3	2.0 ± 0.2	0.012
Prior MI (%)	32.7	41.5	NS
Beta Blockers use (%)	39.8	43	NS
LVEF (%)	46 ± 17	39 ± 17	<0.001
Ischemia by DSE (%)	40.6	61.7	<0.001
Hard events (%)	7.5	15.6	0.028

9:45 a.m.

803-5 Chronotropic Resistance to Beta-adrenergic Antagonists in Patients with Coronary Artery Disease is Greater in Type 2 Diabetes Mellitus

Vivek J. Goswami, John A. Spertus, Robert A. O'Rourke, University of Missouri at Kansas City, The Mid-America Heart Institute, Kansas City, MO, University of Texas at San Antonio Health Science Center, San Antonio, TX

Background: Although autonomic neuropathy is a common complication of diabetes mellitus (DM), little is known about the cardiovascular effects of autonomic neuropathy, especially concerning chronotropic resistance to beta-adrenergic antagonists. The result may be a persistently elevated heart rate (HR) despite high dose beta-blocker therapy. We compared the chronotropic responses to beta-blocker therapy in diabetic and normoglycemic patients.
Methods: 265 outpatients in a coronary artery disease (CAD) clinic were included. Diabetic patients were defined as those with a fasting plasma glucose > 126 mg/dl or any prior documented diagnosis of DM. The control group consisted of normoglycemic CAD outpatients in the same clinic. All patients had objective evidence of myocardial ischemia with preserved left ventricular function. Only patients who received metoprolol as part of aggressive medical therapy were included. Patients taking other medications that may have affected heart rate were excluded. Metoprolol was initiated at 100mg and titrated to a target resting HR of < 60 beats per minute. After at least 30 days of therapy, HR and doses of metoprolol were compared between patients with DM and normoglycemic controls.
Results: The mean HR differed between the 144 diabetics and 121 normoglycemics, being 62.8 and 58.8 beats per minute, respectively. The average beta-blocker dose was 128.8mg for the diabetic patients and 102.9mg for normoglycemic patients. The results were analyzed using the Wilcoxon rank-sum test. The metoprolol dosage was divided into three groups: less than 100mg, 100mg, and greater than 100mg. The differences in HR and dose of metoprolol between diabetic and normoglycemic patients were both statistically significant (P<0.001).
Conclusion: Thus, patients with DM often have an attenuated chronotropic response to beta-adrenergic antagonists despite receiving higher doses than similar CAD patients without DM. This inability to adequately reduce HR in diabetic patients is likely due to cardiac autonomic dysfunction, which may necessitate more aggressive therapy in order to prevent recurrent cardiovascular events.

10:00 a.m.

803-6 The Metabolic Syndrome is Gradually and Independently Predictive for Vascular Events Among Patients Undergoing Coronary Angiography

Christoph H. Saely, Stefan Aczel, Thomas Marte, Peter Langer, Guenter Hoefle, Werner Benzer, Heinz Drexel, Vorarlberg Institute for Vascular Investigation and Treatment (VIVIT), Feldkirch, Austria, Academic Teaching Hospital Feldkirch, Feldkirch, Austria

Background: Prospective data on the cardiovascular risk associated with the metabolic syndrome (MetS) are limited: the impact of MetS on future vascular events in men with established coronary artery disease (CAD) is not known, and data are scarce for patients with diabetes.
Methods: We investigated 750 consecutive patients undergoing coronary angiography for the evaluation of established or suspected CAD. According to Adult Treatment Panel-III criteria, we diagnosed the MetS in the presence of three out of: abdominal obesity, hypertriglyceridemia, low HDL cholesterol, hypertension, and fasting hyperglycemia.
Results: During a follow-up period of 2.2 ± 0.4 years the MetS was an independent predictor of vascular events (adjusted hazard ratio [HR] 2.35; 95% CI 1.47-3.77). Importantly, the MetS proved significantly predictive of vascular events among men with angiographically proven CAD (n = 350; adjusted HR 2.12; 95% CI 1.23-3.66; p = 0.007) and among patients with diabetes mellitus type 2 (n = 164; HR 3.89; 95% CI 1.12-3.52; p = 0.033). Cardiovascular risk increased gradually with an increasing number of MetS risk factors (p for trend <0.001): compared with patients who did not have any MetS risk factor, the respective HRs were 1.98 (95% CI 0.66-5.93), 1.91 (95% CI 0.62-5.87), 2.55 (95% CI 0.82-7.92), 6.03 (95% CI 2.00-18.17), and 11.11 (95% CI 3.15-39.19) for patients with one through five MetS traits.
Conclusions: The MetS is a significant predictor of cardiovascular events in men with established CAD and in patients with diabetes mellitus type 2. Cardiovascular risk increases gradually with an increasing number of MetS traits.

10:15 a.m.

803-7 **High-Carbohydrate Meal Induced Reduction of Ischemic Threshold in Patients with Stable Coronary Disease: Effects of Partial Fatty Acid Inhibition by Trimetazidine**

Chiara Montano, Gabriele Fragasso, Altin Palloshi, Gianluca Perseghin, Giorgio Bassanelli, Giliola Calori, Alberto Margonato, San Raffaele Hospital, Milano, Italy

Background. Previous studies have evidenced a significant reduction of coronary flow reserve after ingestion of meals of different composition. A possible role of increased free-fatty acids levels which are deleterious during acute myocardial ischemia and reperfusion, has been hypothesized. We assessed whether the addition of the partial fatty acid inhibitor trimetazidine (TMZ) to standard conventional therapy in patients (pts) with stable coronary disease, not amenable to revascularization could improve ischemic threshold and stress left ventricular function after fasting (F), and after a high fat (HFM) and high carbohydrate (HCM) meals.
Methods. Ten pts (9 males, age 68±7 yrs) were allocated to placebo (P) and TMZ (40 mg tid), both administered from 24 hrs before F, HFM and HCM, according to a randomized, double-blind design study. All pts underwent stress (treadmill exercise testing-Bruce protocol) echocardiography after F (8hrs), HFM and HCM (3 hrs), on P and on TMZ. Time to 1mm ST segment depression (time 1mm) and stress wall motion score index (WMSI) were evaluated.
Results. On P, the HFM did not affect exercise variables compared to F, whereas HCM resulted in a reduction of the ischemic threshold (time 1 mm from 380±106 to 292±123 sec, p=0.02). Compared to P, TMZ improved time 1mm after F, HFM and HCM (432±153, p=0.04, 438±118, p=0.04, 381±111, p=0.01, respectively). Compared to P, on TMZ stress WMSI decreased from 1.55±0.25 to 1.29±0.14, p=0.001 during F, from 1.64±0.21 to 1.39±0.21, p=0.008 during HCM, and from 1.57±0.10 to 1.39±0.28, p=0.02 during HFM. Interestingly, stress WMSI on TMZ was never different from rest WMSI on P.
Conclusions. In conclusion, in pts with coronary disease a HCM results in a greater impairment of coronary reserve compared to HFM. The observed beneficial effects of the partial fatty acid inhibitor TMZ seem to be independent on meal composition.

ORAL CONTRIBUTIONS

812 Risk Factors and Clinical Outcomes in Acute Ischemic Syndrome

Monday, March 07, 2005, 11:00 a.m.-12:15 p.m.
Orange County Convention Center, Room 230D

11:00 a.m.

812-3 **Frequency, Timing, and Clinical Correlates of Changes in TIMI Risk Score at Emergency Department in Chest Pain Patients**

Francesco Pelliccia, Paolo Salvini, Domenico Cartoni, Loredana Macali, Fiammetta Albi, Bruno Polletta, Giuseppe Mercuro, Pietro Tanzi, San Filippo Neri Hospital, Rome, Italy, San Camillo Hospital, Rome, Italy

Background: TIMI risk score is commonly estimated at triage in Emergency Departement (ED) in pts with chest pain, but it remains undefined if serial, frequent re-evaluations of the score during the following observation period are warranted. Accordingly, the aim of our study was twofold: (i) to assess prospectively the frequency and timing of changes in TIMI Risk Score during ED stay; (ii) to identify which clinical factors at presentation relate to the subsequent change in TIMI risk score.
Methods: Of a total of 4,333 pts who were triaged at ED over a 1-year period because of acute chest pain, 1,747 pts (40%) were risk-stratified as 'low risk' on the basis of a TIMI risk score 0-2, and were managed further at our CPU according to recently developed critical pathways. Pathways include a protocol for ruling out myocardial infarction (i.e. q3 hour ECGs and serum markers of myocardial necrosis for 6 hours) as well as pre-specified indications for Doppler echocardiography, continuous 12-lead ST-segment monitoring, and exercise stress testing. During the observation period at ED, all pts had TIMI risk score re-evaluation every 30 minutes over a 6-hour period.
Results: During ED stay, TIMI risk score became 3 or higher in 1,095 pts (63%, Gr.A), while it did not change in the remaining 652 pts (37%, Gr.B). Timing of TIMI change vs. arrival was <30 min in 128 pts (7.3%), <60 min in 159 pts (9.1%), <90 min in 205 pts (11.7%), <120 min in 309 pts (17.7%), and <150 min in 294 pts (16.8%). Compared to Gr.B, Gr.A pts were significantly (p<0.05) more likely to be female (34% vs 21%), hypertensive (44% vs 24%), hyperlipidemic (67% vs 33%) and to have had a prior MI (19% vs 6%) or PCI/CABG (21% vs 3%). More Gr.A pts were admitted to CCU or transferred to the cath lab (10% vs 2%, p<0.05), while more Gr.B pts were discharged home directly from ED (65% vs 32%, p<0.05).
Conclusion: TIMI risk score may change soon after arrival at ED in half of pts with acute chest pain initially triaged as 'low-risk'. Changes in TIMI risk score are more common in women with multiple risk factors and/or previous diagnosis of CAD. Serial, frequent assessments of the TIMI score during the ED observation period are mandatory particularly in these subsets of pts.

11:15 a.m.

812-4 **Relationships Between Renal Function, Age, and Obesity and Outcomes in High-Risk Patients with Acute Coronary Syndromes: Results from SYNERGY**

Kenneth W. Mahaffey, Glenn Levine, Richard Gallo, John Ducas, Shaun G. Goodman, Yuliya Lokhnygina, Louise Traylor, Elliott Antman, Harvey D. White, Richard C. Becker, Jacques J. Col, Marc Cohen, Robert A. Harrington, James J. Ferguson, Robert M. Califf, for the SYNERGY Trial Investigators, Duke Clinical Research Institute, Durham, NC

Background: Uncertainty remains about the dosing of heparin in the elderly and in pts with renal insufficiency and obesity. In the SYNERGY trial, enoxaparin was dosed as 1 mg/kg every 12 h subcutaneously. Patients undergoing PCI were given a 0.3 mg/kg IV bolus if the PCI was >8 h after the last dose. Unfractionated heparin (UFH) was dosed as a 60 U/kg bolus and a 12 U/kg/h infusion with a target aPTT of 50-70 seconds.
Methods: The relationships between age, renal function, and outcomes were examined by calculating a net clinical benefit (freedom from death, nonfatal MI, urgent revascularization, or transfusion through 30 days post-enrollment) by renal function (creatinine clearance [CrCl]) and age. Outcomes were assessed by clinically relevant body mass index (BMI) groupings (<25 [27.4% of pts], ≥25 and <30 [41.1%], ≥30 and <40 [28.1%], and ≥40 [3.4%]).
Results: The net clinical benefit by renal function and age is shown (Table). Patients with the highest BMI tended to have fewer events than those with the lowest BMI (death or nonfatal MI [14.3% v 15.4%, p=0.593] and bleeding [4.5% v 8.4%, p=0.013]). No evidence of differing efficacy (p=0.700) or safety (p=0.891) existed across BMI groups by treatment (enoxaparin v UFH).
Conclusions: Patients with lower CrCl had worse outcomes, but there was no apparent increase in events in the elderly. Obese pts tended to do better than those with the lowest BMI. No apparent treatment differences between enoxaparin and UFH in these clinically important subgroups were seen.

30-day Freedom From Death/MI/Urgent Revascularization/Transfusion

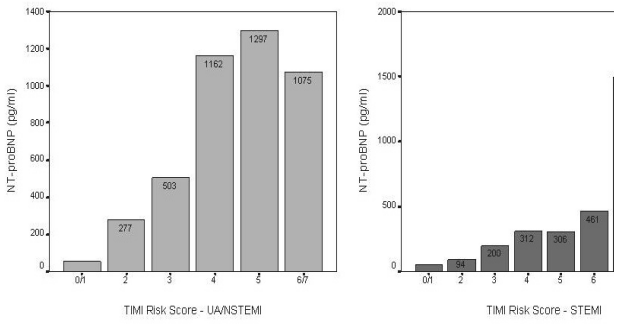
Group	N	Enoxaparin	UFH
CrCl > 60, Age ≤ 75	6589	76.1	76.0
CrCl > 60, Age > 75	870	70.1	69.9
CrCl ≤ 60, Age ≤ 75	1108	61.4	65.1
CrCl ≤ 60, Age > 75	1332	62.7	63.0

11:30 a.m.

812-5 **NT-proBNP Is Strongly Related To The TIMI Risk Score In ACS**

Michael Weber, Albrecht Elsaesser, Christian Kleine, Eva Keil, Matthias Rau, Christian Maikowski, Veselin Mitrovic, Christian Hamm, Kerckhoff Heart Center, Bad Nauheim, Germany

Background: BNP/NT-proBNP) are synthesised and secreted from the myocardium in response to ventricular wall stress and myocardial ischemia. Both markers have proven to be of independent predictive value for an adverse outcome in patients with an acute coronary syndrome (ACS). Therefore we conducted a prospective observational study to investigate the relation of NT-proBNP values to the established TIMI risk score for NSTE-ACS and STEMI in patients presenting with an ACS.
Methods and results: We included 609 consecutive patients with an episode of chest pain within the last 48 hours and an indication for early invasive diagnostic. In all patients NT-proBNP plasma levels were measured at admission. In 261 patients STEMI and in 348 patients NSTE-ACS was diagnosed. We found NT-proBNP values linked to the respective TIMI risk score, either for NSTE-ACS or STEMI (figure, values are given as median). NT-proBNP was correlated to the respective TIMI risk score in NSTE-ACS (Rho=0.43, p<0.01) and in STEMI (Rho= 0.49, p<0.01).
Conclusion: NT-proBNP is elevated in patients with an ACS strongly linked to the respective TIMI risk score for either NSTE-ACS or STEMI. These findings underlines the usefulness of NT-proBNP for risk stratification in patients presenting with an ACS. The therapeutic consequences need to be further investigated.



11:45 a.m.

812-6 **Placental Growth Factor Level is Not an Independent Predictor of Adverse Events in non-ST Elevation Acute Coronary Syndrome**

Bertil Lindahl, Anders Mälarstig, Agneta Siegbahn, Lars Wallentin, Uppsala Clinical Research Center, Uppsala, Sweden

Background: Placental Growth Factor (PlGF) is upregulated in atherosclerotic lesions and may be of importance for plaque instability. A previous study has indicated that PlGF may be an independent predictor of adverse outcome in non-ST elevation acute coronary syndrome (NSTE-ACS). We therefore evaluated the prognostic value of PlGF and compared it with other established prognostic factors in patients enrolled in the FRISC-II trial.
Methods: Blood samples were obtained at inclusion in patients enrolled in the FRISC-II trial (n=1080), evaluating an invasive vs. a non-invasive strategy in NSTE-ACS. PlGF was measured in citrated plasma using a sensitive ELISA (R&D systems). Patients were followed regarding myocardial infarction (MI) and death for 2 years.
Results: The median level of IL-10 was 10.6 ng/L [25:th-75:th percentile; 8.6 - 13.8].

Events at 2 years	PlGF <10.6 ng/L N=533	PlGF ≥10.6 ng/L N=547	p-value
MI (%)	12.6	11.7	0.66
Death (%)	3.0	5.5	0.043

After adjustment for age, gender, treatment strategy and in addition either troponin T, C-reactive protein or NT-pro B-type natriuretic peptide, the Odds Ratio (95 % CI) regarding mortality for PlGF was 1.45 (0.76-2.75), 1.30 (0.67-2.50) and 1.52 (0.79-2.92), respectively. When all these factors were entered in the model the Odds Ratio was 1.19 (0.60-2.39).

Conclusions: Increased plasma levels of PlGF are associated with raised mortality in univariate analysis, but not in multivariate analysis after adjustment for troponin T, C-reactive protein or NT-pro B-type natriuretic peptide. There was no association between PlGF and myocardial infarction.

Noon

812-7 **Increased In-Hospital Mortality in Patients Without Traditional Risk Factors Presenting With Non-ST-Segment Elevation Myocardial Infarction: Insights From the CRUSADE Initiative**

Abdul R. Halabi, Anita Y. Chen, Robert A. Harrington, Sidney C. Smith, Jr., E. Magnus Ohman, W. Brian Gibler, Eric D. Peterson, Matthew T. Roe, Duke Clinical Research Institute, Durham, NC

Background: While traditional risk factors increase the risk of developing coronary artery disease (CAD), their impact on outcomes for patients with non-ST-segment elevation myocardial infarction (NSTEMI) has not been clearly elucidated.
Methods: We compared clinical characteristics and in-hospital outcomes in 74,220 NSTEMI patients (positive CK-MB or Troponin I/T) included in the CRUSADE Quality Improvement Initiative from 476 US hospitals (January 2001-March 2004) according to the presence and number of traditional CAD risk factors (hypertension, diabetes mellitus, current/recent smoking, and dyslipidemia).
Results: There were no major differences in CAD risk factor distribution across gender and age categories. A total of 7,755 patients (10.5%) did not have any CAD risk factors and these patients had the highest frequency of unadjusted mortality (Table). The adjusted risk of mortality was lower in patients with any combination of traditional CAD risk factors (OR 0.92, 95% CI 0.82-1.04, 1 vs. none; OR 0.81, 95% CI 0.72-0.92, 2 vs. none; OR 0.83, 95% CI 0.73-0.95, 3-4 vs. none).
Conclusion: Patients without traditional CAD risk factors represent 10% of the NSTEMI population. Since the absence of traditional CAD risk factors does not yield a favorable prognosis for patients with NSTEMI, further study is needed to delineate the interplay between CAD risk factors, treatment differences, and novel inflammatory risk factors on clinical outcomes in this population.

	Number of Traditional Risk Factors*					
	0	**1**	**2**	**3**	**4**	
Variables	**n=7,755**	**n=22,314**	**n=26,329**	**n=15,422**	**n=2,400**	**P-value†**
Patient Characteristics						
Mean age (yrs)	69.3	68.9	67.8	65.3	60.4	<0.0001
Male sex	61.5	59.5	59.4	61.1	63.9	<0.0001
White race	85.1	82.8	80	77.4	73.4	<0.0001
Prior MI	17.7	23.5	32.7	41.0	46.4	<0.0001
Prior CABG	10.8	13.6	21.8	28.6	27.6	<0.0001
In-Hospital Clinical Events‡						
Death	6.8	5.9	4.6	4.1	3.4	<0.0001
Death or re-infarction	9.2	8.1	7.2	6.7	6.0	<0.0001

*All data percentages unless otherwise noted. †5-way p-values across categories. ‡Unadjusted rates.

POSTER SESSION

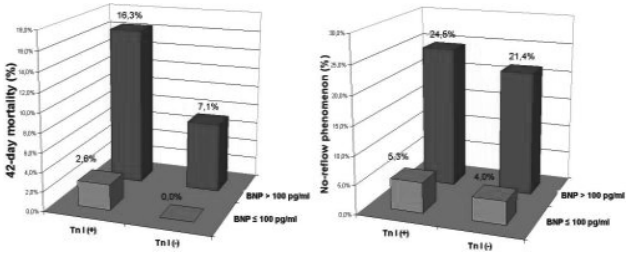
1088 Predictors of Increased Risk Among Patients With ST-Elevation Myocardial Infarction

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1088-203 **Combination of Admission Troponin I and B-type Natriuretic Peptide Levels in Prediction of Mortality and Angiographic Success of Procedure in Patients With Acute ST-Elevation Myocardial Infarction Treated With Primary Angioplasty**

Marcin Grabowski, Krzysztof J. Filipiak, Grzegorz Karpinski, Adam Rdzanek, Zenon Huczek, Grzegorz Horszczaruk, Janusz Kochman, Przemysław Stolarz, Robert Rudowski, Grzegorz Opolski, Medical University of Warsaw, Warsaw, Poland

Background: Troponin I (TnI) and B-type natriuretic peptide (BNP) levels are predictive of mortality in patients with acute coronary syndromes. Few data are available for TnI and BNP levels obtained on admission in patients (pts) with acute ST elevation myocardial infarction (STEMI) treated with primary percutaneous coronary intervention (PCI).
Methods: Blood samples for BNP (median 100 pg/ml) estimation, obtained on admission in 126 consecutive pts (mean age 58,8±10,7 years old) with STEMI were measured before PCI. Follow-up up to 42 days was performed.
Results: There was a significant difference in mortality between the group with positive TnI(+) and BNP >100 pg/ml, and the group without TnI(+) and with BNP ≤100 pg/ml: 16,3% vs. 0%, p=0,045 and significant difference in no-reflow phenomenon between the group with TnI(+) and BNP >100 pg/ml, and the group without TnI(+)and with BNP ≤100 pg/ml: 24,5% vs. 4%, p=0,049. In multivariate model, incorporating BNP, admission TnI and other clinical variables, serum BNP on admission had independent prognostic value to predict death at 42 days (odds ratio [OR]=8,8; 95% confidence interval [CI] 1,1-73,3), TIMI<3 after PCI (OR=3,5; 95%CI 1,2-9,7) no-reflow phenomenon (OR=6,2; 95%CI 1,6-23,2).
Conclusion: Combination of TnI and BNP levels obtained on admission are a powerful, independent predictor of short-term mortality and angiographic success after PCI in pts with STEMI. No-reflow phenomenon may be predicted in STEMI on basis of high serum BNP values on admission.

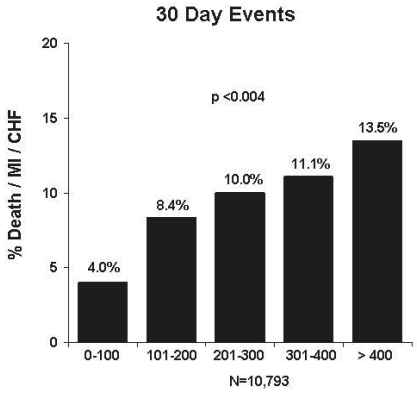


1088-204 **Association of Elevated Platelet Counts and Adverse Clinical Outcomes in the Setting of ST Segment Elevation Myocardial Infarction**

Hung Q. Ly, Ajay J. Kirtane, Jacki Buros, Sabina A. Murphy, Christopher P. Cannon, Eugene Braunwald, C. Michael Gibson, The TIMI Study Group, Brigham and Women's Hospital, Boston, MA, Beth Israel Deaconess Medical Center, Boston, MA

Background: Platelet activation and aggregation play a pivotal role in the thrombotic process leading to myocardial infarction. Prior studies have shown an association between mean platelet volume and adverse outcomes in ST elevation myocardial infarction (STEMI). However, data on platelet counts and their association with clinical outcomes in the setting of STEMI is limited.
Objectives and Methods: We hypothesized that higher platelet counts on presentation would be associated with poorer outcomes. Data was obtained from 10,793 STEMI patients pooled from the TIMI trials database.
Results: Median platelet counts on presentation were 240x10^3/μL. There was an association of increased rates of adverse clinical outcomes at 30 days with increasing platelet counts (Figure). Following multivariate analysis for correlates of elevated platelet counts (age, gender, weight, diabetes, smoking) as well as standard clinical covariates predictive of poorer outcomes in STEMI, increasing platelet counts was significantly associated with the composite end-point of death, reinfarction, and congestive heart failure: levels between 200-300 had an OR=1.20 (95% CI 1.01-1.42; p=0.033), levels 300-400 had an OR=1.43 (95%CI 1.14-1.80; p=0.02) and levels >400 had an OR=1.63 (95%CI 1.05-2.53; p=0.031) compared to the reference group with platelet levels of <200 x10^3/μL.
Conclusion: In the setting of STEMI, elevated platelet counts on presentation was independently associated with adverse clinical outcomes.

Association of Platelet Counts and Clinical Outcomes



1088-205 **Mitral Regurgitation in Myocardial Infarction Complicated by Heart Failure, Left Ventricular Dysfunction, or Both: Prognostic Significance and Relation to Ventricular Size and Function**

Maria Amigoni, Deepa Mangalat, Mikhail Bourgoun, Eric J. Velazquez, Frans Van de Werf, Jalal Ghali, John J.V. McMurray, Lars Køber, Marc A. Pfeffer, Scott D. Solomon, Brigham and Women`s Hospital, Boston, MA

Background: Mitral regurgitation (MR) after myocardial infarction (MI) is associated with increased mortality and other cardiovascular (CV) events. We assessed the relationship between MR, changes in left ventricular (LV) size and function, and CV outcomes in patients (pts) enrolled in the VALIANT echo sub study.
Methods: VALIANT randomized 14,703 pts with heart failure and/or systolic dysfunction after MI to valsartan, captopril, or both. We studied 496 pts who underwent echocardiography 5.0 ± 2.5 days after MI. MR was quantified as the jet area/left atrial area ratio: < 5%, no MR; 5-20%, mild MR; ≥ 20%, moderate to severe MR. Jet eccentricity raised the MR grade by 1 point. MR severity was related to LV size, function, and outcomes.
Results: MR was absent in 231 pts (46.6%), mild in 202 (40.7%), and moderate-severe in 63 (12.7%). MR severity was associated with older age, female sex, history of MI, hypertension, diabetes, and heart failure (p trend<0.02). LV end-diastolic (no MR: 112.1 ± 28.2 ml, mild MR: 123.5 ± 29.5 ml, mod-sev: 139.6 ± 43.3 ml.) and end-systolic (no MR: 67.3 ± 19.8 ml, mild MR: 76.8 ± 23.4 ml, mod-sev: 88 ± 33 ml) volumes increased with worsening MR, and ejection fraction decreased (no MR: 40.4 ± 5.1%, mild MR: 38.4 ± 5.8%, mod-sev: 37.7 ± 7.4%) (p trend<0.0001). Moderate-severe MR was an independent predictor of total mortality, CV mortality, or any CV event (p<0.05).
Conclusions: MR severity is associated with larger LV volumes, worse LV function, and adverse outcomes in pts with LV dysfunction after MI.

Table. Association of moderate-severe MR with outcomes

	Hazard Ratio*	95% - CI	P value
Death	2.3	1.2- 4.5	0.016
CV death	2.2	1- 4.5	0.037
Combined end point (CV death, heart failure hospitalization, recurrent MI, cardiac arrest or stroke)	2.1	1.3- 3.5	0.002

(*Adjusted for age, gender, heart rate, Killip class, PTCI, diabetes, history of heart failure, history of MI, renal insufficiency, ejection fraction, left ventricular diastolic volume)

1088-206 **Transfer to Acute PCI Improves Outcome for Patients With ST-elevation Myocardial Infarction**

Michael Oeff, Harm Ohlmeier, Albrecht Hempel, Hartmut Goos, Hartmut Huget, Antje Goesswald, Ute Wolf, Staedtisches Klinikum Brandenburg, Brandenburg an der Havel, Germany

Early thrombolysis is recommended for the treatment of myocardial infarction with ST-segment elevation (STEMI), if expected time delay to PCI is more than 90 minutes. But discussion about differences in outcome between early thrombolysis and delayed primary PCI is ongoing.
Methods: The multicenter hospital-based Myocardial Infarction Registry Brandenburg - representing a weakly populated German state - included 2391 patients (pts) with acute coronary syndrome (ACS). Survival analysis of pts with STEMI receiving early thrombolysis ± PCI vs delayed primary PCI was performed. Mean follow-up in 99,1% of pts: 1,5±0,2 yrs.
Results: Of all ACS-pts 1099 presented with STEMI (men 67%; mean age 65.3+/- 12 yrs) within 24h after symptom onset. Primary thrombolysis was administered in 451 (41%) followed by PCI in 330 (30%). Primary PCI was performed in 440 (40%), in 208 (19%) no reperfusion therapy was performed within 24h. Median time to thrombolysis was 2.3h to primary PCI was 5.4h.
Following subgroups were compared regarding 30-day-mortality: group A: pts receiving early thrombolysis (<4h) without subsequent PCI (n=66), group B: pts receiving early thrombolysis + PCI (n= 221) and group C: pts after delayed primary PCI within 4-24h (n=211). 30-day-mortality was 15,2; 6,8; 6,2%. Difference in mortality was only significant comparing group A vs C: p=0,02. Comparing the combined group (A+B) vs C mortality was 8.7 vs 6.2% (p=ns).
Logistic regression analysis revealed age (OR:1.09;CI:1.05-1.13), renal failure (OR:4.81;CI:1.58-14.68), cardiac shock (OR:3.64;CI:1.10-12.01), heart failure at admission (OR:2.65; CI:1.05-6.69) and dyslipidaemia (OR: 0.36;CI:0.16-0.80) as independent influencing factors. There is a tendency towards higher mortality-rates in group A, but treatment strategies had no independent influence on outcome.
Conclusion: Outcome after early thrombolysis within 4 hours after symptom onset followed by PCI is comparable to that after delayed primary PCI regarding 30-day mortality. This treatment strategy can be recommended in weakly populated areas with long distances to centers with angioplasty facilities.

1088-207 **High Levels Of Plasma N-terminal Pro-b-Type Natriuretic Peptide in Diabetic Patients With Acute Myocardial Infarction Are Associated With an Increased Risk of In-Hospital Mortality.**

Marianne Zeller, Gilles Dentan, Yves Laurent, Jean-Claude Beer, Luc Janin-Manificat, Hamib Makki, Isabelle L'Huillier, Bruno Vergès, Michel Vincent-Martin, Alexandra Oudot, Jean-Eric Wolf, Yves Cottin, on behalf of the RICO Survey working group, University of Burgundy, Dijon, France, University Hospital, Dijon, France

Background. N-terminal Pro-B-type Natriuretic Peptide (N-BNP), has been shown to provide valuable prognostic information on short and long term mortality in patients with acute Myocardial Infarction (MI). However, only few data on N-BNP levels in diabetic patients after MI are available**.**
Patients and method. From french regional RICO survey, we measured plasma N-BNP (Elecsys, Roche) on admission for MI in 560 patients, including 199 (35%) patients with diabetes mellitus (DM). DM was defined by an history of diagnosed DM or by mean of 2 fasting blood glucose ≥ 7.0 mmol/l (126 mg/l).
Results. In-hospital mortality and cardiogenic shock were strongly associated with supra median plasma N-BNP levels (p<0.0001). In mutivariate analysis, N-BNP levels were inversely associated with creatinine clearance and Left Ventricular Ejection Fraction (LVEF) (both p<0.0001) and directly associated with age (p=0.0002) and diabetes (p=0.002). However, there was no association with CK peak level or hypertension. N-BNP plasma levels were significantly higher in DM patients compared to non-diabetic patients (Median (25^{th}-75^{th}): 245 [81-777] vs. 130 [49-299] pmol/l, p<0.0001). The difference remained statistically significant (p=0.01) even after adjustment for age, creatinine clearance and LVEF. In DM patients, we found no significant correlation between N-BNP and plasma glucose. Moreover, DM patients showed a higher rate of in-hospital mortality (17% vs. 6%, p<0.0001) and cardiogenic shock (16% vs. 7%, p=0.0002). In multivariate analysis, when DM was not an independent predictive factor, both cardiogenic shock and in-hospital mortality were inversely associated with LVEF (p<0.0001 and p=0.0001 respectively) and directly associated with log N-BNP (p=0.0002 and p=0.02, respectively).
Conclusions: 1) In acute MI, DM patients show increased plasma N-BNP levels independently of age, renal function and LVEF 2). This rise in N-BNP levels appears to be strongly associated with the increased incidence of in-hospital mortality and cardiogenic shock observed in DM.

1088-208 **Primary Coronary Intervention and Prevention of Left Ventricular Remodeling: Comparison Between Two Age Groups**

Chiara Agresti, Francesca Innocenti, Giorgio Jacopo Baldereschi, Francesca Caldi, Niccolò Marchionni, Massimo Margheri, Marco Comeglio, Giulio Masotti, Riccardo Pini, University of Firenze and AOU Careggi, Florence, Italy

Background: the study was undertaken to compare, between patients of different age groups, the efficacy of primary coronary intervention (PCI) on prevention of left ventricular (LV) remodeling after anterior ST-elevation myocardial infarction (STEMI).
Methods: one month after PCI for a first anterior STEMI, 116 patients (G1: 93 aged<75, mean age 59±9 years, males 80%; G2: 23 aged≥75, mean age 80±4 years, males 61%) underwent standardized dobutamine stress echocardiography (DSE) and measurement of left anterior descending (LAD) coronary artery flow reserve (CFR) by transthoracic echocardiography during intravenous adenosine infusion (140 /kg/min for 5').
Results: Hyperlipidemia and smoking were more frequent in G1, peripheral vascular disease in G2. CPK peak was significantly higher in G1 (3249±2414 IU/L vs. 1894±1462 IU/L, p<0.05), while time delay between symptom onset and PCI was similar in the two groups (4±2.8 vs. 4±1.5 hours, p=NS). Extension of coronary artery disease, was also comparable. LV end-diastolic diameter (EDD) and volume (EDV) were slightly, though significantly greater in G1, but indexed EDV was similar, probably due to the larger proportion of females, with smaller BSA, in G2 (EDVi: 70±18 in G1 vs. 64±13 ml/m^2 in G2, p=NS). LV ejection fraction was similar and only slightly reduced (G1: 45±11%, G2: 46±10%, p=NS). Wall motion score index (WMSI) was similar in the two groups during the whole stress test, either globally or when calculated separately for necrotic and remote area. CFR was within the lower normal range and similar in the two groups (G1 2.0±0.6 vs. G2 2.1±0.4 p=NS), and LAD diastolic maximal and median flow velocity, both at baseline and after adenosine infusion, were similar as well.
Conclusion: The beneficial effect of PCI on microvascular integrity and left ventricular remodelling is age-independent and is associated with a substantially preserved global LV systolic function after anterior STEMI. This data reinforce the importance of offering older people the benefits of invasive treatment of acute STEMI, particularly in consideration of the highly negative impact of LV dysfunction on the prognosis and the quality of life of this aged subset.

POSTER SESSION

1089 Biomarkers and Risk Assessment in Acute Ischemic Syndrome

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1089-195 Admission α_1- Antitrypsin Levels Predicts Myocardial Infarction Size

Shahar Lavi, Robert Zukerman, Zvi Borochowitz, Oren Zinder, Vardit Adir, Michael Kapeliovich, Yoram Agmon, Walter Markiewicz, Haim Hammerman, Rambam Medical Center, Haifa, Israel, Bnai-Zion Medical Center, Haifa, Israel

Introduction: α_1-antitrypsin (AT) is both an inflammation sensitive plasma protein and a protease inhibitor. Those, its correlation with acute myocardial infarction (MI) could be unique. Our aim was to investigate the time course of α_1-AT levels during acute MI and correlate it with left ventricular function
Methods: Sixty-two patients with first acute ST elevation MI were enrolled. Blood samples were obtained for α1-AT levels on admission, and then for 5 consecutive days. Subjects were genotyped for Z-E342K and S-E264V mutations to exclude allelic influence. Patients were followed for 30 days. Left ventricular wall motion score index (WMSI) as assessed by echocardiography during 2nd-3rd day
Results: None of the patients had the above mutations. Patients were divided into two groups according to median α1-AT levels on admission. Patients with higher admission levels maintained elevated levels throughout hospital course. Anterior wall MI was more frequent in these patients. Other baseline characteristics were similar. α1-AT increased less in patients with higher admission levels as compared to patients with lower levels (47% vs. 37%, p=ns). Admission α1-AT levels were significantly correlated with WMSI (R=0.33, p=0.008). Events rates were low and not different between the groups
Conclusions: Higher levels of α1-AT on admission and during acute MI are associated with larger infarctions. The known ~ 24h delay of α1-AT rise during stress suggest marked inflammatory response in large MI prior to admission.

	admission α1-AT <130 mg/dL (n=31)	admission α1-AT >130 mg/dL (n=31)	p value
Day 2 α1-AT mg/dL	134±3	162±5	0.0002
Day 3 α1-AT mg/dL	157±4	184±6	0.002
Day 4 α1-AT mg/dL	164±6	196±8	0.002
Day 5 α1-AT mg/dL	166±6	190±7	0.01
WMSI	1.5±0.05	1.71±0.06	<0.01
max $CK_{(U/L)}$	2016±269	3371±604	0.05
Anterior wall MI (#)	6	12	ns

1089-196 NT-Pro Brain Natriuretic Peptide Levels Predict the Rate of Death in Diabetic Patients With Acute Coronary Syndromes Without ST Elevation

Oscar Bazzino, Diego Perez de Arenaza, Florencia Rolandi, Jose Navarro Estrada, Juan Fuselli, Fernando Botto, J. Santopinto, Maria Ines Sosa Liprandi, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Background and aims: Patients with diabetes mellitus (DM) with acute coronary syndromes (ACS) are at increased risk of further complications. We examined the clinical characteristics, levels of N-terminal Natriuretic Peptide(NT-proBNP), troponin T (TnT), and C-Reactive Protein (CRP), and clinical outcomes in patients with and without diabetes in a cohort of unselected patients admitted with ACS without ST elevation (NSTE-ACS).
Methods: We undertook a prospective, cohort of 1483 patients admitted to 12 centers with NSTE-ACS that was followed up for 6 months. Centralized measurements of NT-proBNP, TnT, and CRP, were performed 3 h (median) after admission.
Results: A prior diagnosis of diabetes mellitus (DM) was found in 275 (18%) patients. These patients were younger and had higher rates of prior hypertension, hypercholesterolemia, prior myocardial infarction (MI), or peripheral artery disease (PAD) than non-DM patients. Rates of elevated levels of NT-proBNP (>586 pg/mL), TnT (>0.03 ng/mL), and CRP (>3 mg/L) were higher in diabetic compared to non diabetic patients (38% vs 28, p=0.001; 68% vs 57%, p=0.002; 34% vs 27%, p=0001 respectively). The rate of death was 9.1% (n=25/275) in diabetic patients compared to 4.3% (n=52/1208) in non diabetic (p=0.001) and the rate of MI was 5.8% (n=16/275) and 3.1% (n=37/1208) (0.02) respectively. In diabetic patients, characteristics associated with death or MI were elevated NT-proBNP (>586 pg/mL), troponin I (>0.1 ng/mL), ST depression on ECG, age, female sex, prior angina and PAD. In a multivariate logistic regression model of diabetic patients including clinical, ECG, and biomarkers variables NT-proBNP levels (OR 1.91, 95% CI 1.44-2.53, p<0.001) was an independent predictor of death and TnT levels (OR 1.22, 95% CI 1.01-1.46, p<0.001) was an independent predictor of MI at 6 months.
Conclusions: Diabetic patients with NSTEACS have higher risk profile, biomarker levels and clinical outcomes than non diabetic patients. Biomarkers are useful to identify DM patients at high risk of clinical events: NT-proBNP identifies patients at high risk of death and TnT at high risk of MI.

1089-197 A Multimarker Strategy Predicts Short- and Long-Term Mortality in Patients Admitted for Exclusion of Myocardial Infarction

Michael C. Kontos, Rajat Garg, F Philip Anderson, Charlotte S. Roberts, James L. Tatum, Joseph P. Ornato, Robert L. Jesse, Virginia Commonwealth University, Richmond, VA

BACKGROUND: A multi-marker strategy incorporating myoglobin (MYO), CK-MB and troponin I (TnI) has been used to rapidly diagnose myocardial infarction (MI). However, there is little data comparing the additive value of these markers for predicting short- and long-term mortality.
METHODS: Consecutive patients (pts) without ST elevation on the initial ECG were admitted and underwent serial assessment of cardiac markers (CK, CK-MB, and TnI) over 8 hours for diagnosis of MI. MYO was assessed at the time of admission and/or 3 hours later. Pts with positive markers had continued assessment until the markers peaked. Thirty day and one year all-cause mortality were assessed for each marker individually and in combination.
RESULTS: A total of 3,461 consecutive pts without ST elevation were included in the analysis. Overall 30 day and 1 year mortality was 2.4% and 9.7%. The number of pts with (+) markers and mortality are shown in the Table. Mortality was similar and not significantly different in pts with a (+) TnI, MYO or CK-MB. Each additional positive marker was associated with a significant increase in mortality, both at 30 days and 1 year.
CONCLUSIONS: Elevations in any cardiac marker predict mortality. The more markers that are positive, the higher the mortality.

Marker	# Positive (%)	30 Day Death, %		1 Year Death	
		Marker (-)	Marker (+)	Marker (-)	Marker (+)
MYO	675 (20)	1.3 #	7.9	7.6 #	22
CK-MB	421 (12)	1.5 #	8.8	8.4 #	20
TnI	517 (15)	1.6 #	7.2	8.2 #	19
0 markers (+)	2490 (72)	1.0	NA	6.6*	NA
1 marker (+)	533 (16)	NA	3.2	NA	13.7*
2 Markers (+)	234 (6.8)	NA	6.8	NA	20
All Markers (+)	204 (5.9)	NA	12.7	NA	25.5
*=p<0.05 for 0 vs 1, 1 vs 2 or 2 vs 3 makers (+); p<0.001 (+) vs (-) marker					

1089-198 Correlation of Serum Neopterin Levels With Admission TIMI Risk Scores in Patients With Acute Coronary Syndromes

Marios D. Gagos, Douglas T. Johnston, Nicholas Raio, David Shenouda, Louis Ragolia, Kevin Marzo, Mark Davis-Lorton, Joshua DeLeon, Winthrop University Hospital, Mineola, NY

Background: The American College of Cardiology (ACC) and American Heart Association (AHA) guidelines include the use of multiple risk scores in the initial assessment of patients with acute coronary syndromes (ACS). Macrophage activation has been proven to be a vital component of atheromatous plaque disruption resulting in ACS. Serum Neopterin, a pterydine by-product of macrophage activation, has been documented to be elevated in ACS when compared with control subjects. We evaluated the relationship between calculated admission TIMI risk scores and serum neopterin levels in patients with ACS.
Methods: We studied 57 subjects who were admitted with a diagnosis of unstable angina (20 men, 14 women; mean age 62.3 +/- 7 years, range 33 to 88) amd non-ST elevation myocardial infarction (NSTEMI) (12 men, 11 women; mean age 64.7 +/- 6 years, range 41 to 93). All blood samples were drawn on admission, 24 and 72 hours of admission. Serum neopterin levels were determined with a commercially available enzyme-linked immunosorbent assay and compared to admission TIMI risk scores calculated by ACC/AHA guidelines.
Results: Serum neopterin had a strong correlation with the calculated TIMI risk score on admission, r=0.80, n=57, p<0.0001 by the Spearman Correlation. The corresponding mean neopterin levels for patients with ACS stratified with TIMI scores between 1 through 7 were the following: patients with TIMI 1 scores had mean neopterin levels of 3.3 +/- 0.4 nmol/L, TIMI 2 patients 4.6 +/- 0.6 nmol/L, TIMI 3 patients 5.2 +/- 1.2 nmol/L, TIMI 4 patients 7.0 +/- 2.2 nmol/L, TIMI 5 patients 10.3+/- 3.5, TIMI 6 patients 18.4.5 +/- 4.5 nmol/L, and TIMI 7 patients 28.0 +/- 0.0. The sharp rise in Neopterin levels with one-unit increases of TIMI score appear to be non-linear (exponential growth, R-square=0.71, p<0.0001).
Conclusions: Serum Neopterin levels drawn on admission have a high correlation with ACC/AHA calculated TIMI risk scores. Serum neopterin may be useful in estimating coronary disease activity and the non-linearity of the correlation may suggest a more sensitive marker for defining risk in ACS.

1089-199 Myoglobin Predicts Mortality Better Than Troponin I, Even in Patients With Renal Failure

Michael C. Kontos, Rajat Garg, F Philip Anderson, Charlotte S. Roberts, James L. Tatum, Joesph P. Ornato, Robert L. Jesse, Virginia Commonwealth University, Richmond, VA

BACKGROUND: Myoglobin (MYO) can be used as an early marker to diagnose myocardial infarction (MI), and while non-specific for myocardial necrosis, it does appear to be a strong predictor of mortality. Elevations of MYO are commonly present in patients (pts) with renal failure (RF). Whether the predictive value of MYO is secondary to identification of pts with RF has not been studied.
METHODS: Consecutive pts admitted for MI exclusion without ST elevation on the initial ECG underwent serial assessment of cardiac markers (CK, CK-MB, and TnI) over 8 hours. MYO was assessed at the time of admission and/or 3 hours later. Pts with positive markers had continued assessment until they peaked. RF was defined as a creatinine clearance <60 ml/min. Multivariate analysis was performed to identify predictors of one year all cause mortality in all pts and those with RF.

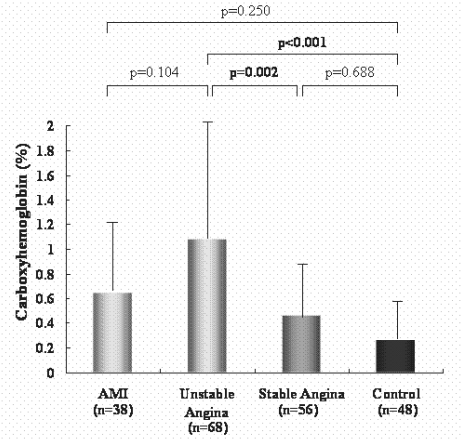
RESULTS: A total of 3,461 pts without ST elevation were included in the analysis. Overall 30 day and 1 year mortality was 2.4% and 9.7%. MYO was elevated in 675 (20%), CK-MB in 421 (12%), and TnI in 517 (15%). Among the 993 pts with RF, MYO was elevated in 43%, CK-MB in 17% and TnI in 21%. MYO was the strongest multivariate predictor of mortality in all pts, as well as in pts with RF. TnI had borderline predictive value, while CK-MB was not predictive in either group. **CONCLUSIONS:** Despite absence of cardiac specificity, an elevated MYO still strongly predicts mortality, even in pts with RF.

	All Patients (n=3,461)		Patients with RF (n=993)	
	OR (95% CI)	P Value	OR (95% CI)	P value
Age>65	2.8 (2.2, 3.6)	<0.001	1.5 (1.0, 2.1)	0.03
Prior MI	1.5 (1.1, 2.0)	0.01	1.6 (1.1, 2.40	0.02
Ischemic ECG	1.6 (1.1, 2.1)	<0.001	2.3 (1.6, 3.4)	<0.0001
MYO (+)	2.8 (2.1, 3.7)	<0.0001	2.3 (1.6, 3.4)	<0.0001
TnI (+)	1.4 (0.96, 2.0)	0.08	1.5 (0.95, 2.3)	0.08

1089-200 **Increase in Carboxyhemoglobin in Patients With Acute Coronary Syndrome**

Soon Jun Hong, Hong Seog Seo, Chang Gyu Park, Seung Woon Rha, Jin Won Kim, Jung Chun Ahn, Woo Hyuk Song, Dong Joo Oh, Young Moo Ro, Cardiovascular Center, Korea University Hospital, Seoul, South Korea

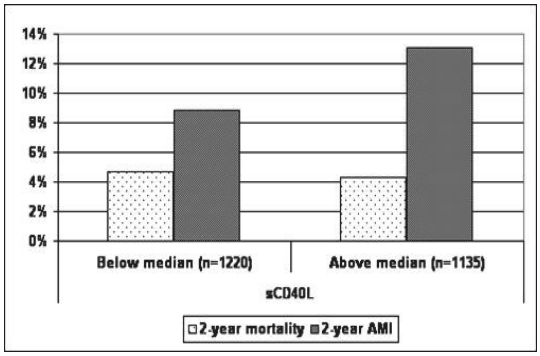
Background: Carbon monoxide (CO), produced within the blood vessel wall, has been known for the regulation of vascular smooth muscle tone. CO is synthesized endogenously by heme oxygenase type 1 in response to ischemic stress. The relation between CO and coronary artery diseases has not been investigated.
Methods: Total of 210 participants (94 women and 116 men) with suspected coronary artery diseases were divided into four groups: acute myocardial infarction (AMI) (n=38), unstable angina pectoris (UAP) (n=68), stable angina pectoris (SAP) (n=56), and control (n=48). All patients underwent coronary angiography (CAG) in evaluation of rest or effort angina. Following the CAG, venous carboxyhemoglobin (COHb) was measured.
Results: COHb level in UAP was significantly higher than those of SAP and control, but COHb level showed no significant difference between UAP and AMI (Figure). Total cholesterol in UAP was significantly higher than that of control (177 ± 40 Versus 144 ± 29 mg/dL, p=0.03). C-reactive protein (CRP) progressively increased from control to AMI; however, only CRP in AMI was significantly higher than that of control (6.2 ± 5.7 Versus 0.8 ± 0.9 mg/L, p<0.01). There were no significant differences in age, body mass index, fasting blood sugar, HDL-cholesterol, and lipoprotein(a) in all groups.
Conclusion: Our results suggest that acute coronary syndrome is associated with higher COHb level, and the increase in COHb may result from the acute compensatory mechanism responding to ischemic stress.



1089-201 **Levels of Soluble CD40L are Associated With Myocardial Infarction, but not Mortality, in Patients With Non-ST Elevation Acute Coronary Syndrome**

Anders Malarstig, Bertil Lindahl, Lars Wallentin, Agneta Siegbahn, Department of Medical Sciences, Clinical Chemistry, Uppsala, Sweden, Department of Medical Sciences, Cardiology, Uppsala, Sweden

Background: Recent data suggest that CD40L and its receptor CD40 is involved in the pathogenesis of NSTE-ACS by acting in the inflammatory and coagulatory systems. The aim of this study was to investigate whether levels of sCD40L at study inclusion was associated with MI and death during follow-up in a large cohort of patients with NSTE-ACS.
Methods: Citrated plasma samples were obtained at inclusion in patients enrolled in the FRISC-II trial (n=2355), evaluating an invasive vs. a non-invasive strategy in NSTE-ACS. Plasma concentrations of sCD40L were determined using an ELISA assay (Bender MedSystems). Patients were followed regarding MI and death for 2 years.
Results: The median level of sCD40L was 0.29 ng/ml [25:th-75:th percentile; 0.19-0.49]. A strong association between sCD40L levels and subsequent myocardial infarction was observed (p<0.001), whereas the mortality rate was equal in patients with sCD40L levels above and below median. The results were similar in patients that received an early invasive treatment and in those that did not. Levels of sCD40L did not correlate to Troponin T, Interleukin-6 or C-reactive protein.
Conclusions: In patients with NSTE-ACS an increased plasma concentration of soluble CD40L is associated with an increased long-term risk of MI , but not with mortality.



1089-202 **N-Terminal Pro-B-Type Natriuretic Peptide in the Prediction of Coronary Artery Disease in Unstable Angina Patients with Normal Troponin I and ECG**

Youngkeun Ahn, Seo Na Hong, Nam Sik Yoon, Sang Yub Lim, Kyoung Ho Yun, Dong Koo Kang, Sang Hyun Lee, Yeon Sang Lee, Kye Hun Kim, Young Joon Hong, Hyung Wook Park, Ju Han Kim, Weon Kim, Myung Ho Jeong, Jeong Gwan Cho, Jong Chun Park, Jung Chaee Kang, The Heart Center of Chonnam National University Hospital, Gwangju, South Korea

Background: Elevation in B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) are associated with symptomatic left ventricular dysfunction. Myocardial ischemia may also cause elevation in level of BNP and NT-proBNP.
Methods and Results: To determine whether elevation of NT-proBNP without elevation of cardiac specific marker could predict the coronary artery disease, we measured serum (s) NT-proBNP level in 179 unstable angina patients (61.8±44.1 years, male 60.9 %) with normal ventricular function (left ventricular ejection fraction > 55 % and no regional wall motion abnormality by echocardiography) and normal troponin I level (≤ 0.05 ng/mL). In these patients, level of CRP, myoglobin and ECG finding are normal. Serum-level of NT-proBNP was higher in patients with coronary artery disease (n=74) than in those without coronary artery stenosis (n=105) (196.8±339.8 vs. 78.4±91.0 pg/mL, p=0.005). At the standard cutpoint of > 200 pg/mL, elevated BNP show high probability of coronary artery disease (odd ratio, 2.98; 95% CI, 1.4 to 8.2; p =0.006).We estimated the extent of coronary artery disease by the Gensini score. The Gensini score was computed by assigning the severity score to each coronary, according to the degree of luminal narrowing and its geographic importance. S-level of NT-proBNP was positively correlated with extent of coronary artery disease (r=0.347, p= 0.001).
Conclusions: NT-proBNP will be a useful screening test for coronary artery disease in unstable angina patients with normal troponin I value and normal ECG.

POSTER SESSION

1090 Diabetes, Lipids, and Thrombosis in Myocardial Infarction Patients

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1090-226 **Primary Percutaneous Coronary Intervention Compared With Thrombolysis for Acute Myocardial Infarction in Diabetes: Results From Randomized Trials of the PCAT Collaboration**

Jorik R. Timmer, Jan Paul Ottervanger, Menko-Jan de Boer, Eric Boersma, Cindy Grines, Cindy Westerhout, Chris Granger, Felix Zijlstra, PCAT collaborators, Isala Klinieken, Iocatie Weezenlanden, Zwolle, The Netherlands, Erasmus Medical Center, Rotterdam, The Netherlands

Background: There is growing evidence for a clinical benefit of primary percutaneous coronary intervention (PCI) compared to thrombolysis as reperfusion therapy in general. However, there are limited data whether this also applies to patients with diabetes.
Methods: Primary PCI was compared with thrombolysis for ST-segment elevation myocardial infarction (STEMI) in patients with diabetes, based on individual patient data derived from clinical trials on behalf of the PCAT collaboration study group. All patients were randomised to thrombolysis or primary PCI. Clinical end-points were mortality, re-infarction, and the combined end-point of mortality or non fatal re-infarction (MACE) after 30 days.
Results: A total of 6,315 patients were included of which 947 (15%) had diabetes. Patients with diabetes were older, were more often female, had more often previous myocardial infarction, and had a longer ischemic time. Mortality (8.8% vs. 5.9%, p<0.001) and incidence of MACE (12.4% vs. 9.8%, p= 0.01) were higher in patients with diabetes. Compared to thrombolysis, primary PCI was associated with a decreased mortality in patients with diabetes (OR 0.5; 95%CI: 0.3 - 0.8) and in patients without diabetes (OR 0.7; 95%CI: 0.5 - 0.9). Recurrent infarction and MACE were also reduced after primary PCI in both patients with and without diabetes.

Conclusion: Diabetic patients with STEMI treated with reperfusion therapy have an increased mortality compared to patients without diabetes. The beneficial effects of primary PCI compared to thrombolysis in patients with diabetes, are at least equal to the effects in patients without diabetes.

1090-227 Long-Term Mortality of Diabetic Patients in Cardiogenic Shock Complicating Acute Myocardial Infarction

Michael E. Farkouh, Krishnan Ramanathan, Eve D. Aymong, John G. Webb, Shannon M. Harkness, Lynn A. Sleeper, Judith S. Hochman, NYU School of Medicine, New York, NY

BACKGROUND: The role of diabetes mellitus (DM) in cardiogenic shock (CS) complicating an acute myocardial infarction (AMI) is not well understood. Previous studies have reported an in-hospital mortality rate for DM patients with CS of > 60%. We sought to compare the 1-year mortality rates of DM and non-diabetic (NDM) patients and to evaluate the impact of a strategy of early revascularization (ERV) compared to initial medical stabilization (IMS) in DM patients with CS.
METHODS: Baseline characteristics, clinical and hemodynamic measures and management were compared for 90 DM (31%) and 198 NDM (69%) who were randomized to ERV or IMS in the SHOCK Trial. Cox proportional hazards regression was performed to evaluate the relationship between DM and treatment strategies for 1-year mortality.
RESULTS: When compared to NDM, DM were of similar age but had higher rates of prior MI (44.4 vs. 27.8%, p=0.007) and hypertension (56.2 vs. 42.5%, p=0.04). The DM group had lower rates of pulmonary artery catheterization (88.9 vs. 97.5%, p=0.007) and fibrinolytic therapy (44.4 vs. 60.1%, p=0.02). For patients randomized to ERV, DM patients had a higher rate of coronary artery bypass grafting (CABG) (50.0 vs. 30.9%, p=0.03) despite similar rates of triple vessel disease. The rates of intra-aortic balloon counterpulsation and coronary angiography exceeded 80% in both NDM and DM.
The 1-year mortality rates in the DM and the NDM groups were equivalent (58.9%). One-year mortality was not associated with diabetes (hazard ratio 1.02, 95%CI 0.73 to 1.42, p=0.91). The magnitude of the benefit of an ERV strategy was similar in the DM and NDM groups [hazard ratio (DM) 0.62, HR (NDM) 0.75, p=0.58]. Even after adjusting for the imbalance in CABG rates between DM and NDM, 1-year mortality was not associated with DM.
CONCLUSION: Diabetes mellitus is not a predictor of 1-year mortality in CS after AMI. The magnitude of benefit from an ERV strategy is similar for DM when compared to NDM. The higher rate of CABG procedures in DM is unlikely to account for the lack of differences in mortality between DM and NDM. The influence of diabetes and the management strategies of DM on mortality in CS deserves further prospective evaluation.

1090-228 Automated External Defibrillator Analysis Specifically Designed for Pediatric Patients

Dianne Atkins, Ian Law, Andrew Blaufox, William Scott, McDonald Dick, Wangcai Liao, Jamil Sohb, Frederick Geheb, James E. Brewer, University of Iowa, Iowa City, IA, ZOLL Medical Corporation, Chelmsford, MA

Background: Electrocardiographic (ECG) rhythm analysis algorithms in automated external defibrillators (AEDs) have been evaluated against pediatric patient rhythms (patients ≤ 8 years old). However, tested algorithms were designed using adult ECG detection criteria. Using adult algorithms to detect nonshockable pediatric supraventricular tachycardia (SVT) has been difficult. This study defined shockable and nonshockable rhythm detection criteria specific to pediatric patients, developed a pediatric rhythm database (PRDB) of annotated rhythms and a pediatric-based AED rhythm analysis algorithm, and determined its accuracy.
Methods: Pediatric rhythm detection criteria were defined for coarse ventricular fibrillation (VF), rapid ventricular tachycardia (VT), and nonshockable rhythms, including pediatric SVT. Pediatric rhythms were collected as sustained, classifiable, rhythms ≥ 9 seconds in length, and were annotated by pediatric cardiologists as clinically shockable or nonshockable based on pediatric criteria. Rhythms were placed into a publicly-available pediatric rhythm database (PRDB); each rhythm was converted to digitally accessible, public-domain, MIT rhythm data format with sampling rate and bit resolution. PRDB was used to evaluate a pediatric-based AED rhythm analysis algorithm.
Results: There were 124 shockable rhythms from 49 patients (sensitivity (SE); coarse VF: 42 rhythms, 100%; rapid VT: 82 rhythms, 94%), for combined SE of 96.0% (119/124). There were 585 nonshockable rhythms from 155 patients (specificity (SP); normal sinus: 208 rhythms, 100%; asystole: 29 rhythms, 100%; SVT: 161 rhythms, 99%; other sinus arrhythmias: 187 rhythms, 100%), for combined SP of 99.7% (583/585). Overall accuracy for shockable and nonshockable rhythms was 99.0% (702/709).
Conclusions: New pediatric rhythm detection criteria were defined, and analysis based on these criteria demonstrated both high sensitivity (coarse VF, rapid VT) and high specificity (nonshockable rhythms, including SVT). A pediatric-based AED can correctly detect shockable rhythms, making it safe and exceptionally effective for children.

1090-229 Specificity Of Metabolic Abnormalities In Young Patients With Metabolic Syndrome And Acute Myocardial Infarction. Data From The Rico Survey

Marianne Zeller, Gilles Dentan, Isabelle L'Huillier, Michel Farnier, Luc Janin-Manificat, Jean-claude Beer, Yves Laurent, Alexandra Oudot, Hamib Makki, Bruno Vergès, Luc Rochette, Yves Cottin, on behalf of the RICO survey working group, University of Burgundy, Dijon, France

Background. Young patients with acute myocardial infarction (MI) are known to have a specific risk factor profile, in particular for tobacco use and dyslipidemia. Little is known, however, about the prevalence and impact of metabolic syndrome (MS) in these patients. We investigated the occurrence and prognosis of MS in young adults (≤ 45 y) with acute (MI).
Patients. We analysed 663 patients included in the RICO survey (French regional survey for acute MI) between 1st January 2001 and 4th May 2004. MS was evaluated at the time of MI and was defined according to the NECP/ATP III by 3 or more of the following criteria: fasting glycaemia ≥ 6.1 mmol/l, triglycerides ≥ 1.7 mmol/l, HDL-cholesterol <1.04 (M)/1.29 (F) mmol/l, blood pressure ≥ 130/85 mm Hg or waist circumference > 102(M)/88(F) cm. Patients were classified according to their age (young (≤ 45y) and old (>45y)) and to the presence of MS.
Results. Of the 663 MI patients included, 63(10%) were young (≤ 45y) (median(25th-75th) age: 41(38-44) y). The prevalence of MS was similar for young and old patients (38 vs 46%, p=0.245). With regard to percentage of females and tobacco use, the data for young MS patients were similar to those for young non-MS patients (respectively, 4 vs 10%, p=0.641 and 79 vs 72%, p=0.566). In contrast, old patients with MS had a higher percentage of females (40 vs 15 %, p<0.001) and lower tobacco use (18 vs 34 %, p<0.001) than patients without MS. Among patients with MS, abnormal fasting glycemia (203(82%)) and hypertension (218(82%)) are predominant in old patients, while low HDL (23(96%)) and elevated triglycerides levels (19(79%)) are the major components of MS in young adults with acute MI.
Conclusion : The prevalence of MS is high but similar for young and old patients with acute myocardial infarction. However, young patients with MS are characterized by a predominance of abnormal serum lipid concentrations. These findings suggest a metabolic abnormality profile specific to young patients with myocardial infarction and therefore define a potential therapeutic target in risk factor management in these patients.

1090-230 Statin Therapy is More Beneficial for Resolving Thrombus of the Culprit Lesion Following Acute Myocardial Infarction

Takahiro Hayashi, Naoya Kobayashi, Masafumi Ueno, Takuo Ishise, Yukiko Miyamura, Takashi Kiyoshima, Masayoshi Matsuura, Hajime Nakamura, Nobutaka Masunaga, Hiroshi Yabushita, Atsuhiro Kurooka, Mitsugu Taniguchi, Akio Kimura, Kinji Ishikawa, Kinki University School of Medicine, Osakasayama, Japan

Backgrounds: Thrombus at the culprit lesion in acute myocardial infarction (AMI) will remain for weeks or months after onset. We hypothesized that statins would help to resolve thrombus of the culprit lesions following AMI.
Methods: We studied 188 AMI patients (161 men, 61.2+/-8.9 years) who had percutaneous coronary stenting within 24 hours after onset. Stented segments were classified into those with or without thrombus using angioscopy at 1 month (36+/-5 days, n=69), 3 months (81+/-40 days, n=49), 6 months (198+/-13 days, n=52) and 9 months later (266+/-42 days, n=18). We investigated the effect of statins on the resolution of thrombus at the stented segments, retrospectively.
Results: Results are shown in the table. The prevalences of thrombus on the stented segments are 73.9%, 53.1%, 26.9% and 16.7% at 1 month, 3 months, 6 months and 9 months after onset, respectively. The patients taking statins showed a lower prevalence of thrombus of the stented segments than those without statins through the observation period. 99.5%, 85.6% of patients were taking aspirin, ticlopidine.
Conclusions: AMI patients have thrombus in the culprit lesion over the long term. Statins achieved a reduction of thrombus in the culprit lesion, which promoted potent plaque stability and antiplatelet and antithrombotic actions.

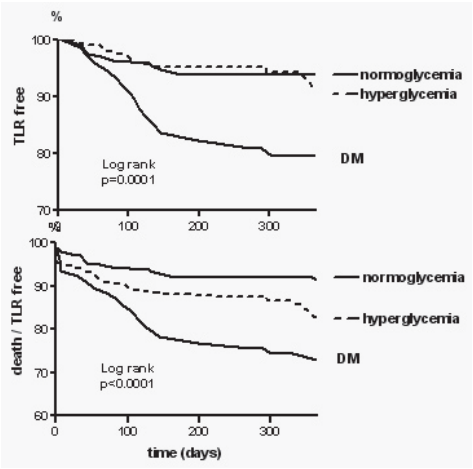
Table. Prevalences of thrombus on stented segments between patients with and without statins

Interval from onset to observation	Statins (n)	No statins (n)	Odds Ratio (95% CI)	P Value
1 month	60.9% (23)	80.4% (46)	0.38 (0.13-1.15)	0.081
3 months	50.0% (16)	54.5% (33)	0.83 (0.25-2.76)	0.765
6 months	12.5% (24)	39.3% (28)	0.22 (0.05-0.92)	0.030
9 months	0.0% (7)	27.3% (11)	0.28 (0.03-3.07)	0.245

1090-231 The Prognostic Impact of Transient Hyperglycemia During Acute Myocardial Infarction in Non-Diabetic Patients who Undergo Primary Percutaneous Coronary Intervention

Shahar Lavi, Michael Kapeliovich, Luis Gruberg, Arthur Kerner, Monther Boulos, Ehud Grenadier, Shlomo Amikam, Doron Aronson, Walter Markiewicz, Rafael Beyar, Haim Hammerman, Rambam Medical Center, Haifa, Israel

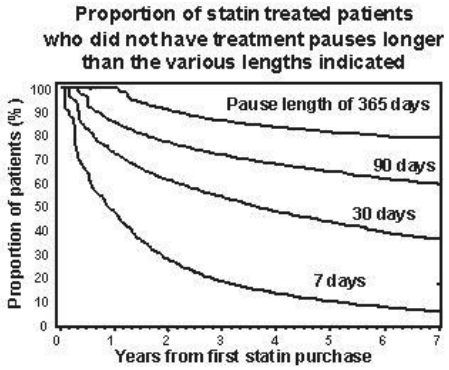
Background: Transient hyperglycemia is common during acute myocardial infarction (AMI) in non-diabetic patients. The outcome of patients who undergo primary percutaneous coronary intervention (PCI) and have transient hyperglycemia is unknown.
Methods: Blood glucose was measured after fasting in 387 consecutive patients who underwent primary PCI. Patients were divided into three groups: normoglycemic (fasting glucose <126mg/dl; n=196); fasting hyperglycemia (fasting glucose≥126mg/dl ; n=113); and overt diabetics (n=78).
Results: In hospital mortality was significantly lower in normoglycemic compared to hyperglycemic and diabetic patients. At one year, the combined endpoint of death and target lesion revascularization (TLR) was lower in normoglycemic patients (HR: 0.28, CI=0.1-0.44, p<0.0001; vs. diabetics) whereas the outcome of patients who had transient hyperglycemia was intermediate (HR: 2.1, CI=1.1-4.3, p=0.02, vs. normoglycemic) and non significantly different from diabetics. One year mortality was highest in patients with transient hyperglycemia (p=0.01). One year TLR rates were identical in normoglycemic and hyperglycemic patients (6% vs. 8%) and higher in diabetic patients (19%, p=0.001).
Conclusions: 1) Transient hyperglycemia in non-diabetic AMI patients who undergo primary PCI is associated with higher in hospital and one year mortality. 2) One year TLR rates were significantly higher in diabetics compared to normoglycemic and transient hyperglycemic patients



1090-232 High Continuation Rate of Statin Treatment Among Patients With Acute Myocardial Infarction

Jeppe N. Rasmussen, Gunnar Gislason, Steen Z. Abildstrom, Søren Rasmussen, Pernille Buch, Steen Stender, Christian Torp-Pedersen, Mette Madsen, National Institute of Public Health, Copenhagen, Denmark, Bispebjerg University Hospital, Copenhagen, Denmark

Background: Most population-based studies of statin adherence are hampered by studying selected populations only. We have studied the unselected population of all acute myocardial infarction (AMI) patients of an entire nation (Denmark).
Method: Via the national patient registry, all patients aged 30 years or older discharged alive after a first AMI from 1995-2002 were identified. Via the national prescription registry, containing all prescriptions filled in Danish pharmacies, each patient's long-term statin use was determined.
Results: A total of 58,420 patients were identified. Of these, 26,810 used statins at some point after discharge. In 1995, 10% used statins within 6 months after discharge, this increased to 56% in 2002. Between 6 months and 2 years after discharge, an average of only further 10% initiated statin,
and this proportion was decreasing during the period (test for linear trend p<0.001).
Among patients using statins, the proportion of days covered (days with a pill available divided by days of observation) was 84%. After 4 years of observation, 50% of the patients had had no pauses longer than 30 days and 70% had had no pauses longer than 90 days. After 7 years, only 21% had had a pause of 365 days or more, including those who discontinued treatment (Fig.).



Conclusion: If AMI patients receive statin treatment, a large proportion continues treatment for many years. If patients are not receiving statin treatment within 6 months after discharge, only few additional patients will initiate treatment.

1090-233 The Streptokinase Regimen in Myocardial Infarction Should be Changed. Final Report of the Romanian Study for Accelerated Streptokinase in ST-Elevation Myocardial Infarction (ROMAS).

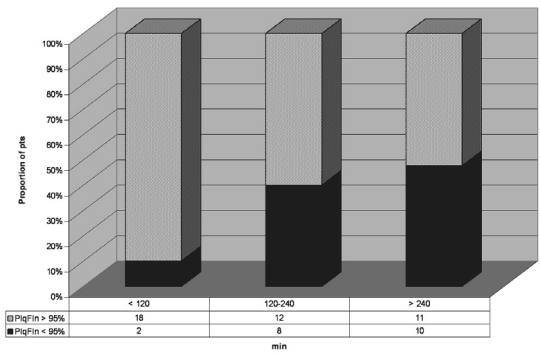
Gabriel Tatu-Chitoiu, Cristina Teodorescu, Monica Dan, Manuela Guran, Petre Capraru, Oana Istratescu, Alexandrina Tatu-Chitoiu, Aurelia Bumbu, Valentin Chioncel, Maria Dorobantu, Spitalul Clinic de Urgenta, Bucharest, Romania

Background. The streptokinase (SK) regimen (1.5 MU/30 -60 min.) in the ST-elevation myocardial infarction STEMI) remained unchanged for the last 20 years.
Objective. To compare the safety and efficacy of two accelerated SK regimens with the one of the classical SK 1.5MU/30-60min. in patients (pts.) with STEMI.
Methods. A group of 1142 consecutive pts. were thrombolised within the first 6 hours after the onset of STEMI with one of the following four SK regimens: 1.SK1.5MU/60 min. (310 pts.); 2. SK 1.5MU/30 min. (168 pts.); 3. SK 1.5 MU/20min (377 pts.); 4.SK0.75MU /10 min. repeated after 50 min.if non-invasive signs of coronary reperfusion (CR) were detected (287 pts.). The CR criteria were: 1.Rapid cessation of the chest pain. 2.Rapid decrease of the ST elevation by more than 50% from the initial value. 3.Rapid increase of CK and CK-MB with a peak within the first 12 hrs.
Results. Similar rates of CR (73.20%, respectively 73.51%) recorded in the SK1.5/20 and SK0.75/10 were higher that the one of 63.20% obtained with SK1.5/60 (p=0.006 and p= 0.009) but not significant higher that the one of 69.64% obtained with SK1.5/30. The in-hospital mortalities were: 13.54% (SK1.5MU/60), 10.71% (SK1.5MU/30), 9.54% (SK1.5MU/20) and 10.80% (SK0.75/10) - non-significant differences. In pts. younger than 75 mortalities from the SK1.5/20 (6.93%) and SK0.75/10 (6.91%) groups were lower that the one of 12.32% recorded with SK1.5/60 (p=0.027 and p= 0.048). In the SK1.5/30 group mortality was 8.60% (not significant different compared with the other three SK regimens). The incidence of hemoragic stroke was 0.64% (SK1.5/60) 0.0% (SK1.5/20 and SK1.5/30) and 0.53% (SK0.75/10). The rates of SK-induced hypotension of 47.33% (SK1.5/20), 44.11% (SK0.75/10) and 42.51% (SK1.5/30) were significant higher that the one of 11.61% recorded in the SK1.5/60 group.Hypotension disappeared within 15 min. in all pts.
Conclusions. 1. The classical SK1.5 MU/60 min. is not the best SK regimen.Higher rates of CR and lower mortalities can be obtain with two accelerated SK regimens at least in pts. younger than 75, without an increased risk. 2. The SK 1.5/30 regimen has an intermediate efficacy between the SK1.5/60 and SK1.5/20 or SK0.75/10 ones.

1090-234 Platelet Function Inhibition by Abciximab is Dependent on Time to Treatment in ST Elevation Myocardial Infarction. ERAMI Substudy.

Luis J. Sargento, Henrique Mesquita Gabriel, J. Marques Costa, P. Canas Silva, J. Oliveira, J. Correia Cunha, M. Celeste Vagueiro, Serv. Cardiologia Hosp Sta Maria, Lisboa, Portugal

Background: Time dependency is well established for thrombolysis in ST elevation myocardial infarction (STEMI), but not for antiplatelet treatment. The aim of the present work is to evaluate the relationship between the pain to abciximab(ABC) bolus time (PBT) and the level of platelet function inhibition (PltFIn) achieved, in STEMI patients undergoing primary PCI.
Methods: Eighty patients (pts) with STEMI participating in ERAMI trial were included in the substudy. All pts were submitted to a 0.25 mg/kg ABC bolus. PltFIn determined with Ultegra at admission and after the bolus, and the PltAgIn rate determined, and grouped according to two pre-specified rates (80% and 95%). Sixty six pts completed all protocol determinations. Pts grouped by PBT into tercis (120 and 240 min). Statistics: Qui square, Fisher test's with odds ratio (OR) determination, and Pearson correlation coefficient.
Results: (1) There is an indirect significant correlation between PBT and PltFIn rate (r= -0.31 p= 0.022). (2) A PltFIn rate lower than 95% was increasingly frequent with longer duration of PBT: 10%, 40.0% and 47.6%, respectively for < 120 min, < 240 min, and greater than 240 min. (3) Pts in the lower tercil (< 120 min) were more likely to reach the 95% PltFIn rate (p= 0.009; OR 0.142 (0.029-0.693)) in relation to the other two tercis.
Conclusion: The earlier the administration of the ABC bolus after STEMI, the greater the effect in PltFIn rate.
Fig.- PltFIn rate dependency on pain to abciximab bolus time (tercis).



1090-235 Relation Between Prothrombotic Markers and Eearly Spontaneous Patency in Acute Myocardial Infarction. An Acute Study of in Patients Triaged to Primary Angioplasty

Marie-Genevieve Huisse, Emilie Lanoy, Annie Bezeaud, Dominique de Prost, Anne Dauphin, Eduardo Angles-Cano, Murielle Mary-Krause, Marie-Claude Guillin, Ph. Gabriel Steg, Hopital Bichat, Paris, France, INSERM EMI 0214, Paris

Background: The determinants of spontaneous early coronary recanalization in acute myocardial infarction (AMI), are poorly understood. We hypothesized that the extent of platelet and leukocyte activation, thrombin generation and/or endothelial damage might differ between patients with early spontaneous recanalization or persistent occlusion at the time of emergent coronary angiography.
Methods: The study was conducted in 126 consecutive pts admitted with ST elevation AMI within 12 hours of pain onset (median 2.2 h) and triaged to primary angioplasty. All pts received aspirin, 5000 U of heparin and underwent immediate coronary angiography, 53 pts had TIMI 2/3 flow and 73 TIMI 0/1 flow in the infarct artery. Blood samples were

collected and processed immediately before angiography to measure platelet activation markers (P-Selectin and PAC-1) and circulating microparticles (MPs) originating from platelets, granulocytes (Gr.) and endothelial cells (Endo.). Soluble platelet glycoprotein V (sGPV), thrombin-antithrombin complexes (TAT) were measured as markers of thrombin generation. Plasmin-antiplasmin complexes (PAP), tissue plasminogen activator (tPA), plasminogen activator inhibitor (PAI-1) were measured as endothelial markers. Comparisons used logistic regression adjusting on baseline characteristics.

Results: Baseline characteristics were similar between groups except for more frequent history of hypertension (p=0.016)or dyslipidemia (p=0.045) in pts with TIMI 0/1 flow. Groups differed by markers oif thrombin generation and endothelial injury which were lower among pts with TMI 2/3 flow: specifically sGPV (53 vs 64 ng/ml,adjusted p=0.002), endo.MPs (12 vs 18 N/µl, adjusted p=0.009) and PAP (88 vs 112 ng/ml, adjusted p=0.037). Categorization of pts using TIMI 3 vs 0/1/2 provided similar trends.

Conclusion: Spontaneous recanalization of the infarct artery compared to persistent occlusion.appears associated with reduced endothelial injury and thrombin generation, but not with platelet activation This implies that improved inhibition of thrombin generation might be more effective than additional antiplatelet therapy for improving acute spontaneous patency.

1090-236 The Influence of Ximelagatran on Plasma Concentration, aPTT and D-dimer in Patients With Recent Myocardial Infarction

Christina Christersson, Jonas Oldgren, Anders Bylock, Lars Wallentin, Agneta Siegbahn, Uppsala University, Uppsala, Sweden

Background: In the ESTEEM study, the risk for new thrombotic events after a myocardial infarction was reduced by placebo controlled long-term treatment with the oral direct thrombin inhibitor ximelagatran, but there was no dose-effect response. We evaluated the influence of the four different doses of ximelagatran on plasma concentration of melagatran (the active compound), aPTT and D-dimer.

Methods and Results: Patients were randomized 6 days (mean) after a myocardial infarction to six months treatment with one of four doses of ximelagatran (or placebo) twice daily together with aspirin 160 mg once daily. Venous blood samples were obtained after 1 and 26 weeks in 339 out of the 1245 ximelagatran patients. For D-dimer, the change (D-dimer) from randomization was individually calculated for each time-point. Results in the table are median levels of plasma concentration, aPTT and D-dimer after 1 week, trough and peak, with Spearman rank correlations at peak (*p<0.001) and within-group comparisons by Kruskal Wallis test†. Similar results were found after 26 weeks.

Conclusion: There was a dose-dependent well-correlated increase in plasma concentration of melagatran and aPTT. However all four ximelagatran dose groups equally decreased D-dimer levels, without correlation to plasma concentration or aPTT. The similar influence on D-dimer levels, indicating decreased thrombin generation and fibrin turnover, corresponded to the equal clinical efficacy of all four ximelagatran doses in the ESTEEM study.

	P-conc, (nmol/L)		aPTT, (sec)		Conc-aPTT	ΔD-dimer, (µg/L)		Conc-ΔD-dimer
	trough	peak	trough	peak	Correlation	trough	peak	Correlation
24 mg	84	291	33	42	r=0.23	-28	-35	r=-0.14
36 mg	141	415	37	47	r=0.67*	-33	-40	r=-0.18
48 mg	222	590	40	52	r=0.68*	-23	-38	r=-0.15
60 mg	261	760	41	53	r=0.81*	-37	-59	r=-0.05
p†	<0.001	<0.001	<0.001	<0.001		0.44	0.41	

POSTER SESSION

1091 New Observations in Emergency Cardiac Care or Cardioversion

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1091-215 Randomized Trial of Biphasic Atrial Flutter Cardioversion

Kai Mortensen, Tim Risius, Tjark F. Schwermer, M. Ali Aydin, Simone Henne, Michelle Ortak, Boris Lutomsky, Thomas Hofmann, Andreas Schuchert, Stephan Willems, Heart Center, University of Hamburg, Hamburg, Germany

Background: Biphasic shocks have been shown to be potentially beneficial for ventricular defibrillation and atrial fibrillation cardioversion. In this prospective trial we evaluated the amount of delivered current neccessary for successful cardioversion using rectilinear biphasic shocks in patients with common type atrial flutter. Additionally, the electrode configuration “anterior-posterior” vs. “anterior-lateral” was determined in a randomized approach.

Methods: 48 consecutive patients (pts.) (61 ± 13 years, male=31) who were admitted to our emergency room with acute common type atrial flutter underwent transthoracic DC cardioversion using a Zoll M-Series defibrillator with Zoll MFE pads. Patients included received a step-up-protocol: 50, 75, 100, 150 or 200 Joule (J.), if necessary. All patients were randomized to either “anterior-posterior” (24 pts.) or “anterior-lateral” (24 pts.) electrode configuration. Successful cardioversion was defined as the cardioversion of atrial flutter to sinus rhythm for ≥30 s after the shock.

Results: External cardioversion of atrial flutter was successful in all patients. The first shock with the lowest energy of 50 J was effective in 23 pts. (48%). In 16 pts. (33%) a second shock of 75 J was successful, 4 pts. (8%) needed a shock of 100 J. 150 Joule were administered to 2 (4%), 200 Joule to 2 (6%) pts.

Between the different electrode positions was no significant difference concerning the mean delivered current (anterior posterior 76 ± 31 J. versus 76 ± 47 J.). The anterior-lateral was superior to anterior-posterior electrode configuration concerning the first sucessful shock (62%/24 pts. vs. 33%/24 pts.).

The two groups were similar with respect to age, sex, weight, underlying cardiac disease, duration of atrial flutter and use of medication.

Conclusions: Our data shows a low success rate (<50%) for the first biphasic shock with 50 J. of atrial flutter. 81 % of the pts. were successfully cardioverted with a maximum energy of 75 Joule. In conclusion we recommend to start biphasic external cardioversion of common type atrial flutter in an emergency room setting with 75 Joule using antero-lateral electrode position.

1091-216 Disparities by Sex in Timing of Initial Electrocardiogram for Patients Presenting with Acute Coronary Syndromes

Deborah B. Diercks, Matthew T. Roe, Anita Y. Chen, Eric D. Peterson, L. Kristin Newby, J. Douglas Kirk, Charles V. Pollack, Jr., W. Brian Gibler, James W. Hoekstra, Sidney C. Smith, E. Magnus Ohman, Judith S. Hochman, University of California-Davis Medical Center, Sacramento, CA

Background: Guidelines for managing patients with non-ST-segment elevation acute coronary syndromes (NSTE ACS) recommend that an electrocardiogram (ECG) be obtained within 10 minutes of hospital arrival, but data on the impact of sex on the timing of the initial ECG are limited.

Methods: Using data from the CRUSADE Quality Improvement Initiative, we compared the clinical features of 63,478 high-risk patients (26,615 women [42%]) with NSTE ACS (designated by positive cardiac markers and/or ischemic ST-segment changes) presenting to the emergency department according to the presence of a delay in initial ECG acquisition. Patients were categorized as delayed (>10 minutes from hospital arrival to ECG acquisition) or non-delayed. Multivariate predictors of delayed ECG acquisition were determined.

Results: A total of 41,397 patients (65.2%) had a delayed ECG. Women were more likely than men to have a delayed ECG (69% vs. 62%). Female sex was the most significant predictor of delayed ECG, followed by non-cardiology inpatient care, non-white race, insurance status, type of institution, and diabetes (Table).

Multivariate Predictors of Delayed (>10 Minutes)
ECG Acquisition

Variables	Adjusted OR (95% CI)	Chi-Square
Female (vs. male)	1.29 (1.25-1.34)	253.0
Off hours (nights and weekends)	0.86 (0.83-0.90)	50.0
Prior PCI	0.86 (0.82-0.90)	48.3
Non-white (vs. white)	1.16 (1.10-1.22)	33.8
No insurance (vs. HMO/private)	0.88 (0.82-0.94)	29.8
Medicaid insurance (vs. HMO/private)	1.07 (1.00-1.14)	
Medicare insurance (vs. HMO/private)	1.06 (1.02-1.10)	
Current/recent smoking	0.91 (0.87-0.94)	23.3
Diabetes mellitus	1.07 (1.03-1.10)	14.4

Conclusion: Only 35% of high-risk NSTE ACS patients had an initial ECG within 10 minutes of hospital arrival. Women are more likely than men to have a delayed ECG. Since the initial ECG is the earliest triage tool for NSTE ACS and ST-segment elevation MI care pathways, emergency departments should focus on reducing the time to initial ECG acquisition in women to improve care in these patients.

1091-217 Internal Thoracic Impedance Monitoring: A New Possibility in Early Diagnosing and Treatment of Acute Heart Failure.

Michael Shochat, Gidon Charach, Aaron Frimerman, Mark Kazatzker, Samir Daka, Paul Rabinovich, Avraham Shotan, Simcha Meisel, Hillel Jaffe Heart Institute, Hadera, Israel, Ichilov Hospital, Tel Aviv, Israel

Treatment of acute heart failure (AHF) is initiated currently only after the appearance of clinical signs such as dyspnea, lung rales (LR), and blood desaturation. These signs signify the alveolar stage of pulmonary edema. Identification of the interstitial stage of AHF, when clinical signs are absent, may enable earlier therapy and prevent the onset of overt AHF. We evaluated the newer impedance monitor that allows recognition of small fluid shifts in the lung as a means to predict evolving pulmonary edema. Study population included AMI patients without clinical and X-ray signs of AHF. Patients were monitored and internal thoracic impedance (ITI), respiratory rate (RR), heart rate (HR), level of LR and blood oximetry (BO) were measured.

382 patients with AMI were studied. Of these, 313 remained without AHF (group 1), 51 patients developed AHF throughout monitoring (group 2), 18 received early treatment (group 3). Group1 patients did not manifest any signs of AHF and ITI decreased in this group by 4.8±2.8% (NS) from initial value (range, 0-11.5%). All group 2 patients developed mild AHF, 78% progressed to moderate AHF and 55% advanced to full pulmonary edema. ITI in patients with mild AHF decreased from initial value by 21.7±3.8% (13-28.9%), with moderate AHF, ITI further decreased by 26.8±5.5% (p<0.05) (range, 19.5-37.9%) and in full pulmonary edema showed an ITI decrease of 34.6±7.5% (25.7-53.3%, p<0.05). All patients in whom ITI decreased >12% developed AHF. Therefore, an ITI decrease of 12% was determined to represent AHF threshold. Time interval from reaching threshold level to onset of LR was minimum 30 min.

Based on this experience we began to treat AMI patients with an ITI decrease>12% despite the absence of AHF. Therapy was initiated in 18 patients at ITI decrease of 13.7±1.61%. 16 patients did not develop AHF. Only 2 patients developed mild AHF. This response was considerably different than expected ($p< 0.0001$ by ^{2} test). Conclusions. The extent of lung impedance decrease correlated with stage of AHF. The impedance monitor enabled the diagnosis of AHF in its preclinical stage, at least 30 before the appearance of LC. Early ITI-guided therapy may prevent AHF at its preclinical stage in most patients with AMI.

1091-218 Endografting For Traumatic Aortic Injury

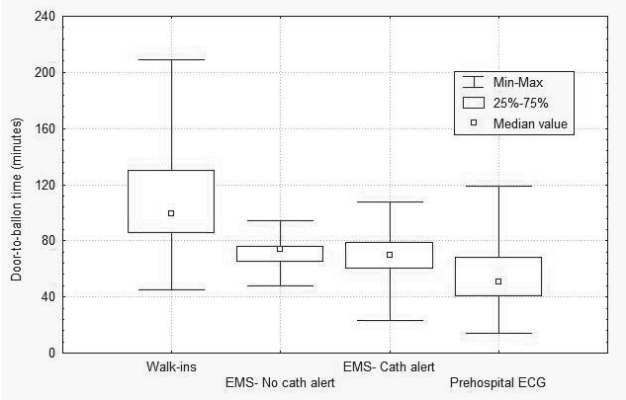
Taro Shimazaki, Shin Ishimaru, Satoshi Kawaguchi, Yoshihiko Yokoi, Kenji Koide, Tokyo Medical University, Tokyo, Japan

Purpose: Patients that sustain traumatic aortic injuries often have multiple concomitant injuries (e.g., brain contusion, hematopneumothorax, leg fractures), which increases this risks associated with conventional open surgery. This study evaluates the safety and efficacy of less invasive procedure, endografting, for traumatic aorta injury.
Methods: Between September 1996 and March 2004, 25 patients with traumatic aorta injury (20 men, 5 women; age range, 20-79 years; mean age, 47 years) underwent endografting. Etiologies of traumatic aortic injury included motor vehicle accidents (n=17), falls (n=7), and assault (n=1). The timing of endografting after the precipitating events was defined as the acute phase (0-3 days; n=11), the subacute phase (3-30 days; n=6) or the chronic phase (greater than 30 days; n=8). Aortic injury occurred at the aortic isthmus in all but one case, and a proximal landing zone of at least 15 mm from left carotid artery was required before endografting was elected. Endografting was performed under general anesthesia, and an original device, constructed from a self-expanding Z shaped stent and thin-wall woven polyester fabric, was used in all cases. The activated coagulation time was maintained >200 seconds by the administration of 50 unit/kg heparin intravenously before the sheath insertion.
Results: Endografting was technically successful in all cases. The mean operating duration was 188 minutes, and the mean estimated blood loss was 236 ml. One case with subarachnoid hemorrhage sustained during a motor vehicle accident died on the seventh postoperative day secondary to rupture of the ascending aorta. Another patient with pelvic fractures underwent endografting without resulting endoleak but died secondary to exsanguination from a chest drain.
Conclusion: Endografting is an effective method for management of traumatic aortic injury and does not require cardiopulmonary bypass with high dose heparin. Therefore, endografting may be preferable to conventional surgery for management of traumatic aorta injury in select populations.

1091-221 "Cath Alert" and Transmission of a Prehospital 12-Lead Electrocardiogram Can Shorten Door-to-Balloon Times in Patients With ST-Segment Elevation Acute Myocardial Infarction

Howard S. Bush, Allen Brown, Kenneth Fromkin, Gian Novaro, Michael Shen, Craig Asher, Sergio Pinski, Cleveland Clinic Florida, Weston, FL, Miami-Dade EMS, Miami, FL

Background: Primary percutaneous coronary intervention (PCI) is the preferred method of revascularization for patients with ST-segment elevation acute myocardial infarction (STEMI). A main outcome determinant after PCI for STEMI is door-to-balloon time (DBT). DBT can be reduced with implementation of strategies for rapid cath lab deployment. This goal could be achieved by the "cath alert", i.e., pre-hospital notification/mobilization of a cath lab team, especially when combined with transmission of a diagnostic 12-lead electrocardiogram (ECG).
Methods: We tested this hypothesis in 153 consecutive patients (age 61±13, 131 male) that presented to our emergency department (ED) with STEMI and underwent primary PCI. Exclusion criteria: prior lytics or hospital transfer. **Results**: 42 patients (pts) self-presented to the ED and 111 were brought by emergency medical services (EMS), of which 106 had pre-hospital notification and 90 of these included transmission of a pre-hospital ECG. The DBT was shorter as more pre-hospital information became available to the cardiac team ($p<0.001$, ANOVA) (Figure). The longest DBT of 106±38 minutes occurred in pts who self-referred to the ED; the shortest DBT time of 54±22 minutes occurred in those with "cath alert" plus pre-hospital ECG.



1091-222 Atrial Flutter: Is Biphasic Superior to Monophasic External Cardioversion? A Randomized Comparison

Tim Risius, Kai Mortensen, Tjark Schwemer, M. Ali Aydin, Simone Henne, Ralf Köster, Thomas Hofmann, Stephen Willems, University Hospital Hamburg - Eppendorf, Hamburg, Germany

Biphasic shocks have been shown to be more effective than monophasic shocks for ventricular defibrillation and atrial fibrillation cardioversion. In this prospective randomised trial we evaluated the efficacy of damped sine wave monophasic to rectilinear biphasic shocks in patients with common type atrial flutter.
Methods: 95 consecutive patients (61 ± 13 years, male=67) who were admitted to the emergency room with common type atrial flutter underwent transthoracic DC cardioversion using either a Physio-Control Lifepak 8 DC defibrillator with Medtronic Fast-Patch Plus Defibrillation/ECG-Electrodes (monophasic) or a Zoll M-Series defibrillator with Zoll MFE pads (biphasic). Patients randomized to the monophasic protocol received sequential shocks of 100, 150, 200, 300 and 360 J, if necessary. Patients randomized to the biphasic protocol received 50, 75, 100, 150 or 200 J, if necessary. Successful cardioversion was defined as the cardioversion of atrial flutter to sinus rhythm for ≥30 s after the shock.
Results: External cardioversion of atrial flutter was successful in all patients, the max. energy was necessary in 4 cases of the monophasic group, in the biphasic group in 3 cases. The first shock with the lowest energy was effective in n=23 in the biphasic group and n=13 in the monophasic group. Successful cardioversion could be achieved with a mean of 76 ± 39 J for biphasic and 175 ± 80 J for monophasic cardioversion. The two groups were similar with respect to age, sex, weight, underlying cardiac disease, duration of atrial flutter and use of medication.
Conclusions: Monophasic and biphasic cardioversion showed similar high success rates. Biphasic shocks significantly reduced the amount of delivered current in patients with common type atrial flutter. Our data suggests that the preferred method for transthoracic DC cardioversion of atrial flutter is the application of biphasic rectilinear shocks.

POSTER SESSION

1092 Off-Pump CABG: Benefits of Avoiding the Machine

Monday, March 07, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 2:30 p.m.-3:30 p.m.

1092-219 Short-Term and Long-Term Outcomes of Off-Pump and On-Pump Coronary Artery Bypass Graft Surgery: The Canadian Off-Pump CABG Registry

Andre Lamy, Forough Farrokhyar, Rosanne Kent, Xiaoyin Wang, On behalf of the Registry Investigators, McMaster University, Hamilton, ON, Canada

Background: To examine the early and one-year clinical outcomes of CABG surgery.
Methods: From 2001 to 2002, 1657 patients had off-pump and 1693 had on-pump CABG surgery. At one year, patients were interviewed by telephone (follow-up = 98%). Clinical events and memory status were recorded. Treatment bias was controlled for by constructing a propensity score. Adjusted rates, odds ratios, and 95% confidence intervals are reported. **Results:** At baseline, the rate of renal dysfunction, previous stroke, carotid stenosis, pulmonary hypertension, chronic obstructive pulmonary disease, peripheral vascular disease were higher in off-pump CABG and left ventricular (LV) ejection fraction, chronic heart failure, previous myocardial infarction (MI) and LV aneurysm were higher in on-pump CABG. Hospital length of stay was significantly lower in off-pump CABG than in on-pump CABG (7.4±8.1 vs. 9.0±11.0, $p<0.01$).

Post-operative, Follow-up and One-year Adjusted Rates and Odds Ratios

	Post-operative	Follow-up	One-year
	Off-pump/On-pump	Off-pump/On-pump	Off-pump/On-pump
Mortality	1.3/1.2(1.04;0.58-1.88)	1.8/1.9(0.96;0.57-1.59)	3.2/3.2(1.00;0.68-1.48)
MI	3.0/1.4(2.18;1.31-3.62)*	0.6/1.3(0.46;0.21-1.00)	3.5/2.7(1.30;0.87-1.96)
Stroke	1.0/1.3(0.77;0.41-1.45)	0.7/1.2(0.60;0.27-1.31)	1.3/2.4(0.55;0.40-1.09)*
Revascularization	0/0	1.7/1.6(1.05;0.60-1.83)	1.7/1.6(1.05;0.60-1.83)
Angiogram	0/0	3.5/4.0(0.87;0.58-1.31)	3.5/4.0(0.87;0.58-1.31)
Recurrent angina	0/0	10.8/17.3 (0.62;0.49-0.72)*	10.8/17.3 (0.62;0.49-0.72)*
* p<0.05			

At one-year, the adjusted rates of mortality and MI were similar between off-pump and on-pump CABG but a 45% reduction of stroke rate was evident in off-pump CABG patients.
Conclusion: Results from a multicenter registry across Canada demonstrate that surgeons use off-pump CABG in patients with more co-morbidities but with a better cardiac function. This registry has shown the safety and efficacy of off-pump CABG and that the results are comparable to that of on-pump CABG. We propose that off-pump CABG should be incorporated into national guidelines as an acceptable technique for coronary revascularization.

1092-220 **Outcomes After Coronary Artery Bypass Grafting in Non-Dialysis Dependent Renal Failure Patients**

Hasmet Bardakci, Veli K. Topkara, Faisal Habib Cheema, Nicholas C. Dang, Timothy Paul Martens, Isaac George, Satish Kesavaramanujam, P. B. Namerow, Mehmet C. Oz, Donald W. Landry, Columbia University College of Physicians & Surgeons, New York, NY

Background: Preoperative renal insufficiency is a risk factor for morbidity and early mortality in patients undergoing CABG.
Methods: The New York State Department of Health Multicenter Database (1997-99) was analyzed for 56457 patients undergoing CABG without requirement for preoperative dialysis. The control group (CTR) with serum creatinine < 2.5 (n=55408) was compared with the renal failure group (RF) with serum creatinine > 2.5 mg/dL (n=1049).
Results: RF group had a higher incidence of postoperative dialysis-dependent renal failure (10.4% vs 0.8%, p<0.001), stroke (4.6% vs 1.9%, p<0.001), sepsis (2.8% vs 0.8%, p<0.001), re-operation for bleeding (3.4% vs 2.2%, p=0.005), gastrointestinal bleeding (2.6% vs 0.8%, p<0.001), and respiratory failure (11.5% vs 3.8%, p<0.001). Hospital length of stay was longer in the RF group compared to CTR (20.4+/-24.0 days vs 10.8+/-11.9 days, p<0.001). Early mortality rate was higher and rate of discharge to home was lower in RF (4.4% vs 1.5% and 66.0% vs 85.3%, p<0.001). Multivariate analysis identified increased age, female gender, emergent operation, decreased EF and Off-pump CABG as independent risk factors for early mortality (Table).
Conclusion: CABG patients with renal failure have significantly increased renal and non-renal morbidity compared to patients with normal or slightly impaired renal function. CABG patients with significant renal failure are an appropriate subgroup for aggressive strategies such as off-pump CABG and hemodialysis on bypass.

Multivariate Analysis of Non Dialysis Dependent Renal Failure:

Early Mortality

Risk Factor	Variable Estimate	Standard Error	p-value	Odds Ratio	95% CI
Age	0.478	0.184	0.010	*1.612	1.123-2.314
Female	0.790	0.326	0.016	2.204	1.162-4.178
Hepatic Failure	2.572	1.440	0.074	13.090	0.779-220.061
Emergent	1.253	0.443	0.005	3.501	1.469-8.343
Ejection Fraction %	-0.271	0.112	0.016	**0.762	0.612-0.950
Off pump surgery	-1.214	0.539	0.297	0.024	0.103-0.854
*	Odds ratio for every 10 years of age				
**	Odds ratio for every 10% of ejection fraction				
Hosmer-Lemeshow Goodness of Fit Test: p-value = 0.153					

1092-223 **The Effect Of Cardiopulmonary Bypass On Cell Junctions; Catenins, Cadherins and Connexins**

Tamer A. Malik, Cesario Bianchi, Frank W. Sellke, Beth Israel Deaconess Medical Center, Boston, MA

Background: The post operative course of patients going for cardiac surgery with blood cardioplegia (CP) and cardiopulmonary bypass (CPB) is often associated with arrhythmias and increased interstitial fluid content. It is hypothesized that this may be due to altered distribution or degradation of gap junctions and/or adherens junctions. Thus, we studied the effect of CPB on different cellular junctions in patients going for coronary artery bypass grafting (CABG) for advanced coronary artery disease.
Methods: Samples were taken from the atrial myocardium and skeletal muscle before and after CPB and immediately frozen in liquid nitrogen. Protein concentration in supernatant from homogenized heart tissue was measured spectrophotometrically at 595-nm wave length with a BCA protein assay kit. Western blot analysis was used to fractionize total protein and to quantify different cell junction proteins using their matching antibodies.
Results: The expression of Gamma-Catenin receptor protein in the human atrial heart tissue was reduced after CP/CPB compared to that found before CP/CPB (169.7 ± 8.2 vs. 183.0 ± 9.5, p=0.04), on the other hand the expression of Beta-Catenin receptor protein was increased after CP/CPB (186.8 ± 5.1 vs. 180.5 ± 4.9, p=0.007) as compared to before CP/CPB. In the skeletal muscle, a Gamma-Catenin signal could not be detected but there was a significant reduction in Beta-Catenin expression after bypass compared to that observed before CP/CPB (117.5 ± 13.1 vs. 97.2 ± 13.9, p=0.01). Protein expression of Connexin-40, Pan-Cadherin or VE-Cadherin were not altered after CP/CPB.
Conclusions: Altered distribution, expression and degradation of cell junctions could explain the increased incidence of irregular heart rhythm, altered vascular permeability and increased interstitial fluid that is often observed after CP under conditions of CPB.

1092-224 **Endothelial Cell Damage Leads To Inflammation In On-pump Coronary Artery Bypass Surgery Patients**

Palaniswamy Vijay, Thomas G. Sharp, Yousuf Mahomed, John W. Brown, Indiana University School of Medicine, Indianapolis, IN

Background: During open-heart surgery, cells exposed to extra-corporal circulation or subjected to relative ischemic conditions can become activated and generate inflammatory mediators. Endothelial cell markers like the adhesion molecules, ICAM and VCAM, are indicators of the degree of damage to myocardial endothelium. We analyzed the release of these markers during on-pump(CPB) and off-pump coronary artery bypass(OPCAB) surgery.
Methods: Patients undergoing surgery with or without cardiopulmonary bypass (CPB, n=40 and OPCAB, n=25) were included. Plasma soluble VCAM-1 (ng/ml), ICAM-1 (ng/ml), and IL-6 (pg/ml) were assayed pre-op, off-pump (end of grafting in the case of OPCAB), 0, 6 and 24hr after surgery. Clinical information was obtained from hospital charts.
Results: Patients in both groups had similar demographics, co-morbidities and number of vessels grafted (2.2±1.4 vs. 2.9±1.8, p=NS). The mean LVEF was 42±15%. The range of aortic cross-clamp and bypass times were 54-98 min and 101-143 min. The levels of IL-6 were 4 times higher (peak) at 6 hrs after surgery in CPB than OPCAB (854±94 vs. 242±45, p=0.001) and remained elevated at 24 hrs (184±94 vs.74±30, p=0.001). Both sVCAM-1 and sICAM-1 levels were significantly greater in CPB than OPCAB patients (p<0.05) at 6 and 24hrs after the surgery. The increase in sVCAM was more pronounced in CPB than in OPCAB. Evenafter 24hrs, the levels of sVCAM and sICAMs were elevated significantly in CPB when compared to 0hr (sVCAM: 1248±180 vs.784±104, sICAM: 563±80 vs.402±90) in CPB, whereas in OPCAB, the levels show a trend to return to 0hr levels (sVCAM: 754±47 vs.600±84, p=0.001, sICAM: 384±50 vs.304±52, p=0.001).
Conclusions: Cardiopulmonary bypass in coronary artery surgery results in a greater inflammatory response as measured by soluble endothelial cell adhesion molecules. This may be due to neutrophil activation and the release of inflammatory cytokines such as IL-6. The activation of inflammatory mediators is reduced by the off-pump approach, which may lead to a smoother postoperative course.

1092-225 **Pro-thrombotic Effects Of On-pump Compared With Off-pump Coronary Artery Bypass Surgery: A Prospective Randomized Controlled Trial**

Neuza Lopes, David Schneider, Roberto Rached, Ludhmila Hajjar, Aecio F. Gois, Deborah Whitaker, Luiz Cesar, Sergio Oliveira, Whady Hueb, Burton Sobel, Jose Ramires, Heart Institute (InCor) University of Sao Paulo, São Paulo, Brazil, University of Vermont, Colchester, VT

Background: To determine whether of on-pump compared with off-pump bypass surgery exerts differential effects on markers of inflammation, coagulation, and thrombosis after surgery, we performed a prospective, controlled trial in which patients were assigned randomly to each.
Methods: All aspects of the surgery other than pump use were the same. The concentrations of C-reactive protein (CRP), fibrinogen, D-dimer, and plasminogen activator inhibitor type 1 (PAI-1) were determined by ELISA before surgery as well as 1 and 24 hours after surgery.
Results: At total of 91 patients were randomized to on-pump (n=51) or off-pump (n=40) surgery. The concentration of CRP did not change appreciably immediately after surgery in either group but was increased 3-fold and comparably 24 hour after either on-pump or off-pump surgery (p<0.001). The concentration of fibrinogen tended to be lower immediately after surgery and increased comparably in both groups 24 hours later. By contrast, the concentration of D-dimer was significantly greater immediately after surgery in the on-pump compared with off-pump group (p<0.0001). Although the concentration of PAI-1 increased significantly in both groups immediately after surgery (p<0.0001), the increment was greater in the on-pump group (p=0.04).
Conclusion: Bypass surgery induces a comparable inflammatory response whether performed on-pump or off-pump. However, on-pump compared with off-pump is more pro-thrombotic as reflected by the increased concentrations of D-dimer and associated with constrained fibrinolysis secondary to increased concentrations of PAI-1

ORAL CONTRIBUTIONS

814 Biologic and Physiologic Markers of Acute Ischemic Syndrome

Monday, March 07, 2005, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Room 304A

2:00 p.m.

814-3 **Multimarker Approach Predicts Adverse Cardiovascular Events in Women Evaluated for Suspected Ischemia: A Report From the NHLBI-Sponsored WISE Study**

Christopher B. Arant, Timothy R. Wessel, Paul M. Ridker, Marian B. Olson, B. Delia Johnson, Barry L. Sharaf, Richard A. Kerensky, Daniel F. Pauly, Eileen Handberg, Issam Zineh, George Sopko, Sheryl F. Kelsey, C. Noel Bairey Merz, Carl J. Pepine, University of Florida, Gainesville, FL, University of Pittsburgh, Pittsburgh, PA

Both inflammatory marker and hemoglobin (Hgb) levels predict cardiovascular (CV) events in selected populations.
As part of the Women's Ischemia Syndrome Evaluation (WISE), we investigated a multimarker approach using inflammatory markers [high sensitivity C-reactive protein (hs-CRP), interleukin (IL)-6, serum amyloid A (SAA)] and Hgb for CV risk prediction in women with suspected ischemia.
Among 595 women, the mean age was 58 ± 12 years, and 26%, 55%, and 58% had diabetes, hypertension, and dyslipidemia, respectively. Angiographically, 65% had no obstructive CAD and mean ejection fraction was 65 ±11%. During a mean follow-up of 3.6 ± 1.8 years, women with no abnormal inflammatory markers had fewer adverse CV events* and deaths compared to women with abnormal inflammatory markers (Table). Adding low Hgb (<12 g/dL) to each category of abnormal inflammatory markers incrementally increased the rate of adverse CV events and mortality for each category (Table). In multivariate analysis women with one, two, three, or four abnormal biomarkers were more likely to have an adverse CV event or die during follow-up compared to women with no abnormal biomarkers (Table). Diabetes (HR 1.79, 95% CI 1.21-2.65) and obstructive CAD (HR 1.65, 95% CI 1.12-2.42) were the only traditional risk factors that predicted CV events.
For women with suspected ischemia, a multi-biomarker approach using inflammatory marker and Hgb levels predicted adverse CV events better than any single biomarker or traditional CV risk predictor.

Table. Relationships between number of markers and outcomes.	Number of Abnormal Inflammatory Markers			
*(Adverse CV Event defined as all-cause death or hospitalization for MI, CHF, stroke or other vascular events)	0	1	2	3
Proportion (%) with adverse CV events (p<0.001 for trend)	12%	18.4%	20.9%	37%
Proportion (%) with All-cause Death (p<0.001 for trend)	1.6%	6.1%	9.1%	17%
	Number of Abnormal Inflammatory Markers with Low Hemoglobin Level (Hgb)			
	0 + Low Hgb	1 + Low Hgb	2 + Low Hgb	3 + Low Hgb
Proportion (%) with adverse CV events (p<0.02 for trend)	20.7%	22.2%	34.8%	45.5%
Proportion (%) with All-cause Death (p<0.005 for trend)	3.5%	6.7%	21.7%	24.2%
	Total Number of Abnormal Biomarkers (Hgb, hs-CRP, IL-6, SAA)			
	1	2	3	4
Risk of adverse CV events (Cox regression HR with 95% CI)	1.90 (1.04-3.46)	1.92 (1.02-3.60)	3.68 (2.00-6.77)	5.50 (2.72-11.14)
Risk of All-cause Death (Cox regression HR with 95% CI)	4.52 (0.99-20.7)	4.56 (0.97-21.5)	11.13 (2.50-49.6)	19.23 (4.08-90.7)

2:15 p.m.

814-4 **Association of the BAT1-NFKBIL1-LTA Region on Chromosome 6 With Susceptibility to Myocardial Infarction**

Petra Hoppmann, Vanessa Jung, Elena Michou, Arne Pfeufer, Thomas Meitinger, Adnan Kastrati, Albert Schömig, Werner Koch, Deutsches Herzzentrum, Muenchen, Germany

Background: Using single nucleotide polymorphisms (SNPs) as disease markers, a 50 kb region on the short arm of chromosome 6 (6p21.3) has been found to be associated with susceptibility to myocardial infarction in a Japanese population. The locus contains the genes *BAT1* (encoding HLA-B-associated transcript 1), *NFKBIL1* (encoding nuclear factor of kappa light polypeptide gene enhancer in B cells inhibitor-like 1), and *LTA* (encoding lymphotoxin-α). We conducted a case-control study to determine whether the *BAT1-NFKBIL1-LTA* region was related to myocardial infarction in Caucasians.
Methods: The group of cases included 3657 patients with myocardial infarction and the control group comprised 1211 individuals without signs or symptoms of previous or acute myocardial infarction. Nine single nucleotide polymorphisms (3 in *BAT1*, 3 in *NFKBIL1*, and 3 in *LTA*) were used as markers for testing the association of the *BAT1-NFKBIL1-LTA* region with myocardial infarction. Genotyping was based on PCR and involved allele-specific fluorogenic oligonucleotide probes (TaqMan technique).
Results: Five of the 9 polymorphisms (1 in *BAT1*, 1 in *NFKBIL1*, and 3 in *LTA*) were significantly associated with a protective effect against myocardial infarction: homozygous carriers of the less frequent alleles were significantly more abundant in the control group than in the group with myocardial infarction (p≤0.045). In addition, we found, that the 9 SNPs were in strong linkage disequilibrium. Protection against myocardial infarction was observed in carriers of a specific haplotype defined by the 9 SNPs (p=0.016), especially in homozygous carriers of the protective haplotype (p=0.0047).
Conclusions: The *BAT1-NFKBIL1-LTA* region on chromosome 6 is a susceptibility locus for myocardial infarction in a population of Caucasian origin. In contrast to previous findings among Japanese, homozygous carriers of the less frequent alleles and carriers of a specific haplotype defined by the 9 SNPs present decreased risk of myocardial infarction..

2:30 p.m.

814-5 **Eosinophils May Have Potential To Promote Occlusive Thrombus In Acute Coronary Syndrome: Histological And Immunohistochemical Analysis**

Tetsuo Sakai, Shin Inoue, Taka-aki Matsuyama, Tsukasa Saito, Yuji Hamazaki, Hiroshi Suzuki, Hidekazu Ota, Takashi Katagiri, Showa University School of Medicine, Tokyo, Japan, Tokyo, Japan

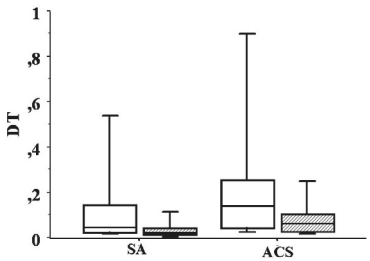
Background: Thrombus aspiration therapy allows us to examine thrombus and atheroma fragments in acute coronary syndrome. It was reported that inflammatory cells and platelet activation play key role in the development of thrombus formation. Among inflammatory cells, eosinophil granule proteins are thought to facilitate the proliferation of thrombus by activating platelets. We performed histological analysis using tissue samples that obtained by thrombus aspiration therapy.
Methods: One hundred nineteen samples from 146 consecutive patients were studied. Thrombus aspiration therapy was carried out in 34 cases with the RESCUE thrombectomy catheter, a PercuSurge GuardWire Plus Temporary Occlusion and Aspiration System was used in 31 cases, and a ThromBuster catheter was used in 54 cases. Samples were stained with hematoxylin and eosin, Elastica van Gieson and phosphotungstic acid hematoxylin. The sample area, percentage of red thrombus (red blood cells and fibrin) area, percentage of white thrombus (platelets and fibrin) area and percentage of atheroma fragments area were calculated. Samples were stained immunohistochemically with antibodies against macrophages, activated platelets (P-selectin) and IL-5 that induces eosinophils migration.
Results: Mixed thrombus was observed in 114 of 119 samples, atheromatous tissue was included in 53 samples. Macrophages, neutrophils and activated platelets were observed in both thrombi and atheroma fragments. Moreover, eosinophil infiltration was observed in the area between the white thrombus and red thrombus in 79 samples. In the contrast, we did not detect eosinophils infiltration into atheroma fragments. The number of local eosinophils was not related to the percentage of peripheral eosinophils. However, the number of eosinophils was significantly related to thrombus size and the percentage of red thrombus area. IL-5 was expressed on granulocytes and macrophages in thrombi.
Conclusions: Presumably, eosinophils may play an important role in coronary occlusion by promoting the growth of red thrombus. Macrophages and neutrophils may act as stimulating eosinophils migration by releasing IL-5.

2:45 p.m.

814-6 **Increased Plaque Temperature In Patients With Type 2 Diabetes Mellitus And Acute Coronary Syndrome: A Synergistic Effect?**

Konstantinos Toutouzas, Virginia Markou, John Mitropoulos, Maria Drakopoulou, Eleftherios Tsiamis, Manolis Vavuranakis, Sophia Vaina, Aris Androulakis, Christodoulos Stefanadis, Hippokration Hospital, Athens, Greece

An increased inflammatory state is observed in patients (pts) with acute coronary syndromes (ACS) and diabetes mellitus (DM). Local inflammatory involvement is correlated with heat generation, which can be recorded by coronary plaque thermography. In this study we investigated whether DM is predisposing in increased plaque temperature in ACS.
Method: In the study we enrolled 108 pts undergoing percutaneous coronary interventions. We included 45 patients with DM and 63 pts without DM. The latter group was matched for all demographic characteristics. Coronary thermography (Medispes, Switzerland) was performed prior to the intervention and temperature difference (DT) between the atherosclerotic plaque and the proximal vessel wall was recorded.
Results: Fifty-three pts suffered from ACS and 55 pts had stable angina (SA). Pts with ACS had increased DT compared to pts with SA (DT: 0.21±0.04 vs 0.09±0.02ºC, p=0.02). Pts with DM had increased DT compared to pts without DM (DT: 0.19±0.04 vs 0.12±0.02ºC, p=0.03). Pts suffering from ACS with DM had greater DT compared to non-diabetic pts (DT: 0.29±0.07 vs 0.15±0.04ºC, p=0.03). In pts with SA there was no difference in DT between pts with and without DM (DT: 0.10±0.02 vs 0.09±0.03ºC, p=0.67).(Figure; DM:White boxes)
Conclusion: The results of this study suggest that DM predisposes to marked increase of local inflammatory activation in pts with unstable syndromes. However, in pts with stable angina DM does not seem to further increase the local inflammatory process.



3:00 p.m.

814-7 **Lipoprotein-Associated Phospholipase A_2 Independently Predicts the Angiographic Diagnosis of Coronary Artery Disease**

Benjamin D. Horne, Jeffrey L. Anderson, Robert L. Wolfert, Joseph B. Muhlestein, Dale G. Renlund, Jessica L. Clarke, Heidi Thomas, Matthew J. Kolek, Tami L. Bair, Robert R. Pearson, Krishnankutty Sudhir, John F. Carlquist, LDS Hospital, Salt Lake City, UT, University of Utah, Salt Lake City, UT

Background: Inflammation in cardiovascular (CV) disease is a much-studied phenomenon for which C-reactive protein (CRP) is a non-specific marker of coronary artery disease (CAD) and CV events. Lipoprotein-associated phospholipase A_2 ($LpPLA_2$) is an enzyme that may be a cardiac-specific inflammatory biomarker. We evaluated the independent association of $LpPLA_2$ to CAD and CV events adjusting for standard factors, lipids, and CRP.
Methods: $LpPLA_2$ (PLAC™ test, diaDexus, Inc.) and CRP were measured from samples donated by consenting patients (N=1,493) enrolled in the registry of the Intermountain Heart Collaborative Study. All patients underwent coronary angiography (1996-1998) to diagnose the presence or absence of CAD. Patients were followed for 6.7±0.5 years (range: 5.7-7.9 years) to determine CV events (all-cause death, ischemic death, non-ischemic CV death, new MI, and cerebrovascular accident [CVA]).
Results: Average age was 63±12 years; 70% were male. $LpPLA_2$ weakly correlated with lipids (LDL: r=0.22, p<0.001; HDL: r=-0.13, p<0.001), but not with CRP (r=0.03, p=0.26). $LpPLA_2$ levels differed between patients with CAD (geometric mean: 369.5 [SE: 6.3] ng/mL) and no CAD (315.3 [8.8], p<0.001) and ischemic death (418.3 [26.2] vs. survivors: 346.4 [6.1], p<0.001). In multivariable logistic regression, increasing quartile (Q) of $LpPLA_2$ predicted increased risk of CAD (vs. Q1) for Q2 (odds ratio [OR]=1.15, 95% CI=0.78-1.71, p=0.48), for Q3 (OR=1.53, 95% CI=1.02-2.31, p=0.042), and for Q4 (OR=2.44, 95% CI=1.58-3.79, p<0.001), while CRP was also predictive (vs. Q1, Q2: OR=1.47, p=0.057; Q3: OR=1.93, p=0.002; Q4: OR=3.43, p<0.001). In multivariable Cox regression, $LpPLA_2$ also tended to predict ischemic death (vs. Q1; Q2: hazard ratio [HR]=1.27, p=0.55; Q3: HR=2.18, p=0.04; Q4: HR=1.73, p=0.14).
Conclusions: $LpPLA_2$ was confirmed to predict increased CAD risk, and extends this to patients undergoing coronary angiography. Uniquely, $LpPLA_2$ was found to predict longitudinal risk of ischemic death, and did so with a similar effect size. This study suggests that $LpPLA_2$ may be considered as an ischemic-specific inflammatory marker of clinical CV risk along with the non-specific CRP.

3:15 p.m.

814-8 **NT Pro-BNP Predicts Clinical Outcomes In Patients With Acute Coronary Syndromes And Preserved Left Ventricular Function**

Florencia Rolandi, Luis Guzman, Jose Gabay, Ricardo Sarmiento, Diego Perez de Arenaza, Natalia Vensentini, José Alvarez, Fernando Rubinstein, José Luis Navarro Estrada, Hospital Italiano, Buenos Aires, Argentina

NT-proBNP has been associated with adverse outcome in patients with non-ST elevation acute coronary syndromes (NSTE-ACS). Little is known about prognostic value of NT-proBNP adjusted by LV function. Our aim was to assess the capacity of NT-proBNP to predict long term events in patients with NSTE-ACS and preserved LV function.
Methods: From a prospective cohort of 1483 patients with NSTE-ACS, 590 underwent in-hospital angiography (median 2 days). Among these, 393 patients had LV ejection fraction >40% and conformed the study population. NT-proBNP was measured at a median of 3 hours and a pre-specified cut-off between low and high levels was 586 pg/ml. The primary endpoint was death and or myocardial infarction (D/MI) at 180 days.
Results: Of the 393 patients with normal LV function, 310 (79%) had NT-proBNP levels < 586 pg/ml and 83 (21%) had = or > 586 pg/ml.
Patients with high NT-proBNP levels had increased risk of death (9.6% vs 2.3%, p=0.002), MI (9.6% vs 3.2%, p=0.01), and D/MI (16.9% vs 5.5%, p=0.001) at 180 days compared to patients with NT-proBNP < 586 pg/ml. In a logistic regression analysis including clinical, ECG and angiographic characteristics, NT-proBNP was an independent predictor of death and D /MI, whereas troponin remained the best predictor of MI. (see table)
Conclusions: NT-proBNP is an independent predictor of clinical outcomes in patients with NSTE-ACS and preserved LV function. It is possible that prognostic information provided by NT-proBNP might be related to other mechanisms than LV dysfunction.

		OR	95% IC	p value
Death or MI	NT-proBNP > 586 pg/ml	2.51	1.12-5.62	0.026
	Diabetes	3.37	1.48-7.68	0.004
	Troponin T > 0.01 ng/ml	2.80	1.12-7.02	0.028
Myocardial infarction	Troponin T > 0.01 ng/ml	3.88	1.06-14.17	0.04
	Diabetes	2.87	1.00-8.20	0.049
	Complex coronary lesion	2.98	1.01-8.81	0.049
Death	Age (per year)	1.06	1.01-1.12	0.029
	Diabetes	3.83	1.26-11.65	0.018
	NT-proBNP > 586 pg/ml	3.14	1.04-9.45	0.042

ORAL CONTRIBUTIONS

822FO Featured Oral Session...Time to Transfer, Time to Treatment and Time of Treatment in ST-Elevation Myocardial Infarction

Monday, March 07, 2005, 4:00 p.m.-5:30 p.m.
Orange County Convention Center, Hall E2A

4:15 p.m.

822-4 **Inter-hospital Delay And Mortality In Patients With ST-Segment Elevation Myocardial Infarction Transferred For Primary Angioplasty**

Giuseppe De Luca, Harry Suryapranata, Menko-Jan de Boer, Jan Paul Ottervanger, AT Macel Gosselink, Jan-Henk E. Dambrink, Jan CA Hoorntje, Arnoud WJ van't Hof, De Weezenlanden Hospital, Zwolle, The Netherlands

Background. Transferring of patients with STEMI for primary angioplasty has been shown to be safe and feasible, with better outcome in comparison with on-site thrombolysis. The aim of the current study was to evaluate the impact of inter-hospital delay on mortality in STEMI patients undergoing primary angioplasty.
Methods. Our population is represented by 616 patients with STEMI transferred for primary angioplasty to our hospital. Patients were divided in 4 groups according to each 30-minute inter-hospital delay (defined as the time between presentation at the referral center and arrival at our hospital): < 30, 30-59, 60-89, ≥90 minutes.
Results. Patients with longer inter-hospital delay had a higher prevalence of multivessel disease, and longer ischemia time. Patient's delay (from symptom onset to admission at the referral hospital) and door-to-balloon time were not different among the groups. Longer inter-hospital delay was associated with impaired perfusion and larger infarct size (Table 1).
A linear relationship was found between inter-hospital delay and 1-year mortality (Table 1, p = 0.01), even after adjustment for major baseline characteristics (age, gender, diabetes, Killip class at presentation, infarct location, multivessel disease, pre and postprocedural TIMI flow) (RR = 1.6 [1.13-2.27], p = 0.008).
Conclusions. The main finding of the present study is that inter-hospital delay is linearly associated with mortality in patients with STEMI transferred for primary angioplasty.

Table 1. Patients" characteristics and outcome according to inter-hospital delay.

Inter-hospital delay (min)	< 30	30-59	60-89	> 90	p trend
Number of patients	94	188	194	140	
Ischemic time (min)	185 (136-289)	190 (156-247)	220 (172-286)	242 (201-389)	< 0.0001
Door-to-balloon time (min)	41 (29-60)	38 (27-51)	37 (25-51)	37 (25-51)	NS
Patient delay (min)	117 (73-198)	105 (70-155)	110 (60-180)	90 (60-180)	NS
Myocardial blush grade 2-3 (%)	81.5	79.0	79.7	71.7	0.09
LDH_{cvs} (U/L)	1150 (698-2510)	1944 (1051-3305)	2131 (1261-3785)	1976 (1103-3300)	0.049
1-year mortality (%)	3.2	6.4	6.2	12.1	0.01

4:30 p.m.

822-5 **Does a 90-Minute Door-to Balloon Time Matter? Observations From Four Current Reperfusion Trials**

William W. O'Neill, Cindy L. Grines, Simon R. Dixon, John J. Griffin, Jack L. Martin, David A. Cox, John G. Webb, Bruce R. Brodie, Roxana Mehran, Raymond J. Gibbons, John Held, Gregg W. Stone, William Beaumont Hospital, Royal Oak, MI, Columbia University, New York, NY

Background: The current AHA/ACC guidelines for percutaneous coronary intervention (PCI) therapy of ST-segment elevation MI (STEMI) promote a 90-minute door-to-balloon time (DBT) as a target for quality. This recommendation is based largely on retrospective observations from clinical registries.
Methods: We sought to determine whether treatment delay has an impact on final infarct size or mortality in four recent PCI trials aimed at infarct size limitation. Data from the EMERALD (n=501), COOL MI (n=357), AMIHOT (n= 269), and ICE-IT (n= 228) were merged and analysis of outcome and infarct size, determined by sestamibi imaging, was performed.
Results: DBT (p<0.0001) and onset-to-door time (p=0.025) remained independent predictors of final infarct size on multivariable analysis
Conclusion: In spite of later time to presentation, patients with short DBT times have a lower mortality, lower 30-day MACE and smaller infarct sizes. These data suggest that "shorter-is-better" concerning DBT, and provide validation for current guideline recommendations.

Results Stratified By Door-to-Balloon Time

DBT (mins)	<60	60-90	90-120	>120	p-value
N	183	296	304	403	
Prior MI	9%	12%	9%	8%	NS
Anterior MI	435	40%	45%	41%	NS
Onset-to-Door (mins)	197 ± 182	140 ± 140	141 ± 151	113 ± 124	<0.0001
Door-to-Balloon (mins)	44 ± 12	75 ± 9	103 ± 8	156 ± 30	-
Onset-to-Balloon (mins)	235 ± 180	216 ± 140	244 ± 150	269 ± 126	<0.0001
Death 30-days	0.6%	0.7%	4.7%	2.5%	0.0037
MACE 30-days	1.6%	2.4%	7.6%	5.5%	0.0034
Infarct Size (% LV)	14.2 ± 15.8	13.2 ± 14.6	18.0 ± 18.0	17.4 ± 18.0	0.0023

4:45 p.m.

822-6 **Door-to-Balloon Time for Acute Myocardial Infarction: Where Can We Improve?**

Elizabeth Bradley, Robert L. McNamara, Jeph Herrin, Yongfei Wang, Martha Radford, David Magid, John Canto, Martha Blaney, Harlan M. Krumholz, Yale University, New Haven, CT

Background: While delays in door-to-balloon times for ST-segment elevation myocardial infarction (STEMI) patients treated with primary percutaneous coronary intervention (PCI) are well-documented, less is known about delays in the specific subinterval components that comprise overall door-to-balloon time. We sought to compare the mean door-to-ECG, ECG-to-cath lab, and cath lab-to-balloon subinterval times for the top performing hospitals (median door-to-balloon less than or equal to 90 minutes) with those at lower performing hospitals (median door-to-balloon times greater than 120 minutes). Understanding how these sub-intervals vary can help identify elements of the door-to-balloon process with the greatest opportunity for improvement.
Methods: Using patient-level data from the National Registry of Myocardial Infarction from 1/2001 through 12/2002 (13,387 patients in 340 hospitals), we estimated hierarchical multivariate models and compared hospitals' geometric mean times for each subinterval in door-to-balloon time, adjusted for patient and hospital characteristics.
Results: Top performing hospitals had significantly shorter adjusted mean times in each subinterval: door-to-ECG (7.8 vs 9.3 minutes, p<0.001), ECG-to-lab (47.3 vs 66.3 minutes, p<0.001), and lab-to-balloon (29.2 vs 38.3 minutes, p<0.001) compared with lower performing hospitals. The subinterval times were positively correlated, indicating that hospitals that performed well in one subinterval were more likely to perform well in other subintervals (p<0.01).
Conclusion: Our data indicate substantial hospital-level variation in the subintervals of door-to-balloon time. Efforts to achieve guideline based door-to-balloon times should initially target the ECG-to-lab subinterval time, where the overall variation in, and opportunity for, reducing door-treatment times are greatest. Setting benchmark door-to-balloon subinterval times, identifying and implementing systems for achieving these times, and monitoring performance may help hospitals achieve guideline based care for patients with STEMI.

5:00 p.m.

822-7 **Time To Treatmant Of Acute Myocardial Infarction (AMI) Can Be Optimized By An Integrated Infarction Networtk According To Guidelines.**

Matthias Rau, Michael Weber, Albrecht Elsaesser, Eva Keil, Christian Maikowski, Christian Hamm, Kerckhoff Heart Center, Bad Nauheim, Germany

Background: Recent studies have demonstrated a benfit of primary PCI for the treatment of patients with an acute ST-segment elevation myocardial Infarction(STEMI). To achieve optimised times till PCI, we initiated a network for the treatment of STEMI.
Methods: Our integrated network incorporates the emergency care system, community hospitals and a cardiac center with a 24h cathlab intervention facility. A twelve lead ECG is recorded preclinically and if STEMI is diagnosed ,the cardiac center is informed immediately and the patient is taken directly to the Cath Lab.
Results: From April 2003 till August 2004 a total of 488 patients with STEMI have been treated. 283 patients (58 %) were admitted directly by the emergency ambulance , 200 (41%) were transferred from community hospitals, n=4 (1%) came without prior informations. 5 % of patients (n=24) had a cardiogenic shock and 7% had a cardiopulmonary resucitation (CPR). Delay from onset of symptoms till arrival in the cathlab was significantly longer for transferred patients (2.4h ± 6.0 vs 6.5 h ± 8.1; p<0,01) Door to balloon- time was short and did not differ between both groops (30 ± 51min vs.25 ± 23 min; ns). In- hospital mortality was 3.2 % excluding those who had CPR. Reinfarcton rate was 1 % at six month time.

Conclusion: In a network for treatment of STEMI with undelayed transportation to the cath lab based on the preclinically recorded ECG a door to balloon time of < 30 min. can be achieved. Short times from onset of symptoms till revascularisation may have an impact on low in hospital mortality raates.

5:15 p.m.

822-8 **Off-hour Primary Angioplasty: Why Is Mortality Higher?**

Srihari S. Naidu, Robert L. Wilensky, Faith Selzer, Warren K. Laskey, Vankeepuram S. Srinivas, James N. Slater, Ruchira Glaser, New York Presbyterian Hospital - Cornell, New York, NY, University of Pittsburgh, Pittsburgh, PA

Background: Percutaneous coronary intervention (PCI) outcome for ST-elevation myocardial infarction exhibits diurnal variation, with higher in-hospital mortality during off-hours. It remains unknown whether differences in clinical or angiographic factors are responsible.
Methods: The incidences of in-hospital and one-year death were collected on 6,676 consecutive patients who underwent PCI in 19 centers during three waves of enrollment between July 1997 and March 2002. Patients undergoing emergent PCI for acute myocardial infarction (n=614, 9.2%) were stratified according to whether intervention occurred off-hour (1900-0659) or during routine hours (0700-1859). Baseline clinical, demographic and angiographic characteristics, as well as in-hospital and one-year mortality were compared.
Results: The majority occurred during routine hours (n=433, 70.5%). Median time from symptom onset to PCI was shorter during off-hours (4.0 vs. 5.1 hours, p=0.05). Clinical and demographic characteristics did not differ, including age, gender, race, diabetes, hypertension, hypercholesterolemia, smoking, history of coronary disease or heart failure, and presentation with cardiogenic shock (off-hours 18.2% vs. 15.0%, p=0.32). Off-hour patients more likely had disease of the left anterior descending (LAD, 79.0% vs. 70.0%, p<0.05), total occlusion of the LAD (40.3% vs. 27.0%, p<0.01), any total occlusion (76.2% vs. 64.0%, p<0.01), and TIMI 0-1 flow (66.8% vs. 55.4%, p<0.01). Stenting rate between off-hour and routine hour patients (77.3% vs. 81.5%, p=0.23) and total angiographic success (88.4% vs. 92.8%, p=0.07) remained similar. Off-hour PCI was associated with higher in-hospital mortality (11.0% vs. 6.0%, OR 1.94 95%CI 1.06-3.58, p<0.05). After adjustment for angiographic differences, odds for in-hospital mortality did not change significantly (OR 2.09, 95%CI 0.96-4.55, p=0.06). Initial differences in mortality persisted at one year (14.2% vs. 10.1%, p=0.13), but were no longer significant.
Conclusion: Increased in-hospital and one-year mortality after off-hour emergent PCI for acute myocardial infarction may be only partially explained by differences in angiographic features.

ORAL CONTRIBUTIONS

824FO Featured Oral Session... Recent Developments in Myocardial Regeneration

Monday, March 07, 2005, 4:00 p.m.-5:30 p.m.
Orange County Convention Center, Room 414A

4:15 p.m.

824-4 **Intravenous Infusion of Mesenchymal Stem Cells During Early Reperfusion Enhances Regional Perfusion and Improves Ventricular Function in a Porcine Model of Acute Myocardial Infarction**

Michael E. Halkos, Faraz Kerendi, Ning-Ping Wang, Rong Jiang, L. Susan Schmarkey, Bradley J. Martin, Arshed A. Quyyumi, Walter L. Few, Hajime Kin, Zhi-Qing Zhao, Robert A. Guyton, Jakob Vinten-Johansen, Emory University School of Medicine, Atlanta, GA

Background: The intramyocardial or intracoronary injection of bone marrow stem cells after acute MI (AMI) has proven efficacious in improving regional perfusion and LV function. Using a closed-chest porcine model of AMI, this study tested the hypothesis that bone marrow-derived mesenchymal stem cells (MSCs) delivered intravenously (IV) during early reperfusion engraft in ischemic myocardium, augment neovascularization, and improve LV function 12 weeks post-infarction.
Methods: The proximal LAD was occluded for 75 min by an angioplasty balloon. At 15 min of reperfusion, Yorkshire pigs randomly received 1 of 4 treatments: vehicle (Control, n=10), 1 x 10^6 MSCs/kg (1 mill, n=7), 3 x 10^6 MSCs/kg (3 mill, n=8), or 10 x 10^6 MSCs/kg (10 mill, n=8). MSCs were pre-labeled with DiI and DAPI fluorescent markers. Myocardial flow reserve (intracoronary adenosine) in scar and border tissue was determined 12 weeks after AMI using 15µm microspheres. LV function was assessed at 12 weeks by pressure-volume analysis (impedance catheter).
Results: MSCs were observed in the scar zone of MSC-treated pigs 12 weeks after IV infusion and expressed muscle-specific proteins by immunohistochemistry. Flow reserve (ml/min/g tissue) in the scar zone was greater in the 1 mill (2.5 ± 0.3), 3 mill (2.9 ± 0.7), and 10 mill (2.9 ± 0.5) groups vs Control (1.1 ± 0.3, p<0.001). Flow reserve in the border zone was also enhanced in the MSC-treated groups vs Control (p<0.001). Vascular density (antibody to vWF) in the scar zone was 23% greater in the 1 and 3 mill groups, and 30% greater in the 10 mill group vs Control (p<0.05). Preload-recruitable stroke work (mmHg) was greater in the 3 mill (39 ± 4.3) and 10 mill (44 ± 2.4) groups, but not in the 1 mill group, compared to Control (26 ± 4.0, p<0.05). Systolic performance (slope of end-systolic pressure-volume relationship, mmHg/ml) was also greater in 3 mill (1.4 ± 0.1) and 10 mill (1.5 ± 0.2) vs Control (1.0 ± 0.1, p<0.05).
Conclusion: In a chronic porcine model of AMI, MSCs delivered IV during early reperfusion engraft into ischemic myocardium, enhance regional perfusion, and improve global LV function in a dose-dependent manner. Functional improvements may be a result of enhanced neovascularization.

4:30 p.m.

824-5 **Autologous Myotissue Transplantation in a Porcine Myocardial Infarction Model Results in Improved Function and Decreased Infarct Size**

Audrey Rosinberg, Pierre Voisine, Guifu Wu, Evan Applebaum, Susan Yeon, Seung Lee, Joseph Carrozza, Frank Sellke, Roger Laham, BIDMC/Harvard Medical School, Boston, MA

Background: Myogenesis is emerging as a potential treatment for myocyte loss in myocardial infarction and heart failure. Cell based therapy has been proposed as a potential treatment strategy. The purpose of this investigation was to determine the safety and efficacy of implanting microtissue containing adult cardiomyocytes in an animal model of myocardial infarction.
Methods: 13 Yorkshire pigs underwent balloon occlusion of LAD for one hour and were randomized to treatment (n=7, septal biopsies via the right ventricle and implantation of 9 tubular biopsies in anterior wall) or control (n=6, septal biopsies and 9 sham injections in anterior wall). Animals were assessed 4 weeks later with hemodynamics, LV function and perfusion (MRI), echocardiography, ultrasonic crystals, microspheres, and morphometric analysis using tetrazolium (TTC) staining, histology, and molecular studies.
Results: All animals tolerated the procedure well. There were no arrhythmias noted and no detectable deleterious effect on basal septum (site of tissue harvest).
TTC staining demonstrated significantly smaller infarcts in the anterior wall in treated animals compared to controls (10.33±4.57% area of mid slice versus 28.9±5.81% respectively, p<0.05). There was no significant difference in the size of the infarct in the untreated septum between treated and control animals (21.63±5.32% and 21.48±2.53%). The volume of infracted myocardium as determined by MRI (delayed enhancement) was significantly lower for treated animals than controls (2.2±0.5% vs 5.4±1.5% of entire LV volume, p=0.04). Anterior/septal wall perfusion ratio (MRI) was significantly higher in treated animals compared to controls (1.2±0.1 and 0.86±.05, p<0.01). dP/dt improved in treated animals vs controls (1235±215 vs 817±91 mmHg/s, p=0.06). There were less expression of VEGF, FGF-2, and CD31 in treated animals compared to controls, but more expression of the anti-apoptotic factor IAP-2 (p=0.04).
Conclusion: This study demonstrates the safety, feasibility, and efficacy of a novel method for myocardial regeneration and protection by implanting autologous myocardial microtissue obtained from preserved myocardial regions.

4:45 p.m.

824-6 **Nestin Expressing Neural Stem Cells Identified in the Scar of the Post-Myocardial Infarcted Rat Heart**

Angelino Calderone, Jessica Drapeau, Jocelyn Dupuis, Viviane El-Helou, Frederic Lefevbre, Montreal Heart Institute, Montreal, PQ, Canada, University of Montreal, Montreal, PQ, Canada

Background: Recent studies have delineated the process of neural remodelling in the infarcted region of the damaged heart. However, it remains equivocal as to whether nerve fiber innervation of the scar occurred via either the growth of pre-existing fibers and/or the recruitment of neural stem cells. Methods;The present study examined the recruitment of neural stem cells to the infarcted region following coronary artery ligation in the adult male rat.
Results: In 1-week post-myocardial infarcted rats, neurofilament-M- and peripherin-positive fibers were visualized in the scar by immunofluorescence. Co-incident with fiber formation, numerous scar-derived cells stained positive for the neural stem cell marker nestin. By contrast, nestin immunoreactivity was not detected in cardiac myocytes of the non-infarcted left ventricle. Following the isolation and culture of scar-derived primary passage cells, nestin-positive cells with a neural morphology were identified, whereas nestin staining was absent in myofibroblasts. FACS analysis of primary passage nestin-expressing neural stem cells indirectly revealed a proliferative capacity as a temporal increase of cell number was observed (Day 7, 6%; Day 11, 47%; Day 18, 68%). Consistent with a progenitor role, nestin and neurofilament-M immunoreactivity were co-localized in primary passage neural cells. To determine the source of nestin-expressing neural stem cells, bone marrow-derived cells labelled with green fluorescent protein (GFP) were administered to irradiated Wistar male rats two weeks prior to coronary artery ligation. Three weeks post-myocardial infarction, numerous GFP-positive cells were identified in the scar, whereas staining was not detected in the non-infarcted left ventricle. Unexpectedly, nestin-expressing neural stem cells in the infarcted region did not co-localize with GFP-positive cells.
Conclusion: These data have demonstrated that nestin-expressing neural stem cells were identified in the infarcted region of the damaged rat heart, possess a capacity to proliferate, were not derived from the bone marrow, and may represent the progenitor cell that subsequently differentiates to a neuronal phenotype.

5:00 p.m.

824-7 **Improvement of Left Ventricular Function by Intramuscular Allogeneic Mesenchymal Stem Cells Transplantation in Postinfarcted Rat Myocardium May Be Transient**

Wangde Dai, Sharon L. Hale, Bradley J. Martin, Jin-Qiang Kuang, Robert A. Kloner, The Heart Institute, Good Samaritan Hospital, University of Southern California, Los Angeles, CA, Osiris Therapeutics Inc., Baltimore, MD

Purpose: The survival, engraftment and differentiation of allogeneic mesenchymal stem cells (MSCs) and their long term effect on left ventricular (LV) remodeling and function were investigated.

Methods: MSCs isolated from ACI rats were labeled with DiI. Phosphate buffered saline (n=36) or allogeneic MSCs (n=39, 2×10^6 cells each) were injected directly into the scar of a 1 week old myocardial infarction in female Fischer rats. Four weeks or 6 months later, LV ejection fraction (LVEF) was assessed by angiogram, and hearts were processed for histology. Immunohistologic confocal microscopy examinations of frozen sections were performed blindly at 6 months.
Results: At 4 weeks, LVEF was significantly greater in MSC treated animals (43.6±1.0 %, n=12) compared to the control group (38.8±1.1%, n=12; p=0.005). At 4 weeks there also was a trend toward smaller post-mortem volumes in the MSC group (0.31±0.01ml) versus the control group (0.34±0.01ml, p=0.16); and infarct scar thickness in the MSC group was 0.48±0.02mm versus the control group at 0.45±0.04mm, p=0.54. However, at 6 months the benefits of MSC treatment were gone (LVEF = 41.8±1.1% in MSC group, versus 42.0±1.0% in control group, p=0.93; volume =0.40±0.02ml in MSC group versus 0.44±0.02ml in control group, p=0.2; and scar thickness was 0.41±0.02mm in MSC group versus 0.41±0.02mm in control group, p=0.85). At 6 months, DiI positive cells were observed in the central scar region of rats in the MSC group, and these cells expressed the muscle-specific markers -actinin, MF-20, phospholamban and tropomyosin, but did not fully evolve into an adult cardiac phenotype. In addition, these cells were found to express smooth muscle actin and von Willebrands factor. No DiI positive cells were found in the control group.
Conclusion: Allogeneic MSCs survive in infarcted myocardium, and express markers suggesting a muscle and vascular phenotype at 6 months after transplantation. MSCs did improve global LV function at 4 weeks with a trend towards less remodeling at this time; however this benefit was transient. Methods to enhance MSC differentiation and continued contribution to contraction are needed to optimize this form of therapy.

5:15 p.m.

824-8 **Indium-111 Oxine Labeling Of Rat Bone Marrow-derived Mesenchymal Stem Cells For In Vivo Imaging During Autologous Cell Therapy Of Myocardial Infarction**

Fatiha Maskali, Nguyen Tran, Joseph Nloga, Marie Héléne Laurens, Pierre-Yves Marie, Gilles Karcher, Faiez Zannad, faiez ZANNAD, nancy, France

Aim: Intramyocardial transplantation of bone marrow mesenchymal stem cells (BMSCs) was reported improving cardiac function in ischemic cardiac disease. However, data concerning the body distribution and the cardiac retention of transplanted cells remain poor. This study was **Aim**ed at assessing the use of Indium-111 oxine labeling of BMSCs for analyzing the retention and distribution of these cells when injected within myocardial infarction areas.
Material and Methods: In a first step, labeling efficiency, cytotoxicity and cell retention of Indium-111 oxine was analyzed in vitro on BMSCs cultures. In a second step, autologous BMSCs labeled with Indium-111 oxine (2x106 cells/50µl) were injected within infarcted myocardial walls one month after left anterior descending artery occlusion in 6 rats. Body pinhole scintigraphic images were recorded at 2 hours and at 1, 3, and 7 days. Cardiac distribution of Indium-111 was also analyzed on cryosections of hearts using a microimager. **Results:** Incubation of BMSCs (2x106 cells in 1 ml) with 15 MBq of Indium-111 oxyne resulted in a time-dependent labeling efficiency and cytotoxicity. Using a 10 min incubation-period, labeling efficiency was high enough (69%) and cell viability remained acceptable (96%). On cell cultures, there were high rates of Indium-111 release from labeled BMSCs, especially during the first day: retentions of Indium-111 within BMSCs were 46% at 2 hours, 28% at day 1, 25% at day 3 and 20% at day 7. After injection of autologous labeled BMSCs in infarcted areas, mean heart-activity determined with pinhole scintigraphy was 26.4±2.3% of the total injected activity at 2 hours, 17.3±2.4% at day 1, 16.8±1.5% at day 2 and 12.7±0.7% at day 7. When these percentages were corrected by the rates of Indium-111 release, documented at the same time-points on cell cultures, it was found that approximately 60% of injected BMSCs were presumably retained within hearts and this, all along the 7 days of in vivo follow-up.
Finally, microimager and histological analyses showed that at day 7, most transplanted BMSCs were still located around the injection sites within infracted areas.

ORAL CONTRIBUTIONS

832 Short- and Long-Term Outcome After an Acute Coronary Syndrome: Role of Inflammatory and Hemodynamic Markers

Tuesday, March 08, 2005, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 304A

8:30 a.m.

832-3 **Systemic Inflammatory Response Syndrome Complicating Acute ST-Segment Elevation Myocardial Infarction**

Rafael Valencia, Salvatore Cavaleri, Christopher B. Granger, Kenneth W. Mahaffey, Gudaye Taissa, Pierre Theroux, Paul W. Armstrong, Michael Hudson, Thomas G. Todaro, Chris Mojcik, Judith S. Hochman, New York University Medical Center, New York, NY

Large myocardial infarction is associated with an intense inflammatory response. The systemic inflammatory response syndrome (SIRS) may play a role in the development of cardiogenic shock (CS).

We analyzed the Complement and ReDuction of Infarct size after Angioplasty or Lytics (CARDINAL) program that investigated pexelizumab, a monoclonal antibody against C5 complement, in STEMI patients to evaluate the relationship between SIRS and the development of CS, CHF and death at 90 days.
The standard definition of SIRS which is the presence of two or more of the following was used: heart rate >90 beats/min, body temperature >38'C or <36'C, respiratory rate >20 breaths/min, or a white blood cell count >12 $x10^9$ / L or <4 $x10^9$ / L.
On presentation, 391 of 1903 (21%) patients met clinical criteria for SIRS. Patients with SIRS tended to be significantly younger (59% vs. 61%), more likely female (32% vs. 26%), diabetic (22% vs. 16%) and active smokers (46% vs. 39%). SIRS patients tended to have higher systolic (138.5 vs. 132.5) and diastolic blood pressures (84 vs. 80) on admission, higher troponin levels (2.0 vs. 1.3), and higher cumulative ST-segment elevation (10.5 vs. 9.5mm). Unadjusted event rates of CS, CHF, death and the composite of CS or death, with and without SIRS are shown below.
SIRS is frequent occurrence in STEMI on presentation and such patients have higher rates of CS and death. The presence of a strong inflammatory response has potential diagnostic and therapeutic implications in the early management of STEMI.

Systemic Inflammatory Response Syndrome in CARDINAL

Outcome	SIRS present (n=391)	SIRS absent (n-1512)	P value
CS developed @90 days	26 (6.7%)	58 (3.8%)	0.016
CHF developed @90 days	34 (8.7%)	95 (6.3%)	0.091
Mortality @90 days	41 (10.5%)	97 (6.4%)	0.006
Composite CS or death @90 days	54 (13.8%)	118 (7.8%)	<0.001

8:45 a.m.

832-4 **Inflammation and Acute Hyperglycemia: A Double Edged Sword in Diabetics With Non-ST Elevation ACS: Analyses From the TIMI Database**

Kausik K. Ray, David A. Morrow, Christopher P. Cannon, Jacqueline Buros, Ajay J. Kirtane, Carolyn Hoss McCabe, Eugene Braunwald, C. Michael Gibson, Brigham and Women's Hospital, Boston, MA, Harvard Medical School, Boston, MA

Background: Inflammation and diabetes (DM) are independently associated with cardiovascular (CV) risk in ACS. In vitro glucose augments the adverse effects of CRP.
Methods: We hypothesized that DM would be associated with increased markers of inflammation & that inflammation would enhance the CV risk in DM. We analyzed non ST elevation ACS patients in the OPUS TIMI-16 trial & validated the results in the TACTICS-TIMI 18 trial (invasive arm).
Results: Median CRP was higher among diabetics (n=541) vs non-diabetics (n=1659) in OPUS (9 vs 7.8mg/l p=0.002) & in TACTICS: diabetics (n=267) vs non-diabetics (n=662) CRP 6.6 vs 5.2 mg/l (p=0.0005). Stratifying by population median CRP in OPUS (fig 1), diabetics with CRP> median were at highest risk of death or MI while non-diabetics with CRP>median and diabetics with CRP<median were at similar risk (p for trend across range<0.0001). Identical observations were made in TACTICS. In addition, among diabetics high glucose levels (tertile 3) increased the CV risk of a high CRP (fig 2). In a Cox-regression model of death and MI, that included DM, glucose and CRP, an interaction was found between glucose and CRP (P_I=0.045).
Conclusion: Diabetics have greater inflammation and hyperglycemia may increase the CV risk associated with this. In diabetics with ACS future strategies that target both better glycemic control and reduction of inflammation, may reduce the CV risk in this high risk population.

Figure 1.
KM estimate of event free survival (Death or MI) By DM and CRP status in OPUS-TIMI 16

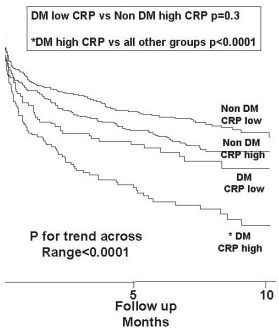
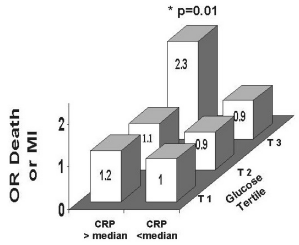


Figure 2.
The interaction between glucose and CRP on Death or MI among Diabetics In OPUS-TIMI 16

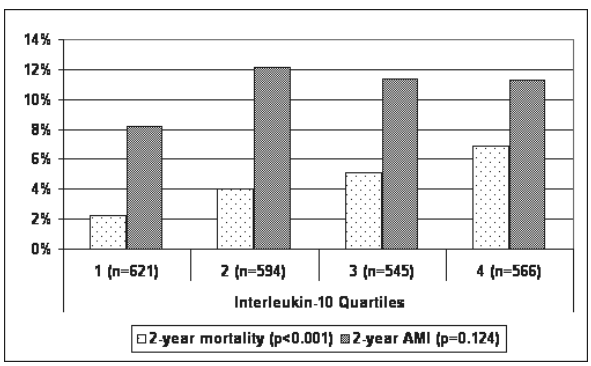


9:00 a.m.

832-5 **Elevated Levels of Interleukin-10 are Strongly Associated with Raised Mortality in non-ST Elevation Acute Coronary Syndrome**

Anders Malarstig, Bertil Lindahl, Lars Wallentin, Agneta Siegbahn, Uppsala Akademiska Sjukhus, Uppsala, Sweden

Background: Interleukin-10 (IL-10) is a cytokine with anti-inflammatory properties. A previous study has suggested that elevated levels of IL-10 are associated with a favorable prognosis in non-ST elevation acute coronary syndrome (NSTE-ACS). The aim of this study was to evaluate the prognostic value of Il-10 in a large group of patients with NSTE-ACS and see whether we could confirm the previous findings.
Methods: Citrated plasma samples were obtained at inclusion in patients enrolled in the FRISC-II trial (n=2326), evaluating an invasive vs. a non-invasive strategy in NSTE-ACS. IL-10 was measured using a highly sensitive ELISA (R&D). Patients were followed regarding myocardial infarction (MI) and death for 2 years.
Results: The median level of IL-10 was 1.06 pg/ml [25:th-75:th percentile; 0.63-1.87]. The mortality and MI rate in relation to quartiles of Il-10 are shown in the figure. The relations were congruent in both patients randomized to an invasive and a noninvasive strategy.
Conclusions: Increased plasma levels of IL-10 were strongly associated with higher mortality in the present study, in contrast to previous findings.



9:15 a.m.

832-6 **Plasma Levels of The Endogenous Nitric Oxide Synthase Inhibitor Asymmetrical Dimethylarginine (ADMA) Predict Outcome in Patients After Acute Myocardial Infarction**

Renke Maas, Heeschen Christopher, Friedrich Schulze, Kenneth Dickstein, Lisa Silberhorn, Thor Ueland, John Kjekshus, Pal Aukrust, Rainer Böger, University Hopsital Hamburg-Eppendorf, Hamburg, Germany, Frankfurt University Hospital, Frankfurt, Germany

The endogenous nitric oxide synthase inhibitor asymmetrical dimethylarginine (ADMA) has been implicated in the development and progression of cardiovascular disease. Elevated plasma ADMA concentrations predict adverse clinical outcome in patients undergoing percutaneous coronary intervention. However, whether elevated plasma ADMA concentrations also provide important prognostic information in patients after acute myocardial infarction (AMI) remains elusive.
Methods: We assayed circulating ADMA levels in 213 patients with AMI and their relation to adverse outcomes (death, AMI, stroke, or resuscitation) during follow-up in patients randomly assigned to angiotensin converting enzyme inhibition (captopril, n=108 patients) or angiotensin II receptor antagonism (losartan; n=105 patients). Blood samples were collected at baseline (median 3 days following AMI) and 1 year.

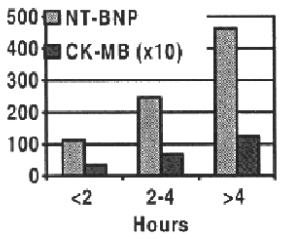
Results: Patients were categorized according to the median of ADMA levels (0.59 [range 0.24-1.13] µmol/l). ADMA levels above the median at baseline were associated with adverse cardiovascular events during a median of 27 months follow-up (univariate hazard ratio 2.10 (95%CI 1.14 - 3.89; P=0.018). Differences in event rates were consistent for all separate endpoints including mortality. The crude event rates for patients with low ADMA levels were 20.8% (combined endpoints), 17.9% (death, AMI), and 10.4% (death) whereas patients with high ADMA levels showed event rates of 35.5%, 31.8%, and 20.6%, respectively (all P<0.05). ADMA remained an independent prognostic indicator after adjustment for other known predictors of mortality and cardiovascular events after AMI (e.g. age, gender, diabetes, smoking, BNP, CRP; adjusted hazard ratio (HR) 2.45 [95%CI 1.25 - 4.80); P=0.009). Intriguingly, plasma ADMA levels were persistently elevated in patients with events during longitudinal testing (baseline: 0.64±0.15; follow-up: 0.67±0.11 µmol/l).
Conclusions: The present study indicates that elevated plasma ADMA concentrations can help to identify patients with myocardial infarction being at high risk for adverse cardiovascular events independently of other risk markers.

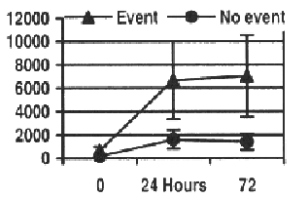
9:30 a.m.

832-7 **Natriuretic Peptide Insights in Acute Myocardial Infarction**

Justin A. Ezekowitz, Pierre Theroux, Wei-ching Chang, Kenneth W. Mahaffey, Christopher B. Granger, W. Douglas Weaver, Paul W. Armstrong, University of Alberta, Edmonton, AB, Canada, Duke Clinical Research Institute, Durham, NC

Background: While natriuretic peptides have prognostic ability, their relationship to acute myocardial necrosis is unclear. We examined the relationship of NT-BNP to infarct size (IS), time from symptom onset and prognosis in ST-elevation MI (STEMI) treated with primary PCI.
Methods: We studied 331 STEMI pts in the COMMA (COMplement inhibition in Myocardial infarction treated with Angioplasty) trial evaluating pexelizumab. NT-BNP (pg/ml) at 0, 24 and 72 hours; CK-MB area-under-the-curve (AUC) at 72 hours; and discharge QRS score were measured. The 90-day composite was death, stroke, shock, and heart failure.
Results: NT-BNP (median & interquartile) was higher with longer time since symptom onset (r=0.354, p<0.001) as was baseline CK-MB (r=0.328, p<0.001), **Lt Panel.** NT-BNP was correlated to measures of IS including AUC (r=0.445, p<0.001), and QRS score (r=0.354, p<0.001); Pts at the 90-day endpoint had markedly higher NT-BNP at all times p<0.001, **Rt Panel.** NT-BNP at all time points was the strongest independent predictor of the 90-day composite endpoint multivariate model: at 24 hrs, only age and 24 hr NT-BNP were sig. predictors of 90-day events (c-index 0.825). Similarly, in the 72 hr model, only age, Killip class and NT-BNP were predictors of a poor outcome (c-index 0.850).
Conclusions: NT-BNP at presentation is highly correlated with duration of symptoms, with IS at 24 hours, and at all timepoints is strongly related to poor outcomes. Sequential measures offer powerful prognostic information in STEMI.





9:45 a.m.

832-8 **Population Studies of Cardiovascular Disease Risk Are Limited If They Lack Angiographic Data**

Benjamin D. Horne, Joseph B. Muhlestein, Dale G. Renlund, John F. Carlquist, Tami L. Bair, Heidi Thomas, Beverly A. Campbell, Jeffrey L. Anderson, LDS Hospital, Salt Lake City, UT, University of Utah, Salt Lake City, UT

Background: The predictive strength of novel markers of cardiovascular (CV) risk, such as C-reactive protein (CRP), can vary between epidemiological studies. We hypothesized that this may result in part from variable presence of asymptomatic CV disease in control groups. Specifically, a recent report claims that CRP only moderately explains CV risk, thus we tested whether CRP is a stronger predictor of events when a clean control group of event-free, non-coronary artery disease (CAD) patients is used than among an admixed control of non-event CAD patients.
Methods: A cohort of 3,688 patients free from acute MI and undergoing angiography for CAD assessment had CRP tested. Events during 6.0±1.7 years of follow-up (range: 2.8-9.4 years) included MI, cerebrovascular accident, and death (all-cause, ischemic [ICD-9: 410-414], and non-ischemic CV). Readmission for congestive heart failure was also determined.
Results: Age averaged 64±12 years; 67% were male. CRP quartiles (Q) 1, 2, 3, and 4 had median hsCRP=0.9, 1.7, 3.5, and 13.1 mg/L, respectively. Overall, 717 (19%) patients died and 945 (26%) had a non-fatal event. CRP predicted (adjusted p<0.05) ischemic death, all-cause death, MI, all events combined, and congestive heart failure readmission. Adjusted Cox hazard ratios (HR) for death were greater when controls were non-CAD patients (n=882; HR=1.0, 1.27, 1.99, 2.23 for CRP Q1-Q4; p<0.001) than when controls had CAD (n=1036; HR=1.0, 1.11, 1.60, 1.59; p=0.001). This dichotomy held for the other endpoints (the statistical interaction of CRP*CAD for all events had p=0.002 for Q4). ROC AUC for death was 0.60 for CRP, 0.70 for CRP and age, and only 0.76 with addition of all 18 other variables.
Conclusions: As demonstrated for CRP, the strength of association for a novel risk marker and CV events may differ by presence or absence of CAD. This suggests that control groups in CV studies must be well characterized (eg., by coronary angiography). Studies where the control group is heterogeneous mixture of both healthy subjects and event-free subjects with undiagnosed CAD may underestimate a marker's predictive power. In this case, CRP remains one of the more important indicators of future CV risk

POSTER SESSION

1117 Protecting the Ischemic Myocardium I

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1117-203 **Human Hibernating Myocardium: Altered Calcium Regulatory System Contributes to Contractile Dysfunction**

Holger M. Nef, Helge Möllmann, Thorsten Dill, Roland Brandt, Woitek Skwara, Birgit Bölck, Robert H.G. Schwinger, Jutta Schaper, Albrecht Elsässer, Kerckhoff Heart Centre, Bad Nauheim, Germany, Laboratory of Muscle Research and Molecular Cardiology, Cologne, Germany

Background: Human hibernating myocardium (HHM) is characterized by a contractile dysfunction during chronic ischemia. We tested the hypothesis that a disturbed expression of calcium regulatory proteins and an altered SR-Calcium-ATPase activity contribute to a reduced function.
Methods: In 14 patients with coronary artery disease and reduced left ventricular function HHM was detected preoperatively by thallium scintigraphy, dobutamine echocardiography and magnetic resonance imaging. All clinical investigations were repeated three months after revascularization. During open-heart surgery transmural biopsies were taken from areas defined as HHM. Protein expression of SR-Calcium-ATPase (SERCA2a), phospholamban (PLN), sodium-calcium-exchanger (NCX) and ryanodine receptor (RyR2) were evaluated by Western blot analysis. SERCA2a activity was determined with an enzyme-coupled assay. Donor hearts not used for transplantation represented control myocardium.
Results: In all patients functional normalization of the HHM regions were documented after successful revascularizaton. The protein amount of phosphorylated PLN represented by the binding-sites Ser16 and Thr17 was significantly reduced (Ser16: 1.0±0.1 vs. 0.6±0.1, p0.05), and RyR2 (0.9.±0.1 vs. 1.0±0.2, p>0.05). Furthermore in HHM maximal SERCA2a activity (Vmax) was significantly reduced (419.9±19.9 vs. 526.8±25.4 nmol ATP/mg protein/min, p<0.05).
Conclusions: We postulate that in HHM a reduced SERCA2a activity contributes to a changed intracellular calcium handling. The regulation of SERCA2a activity depends on the phosphorylation of PLN. Therefore the decreased protein expression of Ser16-PLN and Thr17-PLN explains impaired calcium uptake into the sarcoplasmic reticulum thereby leading to contractile dysfunction in HHM.

1117-204 **Beneficial Effects Of Cardiac Denervation On Ischemia-Reperfusion Injury Result From Decreasing Direct Norepinephrine Toxicity, But Not From Decreasing Norepinephrine-Derived Free Radical Formation**

Makoto Nonomura, Takashi Nozawa, Akira Matsuki, Teruo Nakadate, Norio Igarashi, Bun-ichi Kato, Nozomu Fujii, Akihiko Igawa, Hidetsugu Asanoi, Takashi Kondo, Hiroshi Inoue, Toyama Medical and Pharmaceutical University, Toyama, Japan

Background: Norepinephrine (NE) released from the sympathetic nerve terminals during ischemia is the source of reactive oxygen species and NE-derived free radicals may cause the injury of myocyte. Accordingly, we studied influences of cardiac NE release and NE-derived free radicals on myocardial ischemia-reperfusion injury.
Methods: Using Wistar rats, cardiac denervation was induced by painting a solution of 10% phenol on the proximal region of left coronary artery 1 week before inducing ischemia. In rats without denervation, atenolol (0.5mg/kg) was administered intravenously 10-min before coronary occlusion. The proximal portion of left coronary artery was occluded for 30-min and thereafter reperfused. Cardiac interstitial levels of NE (iNE) and free radicals were determined using microdialysis and electron paramagnetic resonance (EPR) spin trapping in cardiac microdialysate containing 5,5-dimethyl-1-pyroline-n-oxide (DMPO), respectively.
Results: During coronary occlusion, there were no differences in cardiac hemodynamics between phenol group (n=7) and control group (n=9), but heart rate and blood pressure were lower in atenolol group (n=6) than in other two groups. The ratio of infarct size to the ischemic area at risk was lower in phenol and atenolol groups than in control group (28.5±10.3, 31.8±10.7 vs 49.2±14.5 %, respectively, P<0.05). iNE increased more than 200 times during 30-min ischemia in rats with innervation but was unchanged in rats with denervation, associated with the depletion of myocardial NE contents. EPR signal intensity corresponding to ·OH adduct of DMPO was not different between phenol and control group at 30-min (0.31±0.01 vs 0.28±0.11) and 60-min (0.45±0.19 vs 0.32±0.15) after reperfusion. **Conclusions**: Cardiac denervation protected myocytes against ischemia-reperfusion injury primarily through decreasing direct NE toxicity via -adrenergic signal activation, but not through suppressing NE-derived free radical formation.

1117-205 **Glutathione Monoethyl Ester Provides Histological, Hemodynamic, and Echocardiographic Evidence of Cardioprotection in the Rodent Myocardial Ischemia-Reperfusion Injury Model**

Nicholas C. Dang, Veli K. Topkara, Joy Kay, Michael S. Aboodi, Steve Xydas, Shi-Xian Deng, Matthew J. Szabolcs, Donald W. Landry, Mehmet C. Oz, Columbia University, College of Physicians and Surgeons, New York, NY

Background: Reduced glutathione monoethyl ester (GSHme) is a powerful antioxidant that detoxifies harmful oxygen free radicals and peroxides. We sought to examine the cardioprotective effects of exogenous GSHme in a rodent myocardial ischemia-reperfusion (IR) model.

Methods: Forty-eight adult Sprague-Dawley rats were divided into 4 groups: sham-thoracotomy + dextrose (Group 1), sham-thoracotomy + GSHme (Group 2), left anterior descending (LAD) artery ligation-release + dextrose (Group 3), and LAD ligation-release + GSHme (Group 4). Subjects were survived to 4 weeks and underwent echocardiographic and hemodynamic assessment. Hearts were sectioned for histological analysis.
Results: End-diastolic pressure (EDP) was higher (24.08 mm Hg) in Group 4 than in Groups 1 and 2 (20.71 and 19.73 mm Hg, respectively; p<0.05), but lower than in Group 3 (30.58 mm Hg, p<0.05). Myocyte size (hypertrophy) was increased in Group 4 compared to Group 2 (116.91 μ^2 vs. 101.70 μ^2, p=0.02), equivalent to Group 1 (104.58 μ^2, p=0.06), and decreased compared to Group 3 (133.68 μ^2, p=0.01). Left ventricular free-wall sum/sample collagen content was lower in Group 4 than in Group 3 (61% vs. 71%, p<0.05), but comparable to Groups 1 and 2 (61% and 61%, respectively; p=0.87 and p=0.88). Fractional shortening (FS) was higher in Group 4 than in Group 3 (30.26% vs. 22.07%, p<0.05), but comparable to Groups 1 and 2 (33.83% and 31.71%, respectively; p<0.05 and p=0.67). Vascular density and mean aortic pressure were similar among all groups.
Conclusions: These findings suggest GSHme has a sustained cardioprotective effect in a rat IR model manifest as lower EDP, preserved myocyte size, decreased collagen scar formation, and higher FS. Future studies may determine a clinical role for this compound in common IR syndromes.

1117-206 **Cardioprotective Effect of KP-102, a Synthetic Growth Hormone-Releasing Peptide, in Ischemia-Reperfusion Injury**

Tadashi Ohyama, Sadayoshi Furuta, Toshimitsu Hori, Haruyoshi Ueo, Noriko Shiraishi, Masahiro Amakawa, Takahiko Murata, Kaken pharmaceutical Co., Ltd., Kyoto, Japan

Background: KP-102 (GHRP-2: pralmorelin) is a synthetic growth hormone (GH)-releasing peptide that not only induces GH release but also exerts a variety of cardiovascular effects. The aim of the present study was to determine the direct protective effects of KP-102 on cardiomyocytes and the effects of acute treatment following myocardial infarction in dogs.
Methods and Results: 1) Ischemia/hypoxia-induced injury to rat cardiomyocytes was elicited by incubating the cells for 4 h in an ischemia buffer under hypoxic conditions. Cardiomyocyte apoptosis and death were then respectively evaluated using the TUNEL method and by visual assessment of detached cells. Treatment with KP-102 (0.1 -10 μM) after induction of ischemia/hypoxia reduced the number of apoptotic and detached cells in a concentration-dependent manner by exerting a direct, GH-independent cardioprotective effect. 2) Myocardial infarction was induced in dogs by occluding the left anterior descending coronary artery (LAD) for 90 min; this was followed by 3 h of reperfusion. Intravenous administration of KP-102 (1 μg/kg + 0.1 μg/kg/min) was begun 50 min after LAD occlusion and continued to the end of the experiment. Collateral blood flow to the ischemic region was measured 30 min after occlusion using colored microspheres.

Infarct size was determined by TTC staining and was expressed as a percent of the area at risk based on collateral blood flow of <0.03 mL/min/g. Treatment with KP-102 significantly reduced infarct size, as compared to saline-treated controls (38.7±4.6 %, n=7 versus 55.2±4.0 %, n=7, p<0.05). Plasma troponin T levels, which served as an index of myocardial injury and were measured after 60 min of reperfusion, were also significantly reduced in KP-102-treated dogs (0.93±0.27 ng/mL versus 1.59±0.20 ng/mL, p<0.05).
Conclusions: KP-102 protects against ischemia-induced cardiomyocyte injury via a GH-independent mechanism. It also reduces infarct size when administered following ischemia in a canine model of acute myocardial infarction. These findings suggest that KP-102 could be beneficial in the management of ischemic cardiovascular disease, including acute myocardial infarction.

1117-207 Brief Renal Ischemia Applied Before Coronary Reperfusion (Remote Postconditioning) Protects Against Myocardial Reperfusion Injury via Adenosine Receptors

Faraz Kerendi, Hajime Kin, Michael E. Halkos, Rong Jiang, Zhi-Qing Zhao, Robert A. Guyton, Jakob Vinten-Johansen, Emory University School of Medicine, Atlanta, GA

Objectives: A series of brief coronary artery reperfusions and reocclusions applied during the early minutes of coronary reflow (myocardial "postconditioning") attenuates reperfusion injury. Using a model of infarct-inducing coronary artery occlusion-reperfusion, this study tested the hypothesis that a single 5 minute episode of renal artery (RA) occlusion and reperfusion applied immediately before the onset of *coronary reperfusion* ("remote postconditioning", or RPC) would be cardioprotective by mechanisms involving adenosine receptor activation.
Methods: Anesthetized rats undergoing 30 min of left coronary artery occlusion and 3 hours of reperfusion were randomized to: 1) CON (control, no RA occlusion); 2) RPC (RA was occluded for 5 min and released 1 min *before* coronary reperfusion); 3) Permanent RA occlusion (RA was permanently occluded 5 min before coronary reperfusion); 4) Delayed RPC (RA was occluded for 5 min, but its release was delayed until 1 min *after* coronary reperfusion); 5) CON+SPT (same as CON, but received 10 mg/kg IV of the adenosine receptor antagonist 8-sulfophenyltheophylline [SPT] 5 min before coronary reperfusion); and 6) RPC+SPT (same as RPC, but received 10 mg/kg IV SPT 5 min before coronary reperfusion). **Results:** Infarct size (percentage necrosis/area at risk, expressed as mean ± SEM) was reduced by 50% in RPC (25 ± 4%) compared to CON (49 ± 4%, p=0.003), consistent with reductions in plasma CK activity (44 ± 5 vs. 67 ± 6 U/ml, p=0.023). In contrast, permanent RA occlusion failed to reduce infarct size (47 ± 5%). Delaying the release of the RA in delayed RPC abrogated the protective effect of RPC (48 ± 6%). SPT alone had no effect on infarct size (47 ± 4% in CON+SPT vs. 49 ± 4% in CON); however, RPC+SPT reversed the protective benefit of RPC (50 ± 3% in RPC+SPT vs. 25 ± 4% in RPC).
Conclusions: Remote renal postconditioning applied immediately before the onset of coronary reperfusion provides potent cardioprotection likely exerted during the first minutes of coronary reperfusion. This phenomenon is likely mediated by adenosine receptor activation as the protective benefit is inhibited by the simultaneous administration of a non-selective adenosine receptor inhibitor.

1117-208 Mixed L-amino Acids Provide Cardioprotection Mediated By Translational And Transcriptional Regulation Of De Novo Protein Synthesis

Carol Chen-Scarabelli, Zuhair Allebban, Ruggero Ama', Howard Rosman, Louis Saravolatz, Julius Gardin, Tiziano Scarabelli, VA Ann Arbor/University of Michigan, Ann Arbor, MI, St John Hospital/Wayne State University, Detroit, MI

Background: We previously showed that long-term oral supplementation with mixed L-amino acids (AA) attenuates the extent of ischemia(I)/reperfusion(R) injury in the rat heart (Am J Cardiol. 2004;93(8A):35A-40A). Aims of this study were a) to determine whether a single dose of L-AA protects the rat heart against I/R; b) to investigate the mechanisms of this hypothesized cardioprotection; and c) to address whether it is mediated by transcriptional and/or translational effects.
Methods and Results: Isolated rat hearts were randomly divided into 5 groups (n=8): Control: perfused for 60 mins; I/R control: exposed to 35 mins I and 120 mins R; treated group: given a single oral dose (1g/Kg) of 11, mainly essential, mixed AA, and exposed, after 6 hours, to IRI; actinomycin D (ActD) and cycloheximide (Chx) groups: pretreated with ActD (1.5 mg/kg, i.p.), inhibiting transcription (DNA→mRNA), or Chx (1 mg/kg, i.p.), inhibiting translation (mRNA→protein), 1 hour prior to AA supplementation, and exposed to IRI. AA reduced infarct size and release of creatine kinase, promoting postischemic recovery of cardiac function; lessened myocyte apoptosis, processing of caspase-9, although not caspase-8, and reduced mitochondrial leakage of cytochrome c (all p<0.05). AA also enhanced ATP content and rate of ATP production in isolated mitochondria, increased O_2 consumption rate in myocardial skinned bundles, and elevated ratio of Bcl-2 to Bax (all p<0.05). These effects were reduced by pretreatment with both Chx (~80%), and ActD (~60%). Although differences in dry/wet weight ratios between hearts from different groups were not significant, AA induced an increase in myocardial protein content (5930±76 ug/g vs 4732±175 ug/g), which was averted by pretreatment with both Chx and ActD (all p<0.05).
Conclusions: AA reduced postischemic cardiac cell loss, with recovery of cardiac function, and preservation of mitochondrial production of high-energy phosphates. These effects are largely dependent upon protein synthesis, regulated at both transcriptional and translational level. However, since cardioprotection was not fully abolished by blocking protein synthesis, direct effects of one or more AA cannot be ruled out.

POSTER SESSION

1118 Adjunct Pharmacology and Therapy in Patients With Acute Ischemic Syndrome

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1118-215 Enoxaparin is Consistently More Effective Than Unfractionated Heparin Across the Spectrum of Risk in Non-ST Elevation Acute Coronary Syndrome Patients: Insights from the INTERACT Trial

Andrew T. Yan, Raymond T. Yan, Mary Tan, Paul W. Armstrong, Christopher B. Granger, Omar Dabbous, Keith A.A. Fox, Kim A. Eagle, Thao Huynh, David H. Fitchett, Anatoly Langer, Shaun G. Goodman, St. Michael's Hospital, Toronto, ON, Canada, Canadian Heart Research Centre, Toronto, ON, Canada

Background: The Global Registry of Acute Coronary Events (GRACE) risk score accurately predicts in-hospital mortality across the broad spectrum of acute coronary syndromes (ACS).
Objective: To determine whether GRACE risk score predicts recurrent ischemia and different treatment response in ACS.
Methods: In INTERACT, 746 ACS patients receiving aspirin and eptifibatide were randomized to enoxaparin or unfractionated heparin (UH). Holter (48-hour) monitoring was analyzed by an automated algorithm and reviewed by a blinded cardiologist. Events at 30 days were centrally adjudicated in a blinded fashion. We examined the prevalence of Holter-ischemia (HI) and enoxaparin effect among patients stratified by the median GRACE risk score.
Results: The median GRACE score was 117 (range 53 to 233); HI was detected in 19.3% of patients. The GRACE score was positively correlated with HI and death/MI (both P<0.001).

	GRACE Score		Adjusted Odds Ratio (95% CI)	P value
	≤median N=358	>median N=353		
HI	12.6%	26.2%	2.63 (1.75-3.96)	<0.001
Death/MI (30d)	4.5%	9.9%	2.37 (1.28-4.39)	0.006
Major bleeding (30d)	5.1%	7.4%	1.24 (0.69-2.24)	0.47

The beneficial effects of enoxaparin were uniform on HI (pooled OR=0.43, 95% CI 0.29-0.64, P<0.001) and on death/MI (pooled OR=0.49, 95% CI 0.27-0.90, P=0.02) across the high and low-risk subgroups (P for heterogeneity =0.53 and 0.16, respectively).
Conclusions: The GRACE risk score identifies ACS patients at increased risk for early recurrent ischemia detected by Holter monitoring, and death/MI at 30 days. When combined with eptifibatide, enoxaparin is consistently more effective than UH regardless of baseline risk and thus the greatest absolute treatment benefit is seen in higher risk patients.

1118-216 Effects of Tirofiban Plus Clopidogrel Versus Clopidogrel Alone on Biomarkers of Myocardial Necrosis in Aggressively Treated Patients With Non-ST-Elevation Acute Coronary Syndromes Treated With Early Aggressive Approach: Results of the CLOpidogrel, Upstream TIrofiban, in Cath Lab Downstream Abciximab (CLOTILDA) Study

ALESSANDRO POLITI, Mario Leoncini, Anna Toso, Francesco Bellandi, Mauro Maioli, Fabio Frascarelli, Stefano De Servi, Roberto Piero Dabizzi, S.Anna Hospital, Como, Italy, Misericordia e Dolce Hospital, Prato, Italy

Objectives. In non-ST-elevation (NSTE) acute coronary syndromes (ACS) patients undergoing early invasive strategy (coronary angiography within 48 hrs) and pre-treated with aspirin, heparin, and clopidogrel, we evaluated whether the adjunctive treatment with upstream tirofiban significantly reduced the peak levels of troponin (cTn) I and creatine kinase (CK) - MB fraction.
Background. In NSTE-ACS a strong correlation has been found between adverse clinical events and peak values of myocardial necrosis markers.
Methods. A total of 250 patients were randomized to receive (group 1; n =128) or not (group 2; n = 122) tirofiban administered "upstream". Serial blood samples were collected before and after coronary angiography or pecutaneous coronary intervention (PCI) if performed.
Results. Between the 2 groups no differences in clinical and angiographic findings were observed. PCI was globally performed in 163 patients (86 of group 1 and 77 of group 2). Twenty (26%) out of 77 group 2 patients undergoing PCI received abciximab just prior to PCI because of high-risk clinical and angiographic characteristics. Mean cTn I and CK-MB values at admission, 6, 12, 24 hrs thereafter, peak values before coronary angiography, and peak values of index event were not significant different between the 2 groups. Major bleeding rate was 2.3% in group 1 and 1% in group 2 (p = ns). Composite incidence of death, myocardial infarction or re-hospitalization for ACS at 30-day was 10% in both groups.
Conclusions. In NSTE-ACS patients undergoing early invasive strategy, the adjunctive administration of upstream tirofiban did not reduce the peak values of cTn I and CK-MB compared to a regimen including aspirin, heparin, and clopidogrel given on admission and associated with a selective use of abciximab just prior to PCI in high risk patients.

1118-217 Celecoxib Reduces Angina Episodes and Inflammatory Markers in Refractory Unstable Angina by Down-Regulating Monocyte COX-2 Expression

Donatella Lomaglio, Luigi M. Biasucci, Giovanna Liuzzo, Matteo Santamaria, Giovanna Di Giannuario, Valeria Colafrancesco, Julia Mela, Michela Narducci, Maddalena Piro, Filippo Crea, Attilio Maseri, Institute of Cardiology-Catholic University of the Sacred Heart, Rome, Italy

Background. Treatment of refractory unstable angina (RUA) in patients (pts) not suitable for revascularization is a clinical challenge. In this setting COX-2 inhibition may provide profound anti-inflammatory activity without interfering with ASA antiplatelet effects. Accordingly, we sought to assess whether celecoxib (C) may reduce angina episodes and inflammation in patients with untreatable RUA.
Methods: Nine pts (age 71±8; 7 males) with RUA not suitable for revascularization were treatred with C 800 mg/d for 1 week. In all pts number of ischemic episodes before and after treatment and CCS classes were recorded. Pts were followed for 3 months. Before C and after 1 week, 1 and 3 months, CRP levels, interleukin (IL)-6 production after Lypopolysaccaride (LPS) stimulation and monocyte COX-2 expression by Western Blot (WB) assay were assessed in order to evaluate the anti-inflammatory effect of treatment.
Results. All 9 pts were in CCS IV class at entry, with a mean of 3.1 daily ischemic episodes: all but 2 had a subjective improvement at one week that was still present at 3 months in 5 pts (CCS class II, mean number of ischemic episodes 0.4±0.2), 1 pts died 2 months after the end of treatment, 3 had no improvement. None of the pts had myocardial infarction, episodes of heart failure or hematological abnormalities during treatment. CRP decreased rapidly and markedly during the first week (from a median level of 10.9 mg/L at admission to 4.6 at 48 hours, and 3.1 at 1 week) persisting low in pts with symptomatic improvement at 3 months. IL-6 production after LPS significantly decreased at 48 hours, remaining significantly reduced at 1 week, and 3 months (4053 pg/mL at admission, 1805 at 48 hours, 1305 at 1 week, 1328 at 3 months respectively; p<0.05). In pts with reduction of symptoms and of inflammatory markers after C, monocyte COX-2 expression by WB was intense at baseline but was markedly reduced at 48 hours, 1 week and 3 months.
Conclusions. One week of treatment with the selective COX-2 inhibitor C is safe and effective in improving symptoms in RUA. The clinical effects are persistent in the majority of pts and are associated with suppression of monocyte COX-2 expression and reduction in CRP levels, IL-6 production after LPS.

1118-218 Consistent Therapy With Enoxaparin Is Superior to Unfractionated Heparin in SYNERGY

Kenneth W. Mahaffey, Robert M. Califf, Marc Cohen, Karen S. Pieper, Harvey D. White, Louise Traylor, James J. Ferguson, for the SYNERGY Trial Investigators, Duke Clinical Research Institute, Durham, NC

Background: Of patients in the SYNERGY trial, 75% were on antithrombin therapy prior to enrollment, 12% assigned enoxaparin were treated with unfractionated heparin (UFH), and 4% assigned UFH received enoxaparin post-randomization ("crossovers").
Methods: To explore the potential impact of switching therapy, a prespecified analysis was planned to analyze the rates of death or nonfatal myocardial infarction (MI) at 30 days and the incidence of bleeding among patients that received consistent therapy (defined as no prerandomization therapy, prerandomization therapy same as assigned therapy, and no crossovers). Censored and time-dependent covariate analyses were performed to adjust for potential confounders.

Results: Of the 9978 patients in SYNERGY, 5637 (56.5%) received consistent therapy. Outcomes in the overall trial and in the consistent therapy group with and without modeling are shown. The results were similar after adjustment for baseline demographics (death/MI hazard ratio [HR] of 0.86 [95% confidence interval {CI}, 0.75-0.99; p=0.032] and TIMI major bleeding HR of 1.17 [95% CI, 0.97-1.42; p=0.1]) and using the time-dependent covariate techniques (death/MI HR of 0.93 [95% CI, 0.84-1.03]).
Conclusions: In patients in SYNERGY treated with consistent therapy, a significant reduction in death or nonfatal MI with enoxaparin was observed with no excess of bleeding with and without modeling. These data suggest that consistent use of enoxaparin is superior to UFH in acute coronary syndromes.

	30-Day Death / MI (%)Enoxaparin vs UFH	Death / MI HR and 95% CI	TIMI Major Bleeding (%)Enoxaparin vs UFH
Overall	14.0 vs 14.5	0.96 (0.86-1.06)	9.1 vs 7.6 (p=0.008)
Consistent Therapy	12.8 vs 15.6	0.81 (0.70-0.93)	8.1 vs 7.5 (p=0.374)
Adjusted - Censored Analysis	8.4 vs 8.5	0.82 (0.71-0.93)	5.1 vs 4.1 (p=0.378)

1118-219 Effect Of Dual Antiplatelet Therapy On Platelet Activation In Patients With Acute Coronary Syndromes In The Presence Of Elevated Crp And Soluble Cd 40 Ligand.

Manolis Vavuranakis, Dimitris Aggelis, Sophia Vaina, Maria Drakopoulou, Konstantinos Toutouzas, Irini Bosinakou, Theodoros Papaioannou, John Mitropoulos, Christodoulos Stefanadis, Hippokration Hospital, Athens, Greece

In patients (pts) with unstable angina and acute myocardial infarction without ST elevation (ACS), an increase risk for adverse outcome has been observed if high sensitivity C-reactive protein (hs-CRP) and serum soluble CD 40 Ligand (sCD-40L) are elevated. Platelet activation, as reflected by soluble p-selectin(s-PS) has been used in clinical trials for the in vivo evaluation of platelet activity in patients with ACS. Aspirin is an effective therapy for ACS but the addition of clopidogrel, further improves clinical outcome. However, s-PS a marker of platelet activation has not been predictably altered.
Aims: We evaluated the effect of clopidogrel on s-PS in association with hs-CRP and sCD-40 L levels.
Methods: From 86 consecutive pts who were admitted for ACS, 43 pts (mean age 70±4 years, 36 males, 7 females) were randomized to receive aspirin (325 mg, daily) and clopidogrel (300 mg loading dose followed by 75 mg daily) (group: Asp+Clop), and 43 pts (mean age 67±6 years, 34 males, 9 females) to receive aspirin (group: Asp), additionally to usual medical therapy. Blood samples were collected at 0, 8, 48 hours and on day 6. hs-CRP, s-PS and sCD-40 L were determined by immunoturbidimetric assay and ELISA as appropriate.
Results: Pts on Asp+Clop compared to pts on Asp alone had at baseline similar clinical characteristics. Overall, s-PS levels were similar among the two groups at 0, 8 and 48 hours and at day 6 (Asp+clop vs Asp: 55.6±23 vs 53.75±22.9 ng/ml p=0.4, 52.41±16 vs 54.14±20 ng/ml p=0.5, 50.17±13.7 vs 60.8±37.9 ng/ml p=0.1, 50.53±17.5 vs 54.64±18.97 ng/ml p=0.4). However, pts with levels of sCD-40 L > 5.0 μg/dl who also belonged to the highest CRP quartile (CRP >2.26 mg/l) had a significant increase in s-PS at 8 hours, if they received Asp only (53±12 to 68.41±21 ng/ml, p=0.043), and levels of s-Ps were greater than in pts on Clop+Asp (Clop+Asp vs Asp: 47.6±14 vs 68.41±21 ng/ml, p=0.01). This difference was not maintained at 48 hours and 6 days.
Conclusions: In pts with ACS and high hs-CRP and sCD-40 L, treatment with Asp+Clop is better than Asp alone in prohibiting early P-selectin elevation. This could be related to the greater intensity of platelet activation in these pts.

1118-220 Impact of Glycoprotein IIb/IIIa Inhibitors in Patients With Acute Coronary Syndromes Without ST-Elevation in the "Real World"

Pedro Monteiro, on behalf of the Portuguese Registry for Acute Coronary Syndromes investigators, Coimbra University Hospital, Coimbra, Portugal

Background: Glycoprotein IIb/IIIa inhibitors (GPI) are a major advance in the treatment of acute coronary syndromes (ACS) without ST-elevation. However, their real impact in an unselected population of ACS patients (pts) is still poorly documented.
Aim: To evaluate, in pts admitted with ACS without ST-elevation, the impact of GPI therapy in the in-hospital clinical outcome.
Population and Methods: Retrospective analysis of a nationwide database with data from 7067 pts, admitted for ACS in CCU´s or Cardiology wards since 2002; 3871 pts were found to be admitted for ACS without ST-elevation EMI and had data regarding in-hospital therapy. This subpopulation was divided in two groups, as they had (Group A: n=1252) or had not (Group B: n=2619) received GPI. Groups were analyzed regarding demographic, epidemiological and clinical data (see table).
Results: Pts treated with GPI had a higher risk profile, with a higher incidence of previous revascularization and a more adverse coronary anatomy (left main and/or 3-vessel disease - 24% *versus* 14%; p<0.05). Although GPI-treated pts had a worse clinical profile and a higher incidence of non-ST elevation AMI (NSTEMI) (71% *versus* 59%; p<0.05), they had a lower in-hospital mortality (3% *versus* 5%; p=0.03) - see table. A multivariate analysis showed that this was mainly due to a lower incidence of LV dysfunction (p=0.029).
Conclusions: Even in an unselected ACS without ST elevation patient population, the use of GPI is associated with better in-hospital mortality.

Table I - Results

Groups/Parameters	Group A (GPI)	Group B (without GPI)	p
Male Gender	71%	65%	<0.05
Hypercholesterolemia	51%	43%	<0.05
Smoking habits	26%	17%	<0.05
Previous PCI	10%	8%	<0.05
NSTEMI	71%	59%	<0.05
Unstable angina	29%	41%	<0.05
Left main and/or 3-vessel disease	24%	14%	<0.05
In-hospital Mortality	3%	5%	0.03

1118-221 Treatment With the Selective Serotonin Reuptake Inhibitor Sertraline in the Early Phase of Acute Coronary Syndromes: A Double-Blind, Placebo-Controlled, Pilot Study

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Background: Selective serotonin re-uptake inhibitors (SSRIs) can improve outcome of pts with coronary artery disease and depression, but it remains unknown if they can be given in acute coronary syndromes (ACS). We planned a pilot randomized study to verify the effects and safety of the early administration of sertraline, a SSRIs, in patients with ACS and depression.
Methods: We studied 20 pts who arrived to our ED because of acute chest pain and were found to have ACS and depressive symptoms. Depression was assessed using the 21-item self-report Beck Depression Inventory (BDI) and was defined as a score≥10. Within 6 hrs from arrival, pts were randomly assigned to a double-blind treatment with 50 mg b.i.d. of sertraline (n=10) or placebo (n=10). All pts had clinical and biochemical evaluation, echocardiography and coronary angiography within 48 hrs from admission to ED. In-hospital major adverse cardiac events and pre-discharge BDI scores were recorded in all pts.
Results: At entry, there were no differences between the two groups in age, sex, smoking (50% vs 60%, NS), diabetes (30% vs 20%, NS), hypertension (40% vs 30%, NS), and previous MI (20% vs 10%, NS). The two groups had similar BDI scores (13±5 vs 14±6, NS). Also, pts exhibited similar TIMI risk score (5±3 vs 4±2), peak CK-MB (125±35 vs

139±80 ng/ml, NS), peak Troponin I (20±11 vs 25±15 ng/ml, NS), LV ejection fraction (53±15% vs 50±17%, NS), and number of diseased vessels at coronary angiography (1.4±0.8 vs 1.6±0.7, NS). During hospital stay, no deaths occurred and recurrence of myocardial ischemia was seen in 1 patient on sertraline but in 4 pts on placebo. No differences in the frequency of arrhythmia or in QTc interval were detected between the two groups. At time of discharge, BDI score was significantly lower in sertraline-group than in the placebo-group (6±5 vs 13±4, p<0.05). Notewhorthy, a BDI score<10 was seen in 6/10 pts on sertraline and in 1/10 pts on placebo (p<0.05).
Conclusion: Early treatment with sertraline in this pilot study was safe and effective for treating depressive symptoms in pts with ACS and was associated with a better in-hospital outcome. A multicenter randomized study is now ongoing and complete results will be available by 2005.

1118-222 **Blood Transfusions in Patients Admitted With Non-ST-Segment Elevation Acute Coronary Syndromes: Results From CRUSADE**

Eric D. Peterson, Anita Y. Chen, Xin Yang, Matthew T. Roe, Sunil V. Rao, Ralph G. Brindis, W. Brian Gibler, E. Magnus Ohman, Duke Clinical Research Institute, Durham, NC

Background: The management of non-ST-segment elevation acute coronary syndromes (NSTE ACS) now includes more aggressive antithrombotic therapies and interventional procedures. Meanwhile, the NSTE ACS patient population has grown older with more comorbidities. The degree to which these factors have affected the need for blood transfusions has not been well studied in community practice.
Methods: We examined 74,271 patients with NSTE ACS (positive cardiac markers and/or ischemic ST-segment changes) admitted to 430 U.S. hospitals participating in the CRUSADE quality improvement initiative from 2002-2003. Bypass surgery-related bleeding was excluded. We identified the percentage of patients requiring one or more in-hospital red blood cell transfusions as well as the multivariable baseline patient predictors of transfusion. Variation in transfusion rate among hospitals was also analyzed.
Results: The overall in-hospital blood transfusion rate was 9.4%. The top five patient predictors of blood transfusion included the following: renal insufficiency (odds ratio [OR] of 2.35 [95% confidence interval {CI}, 2.21-2.50]), systolic blood pressure (per 10 mmHg drop) (OR of 1.08 [95% CI, 1.06-1.09]), female gender (OR of 1.49 [95% CI, 1.41-1.59]), diabetes mellitus (OR of 1.40 [95% CI, 1.33-1.48]), and age above 75 (vs below 55) (OR of 2.82 [95% CI, 2.48-3.20]). There was a concurrent rise in transfusion rate with increasing number of antiplatelet and anticoagulant agents used in combination among those above age 75. This was not observed among those below age 55. There was >3-fold variation in transfusion rate among participating hospitals.
Conclusion: Blood transfusion is often required in contemporary NSTE ACS management. Patient factors associated with antithrombotic drug distribution and clearance are highly associated with transfusion risks and emphasize the need for individualized dosing to improve the safety of ACS care. Furthermore, wide inter-hospital variability in transfusion emphasizes the need for more studies to quantify the risk and benefit of transfusion in the management of NSTE ACS.

POSTER SESSION

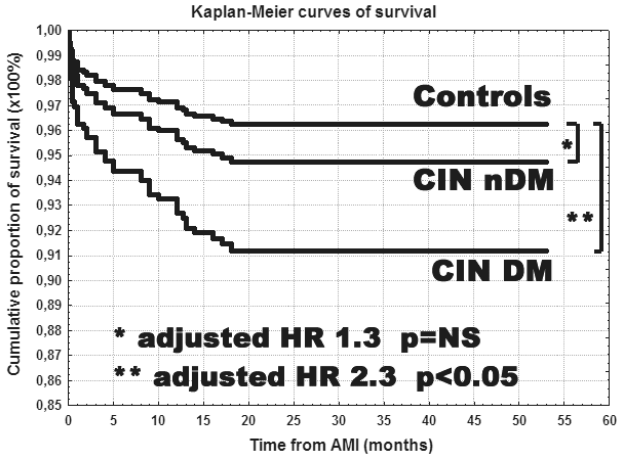
1119 Risk, Complications, and Outcomes Following Acute Myocardial Infarction

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1119-195 **The Impact of Contrast-Induced Nephropathy on Survival Rate in Patients after Acute Myocardial Infarction**

Jacek Kowalczyk, Radoslaw Lenarczyk, Zbigniew Kalarus, Janusz Prokopczuk, Grzegorz Honisz, Teresa Zielinska, Joanna Stabryla-Deska, Patrycja Pruszkowska-Skrzep, Oskar Kowalski, Agata Musialik-Lydka, Mariusz Gasior, Lech Polonski, Medical University of Silesia, Zabrze, Poland, Silesian Centre for Heart Diseases, Zabrze, Poland

Renal insufficiency is associated with poor prognosis in patients (pts) with coronary heart disease.
Aim: to determine impact of contrast-induced nephropathy (CIN) on long-term outcome in pts with acute myocardial infarction (AMI), who underwent coronary angioplasty (PCI).
Methods: CIN was defined by serum creatinine level < 133 µmol/l on admission and its 25% increase, with value > 133 µmol/l within 24 hours after PCI. One-center analysis of 1027 consecutive AMI pts who underwent PCI was performed. 89.8% of them had proper renal function (controls, n=922) and 5.9% had CIN (n=61). CIN group was divided into diabetic (CIN DM, n=28) and non-diabetic pts (CIN nDM, n=33). Cumulative survival during mean 26.4 months follow-up was compared using log-rank, independent predictors of death selected with multivariate Cox regression model.
Results: Remote survival in CIN pts was lower than in controls (68.4% vs 90.0%, p<0.001). CIN pts were older, more often diabetic, hypertensive, with lower EF and greater prevalence of cardiogenic shock (all p<0.05). When incorporating the significant parameters into multivariate analysis, CIN was shown to be still an independent predictor for any-cause death only among CIN DM pts. Adjusted hazard ratio (HR) for death in CIN DM vs controls was 2.35 (CI: 1.95-2.75, p<0.05), in CIN and CIN nDM vs controls HR was not significant.



Conclusion: CIN in diabetic pts significantly and independently influences survival in AMI pts treated with PCI and is associated with increase of death hazard.

1119-196 **Excellent Clinical Outcomes in High Risk Non-Shock Acute Myocardial Infarction Patients Treated in the Contemporary Mechanical Reperfusion Era: A Pooled Analysis of 4 Clinical Trials**

William W. O'Neill, Simon R. Dixon, Gregg W. Stone, John J. Griffin, David A. Cox, John G. Webb, Roxana Mehran, Bruce R. Brodie, Jack L. Martin, Raymond J. Gibbons, John Held, Cindy L. Grines, William Beaumont Hospital, Royal Oak, MI, Columbia University, New York, NY

Background: Recent reports have suggested that the excellent clinical results observed in the CADILLAC trial was attributable to enrollment of low-risk patients. We therefore examined the early clinical outcomes in 1,122 high-risk non-shock acute myocardial infarction (AMI) patients enrolled in 4 contemporary mechanical reperfusion trials.

Methods: We performed a pooled analysis of the EMERALD, COOL-MI, ICE-IT and AMI-HOT randomized clinical trials. These studies were conducted from September 2001 to December 2003. All trials required electrocardiographic evidence of acute anterior or large infero-posterior myocardial infarction for enrollment. Patients with cardiogenic shock were excluded. In three trials, patients presented within 6-hours of symptom-onset; in AMIHOT patients were eligible for up to 24-hours from AMI onset. Clinical outcome was evaluated at 30-days.
Results: 1,122 patients were enrolled in the 4 trials (mean age 59 ± 12yrs; 77% male). Baseline demograhics included: diabetes 14%, hypertension 43%, and prior MI 28%. Almost all patients (99%) had a native vessel culprit. 43% patients had anterior wall infarction and 52% had multi-vessel coronary disease. Stenting was performed in 96% patients; 83% received a glycoprotein IIb/IIIa inhibitor. The mean infarct size at 30-days was 16% of the left ventricle. Following PCI, TIMI-3 flow was achieved in 92% of patients. At 30-days, the incidence of major adverse cardiac events was 4.5% (death 2.0%, myocardial infarction 1.5%, TVR 2.1% and stroke 0.8%).There was no significant difference in MACE rates between anterior and non-anterior patients (4.6% vs. 3.3%, p=NS).
Conclusion: In the current era, mechanical reperfusion is associated with excellent clinical results even in high risk non-shock AMI patients, with similar outcomes in anterior and non-anterior infarct patients.

1119-197 **Impact of Plaque Characteristics on Myocardial Tissue Reperfusion in Acute Myocardial Infarction.**

Shigeo Kawano, Hiroshi Ito, Katsuomi Iwakura, Atsunori Okamura, Toshiya Kurotobi, Motoo Date, Koichi Inoue, Yoshimune Hiramoto, Noriyuki Hanibuchi, Norihiro Hayashi, Takahiro Hashimoto, Hiroyuki Nagai, Masao Takeda, Kenshi Fujii, Sakurabashi Watanabe Hospital, Osaka, Japan

Background: Previous studies have demonstrated that the microvascular embolization of intracoronary thrombus and plaque components reduces the benefit of reperfusion therapy for AMI. However, it is unknown whether the plaque burden of culprit lesion impacts the microvascular embolization and the tissue reperfusion.
Methods: In 83 consecutive patients (pts) with AMI within 6 hours after symptom onset, we performed IVUS to evaluate the plaque characteristics after thrombectomy with RescueTM PT catheter. All pts underwent the subsequent angioplasty with or without stenting after IVUS assessment. Myocardial tissue reperfusion was assessed based on TIMI perfusion grade (TMPG)
Results: TIMI-3 flow was observed in 53 pts (64%) after thrombectomy alone and 65 pts (78%) after adjunctive angioplasty. There were 58 pts (70%) with TMPG-3 in final angiography. In a logistic regression model, RCA culprit was the strongest predictor of TMPG<=2. Large plaque area, presence of lipid-pool like image and angiographic collateral grade were independent predictors of poor tissue reperfusion (Table).
Conclusions: These results suggest that the PCI induced embolization of unstable plaque materials impacts on microvascular dysfunction. Intracoronary thrombus removal is not enough to prevent microvascular embolization and the evaluation of plaque characteristics by IVUS is promising to determine the indication of distal protection strategy to obtain tissue reperfusion in AMI.

	TMPG3	TMPG<=2	OR(95%CI)
RCA culprit, n(%)	14(24%)	15(60%)	10.7(1.04-110)
Plaque area, mm2	14.5±4.4	18.5±4.9	1.4(1.03-1.9)
Lipid pool like image, n(%)	9(16%)	6(24%)	9.6(1.2-79)
Collateral grade	0.9±0.9	0.6±0.6	0.17(0.04-0.74)

1119-198 Long-Term Prognostic Implications of Nonoptimal Primary Angioplasty for Acute Myocardial Infarction

Guido Parodi, Renato Valenti, Gentian Memisha, Nazario Carrabba, Angela Migliorini, Giovanni Maria Santoro, David Antoniucci, Careggi Hospital, Florence, Italy

Background: The long-term outcome of a non-optimal result of a primary percutaneous coronary intervention (PCI) for acute myocardial infarction (AMI) has not been investigated.
Methods and Results: An optimal PCI result was defined as TIMI flow grade 3 and residual stenosis < 20%, otherwise the procedure result was considered non-optimal. Long-term (51±21 months) clinical follow-up data were collected from 1,009 consecutive patients with AMI who underwent primary PCI.
Overall, an optimal primary PCI result was achieved in 958 patients (95%). Cardiogenic shock (OR 2.921, 95% CI 1.462-5.837; p=0.002) and age (OR 1.029, 95% CI 1.002-1.058; p=0.033) were independent predictors of non-optimal primary PCI result. Patients with a non-optimal PCI had a higher (3588±3716 U/L versus 2443±2143 U/L, p=0.002) and delayed (11±6 hours versus 7±4 hours, p=0.0001) peak creatine kinase values, as compared to patients with optimal PCI. At 5-year follow-up, patients with non-optimal PCI showed higher rate of all cause mortality (47% vs 19%; p<0.00001 by log-rank test) than those with an optimal mechanical reperfusion. Fifty-two percent of the deaths in the non-optimal PCI group occurred within the first month. Interestingly, after this period, estimated survival of 30-day alive patients was not significantly different to that of patients with an optimal PCI (p=0.06 by log-rank test). Moreover, at long-term follow-up, cumulative rates of nonfatal reinfarction, hospitalization for heart failure, and additional revascularization procedures were similar in the 2 groups (4% vs 5%, p=0.695; 4% vs 5%, p=921; and 22% vs 20%, p=0.816, respectively).
Conclusion: A non-optimal primary PCI result is an uncommon occurrence, but it represents a very serious event because of the high early mortality.
However, in patients surviving the early phase, long-term patient care should be the same of successfully reperfused AMI patients, since the incidence of clinical events is similar.

1119-199 Blood Loss After Primary Percutaneous Intervention Is Associated With Death and Major Adverse Cardiac Events in Acute Myocardial Infarction

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Background: Hemorrhagic complications are not infrequent after primary percutaneous coronary intervention (PCI) in acute myocardial infarction (AMI). The clinical impact of blood loss after primary PCI has not been studied.
Methods: Data was pooled from 4,357 patients undergoing primary PCI from 7 randomized trials from the PAMI and CADILLAC databases. The impact of decline in hematocrit (HCT) from baseline to nadir on clinical outcomes was examined..
Results: The absolute HCT drop from admission to nadir was >10% in 18.7% of pts, and was >15% in 4.7% of pts. Independent predictors of HCT drop included dialysis (odds ratio (OR) = 44, p<0.0001), final thrombus present (OR=3.0, p<0.0001), ejection fraction <50% (OR=2.2, p=0.0006), no stent (OR=2.2, p=0.0014), female gender (OR=2.0, p=0.03), and age >70 (OR=2.1, p=0.001). In-hospital major adverse cardiac events strongly correlated with the degree of blood loss (Table). By multivariate analysis, HCT drop was an independent predictive of mortality (OR=3.5, p=0.001), reinfarction (OR=7.8, p<0.0001), target vessel revascularization (OR=3.1, p=0.0009), and composite major adverse events (OR=4.1, p<0.0001).
Conclusions: Significant blood loss after primary PCI in AMI occurs in nearly one in five patients, and is strongly associated with adverse clinical events. Future studies are warranted to examine whether alternative routes of vascular access or anti-thrombotic agents can reduce blood loss after primary PCI to improve event-free survival.

Adverse Events are Increased with Increased Blood Loss

Event	≤ 10% HCT Drop	11-15% HCT Drop	≥15% HCT Drop	P value
Death	1.2%	3.3%	8.3%	<0.0001
Reinfarction	0.6%	1.7%	6.4%	<0.0001
Revascularization	1.7%	4.8%	5.9%	<0.0001
Disabling Stroke	0.08%	0.3%	1.0%	0.011
MACE (combined)	3.2%	8.1%	16.2%	<0.0001

1119-200 Higher Presentation Acuity and Medical Comorbidities Limit Utilization of Early Invasive Therapies in Acute Myocardial Infarction With Cardiogenic Shock, Decreasing Survival to Hospital Discharge

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Background: Although early invasive therapies are beneficial in myocardial infarction (MI) complicated by cardiogenic shock (CS), the interaction between clinical factors, selection for angiography and mortality is unclear. Current treatment patterns and predictors of early mortality in CS were investigated in a retrospective cohort analysis.
Methods: Data from 181 pts admitted for MI with CS over 54 months at 2 tertiary care centers, were compiled and analyzed via multivariate logistic regression. MI pts with CS, defined as sustained peri-infarct SBP<90 or MAP<60 mm Hg, were identified by DRG code and adjudicated by chart review.
Results: 56.9% of pts survived to hospital discharge. 84.0% pts underwent angiography, 37.6% pts received IABP support and 69.1% pts were revascularized (53.6% PCI, 15.5% CABG). Deferral of angiography, first SBP≤100, any SBP≤70 or DBP≤30 mm Hg and LVEF≤30% each independently predicted in-hospital mortality (Fig.1a). Prior CABG or CHF, earlier development of CS after admission and pressor use were linked with deferral of angiography (Fig. 1b). No interaction between age, DM and death was noted, irrespective of revascularization status.
Conclusions: Deferral of angiography was more likely in pts with earlier onset of hypotension, prior CABG, CHF or pressor needs, which in turn was strongly predictive of early mortality. This suggests that selection bias may limit utilization of life-saving therapies in the most critically ill pts, who have the most adverse prognosis overall.

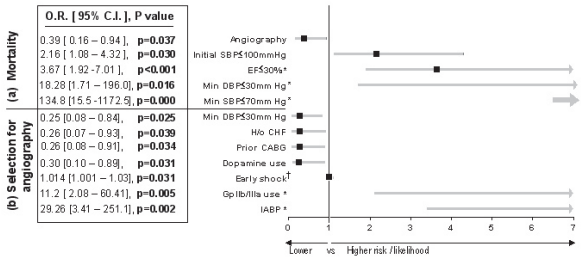

Figure1: (a) Risk of mortality and (b) Factors affecting selection for coronary angiography in patients with cardiogenic shock

* Odds ratio (OR) and/or limits of 95% CI exceeds 7.0 (denoted by arrow)
† Approx 1.4% increase in likelihood of angiography per hour elapsed from admission to onset of shock

1119-201 The Safety of Antithrombin Therapy in Non-ST-Segment Elevation Acute Coronary Syndromes Patients: Results From the CRUSADE Initiative

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Background: In the SYNERGY trial, the use of low molecular weight heparin (LMWH) was associated with a higher risk of bleeding than unfractionated heparin (UFH), particularly when treatment crossover occurred. The relative safety profiles of these antithrombin therapies have not been examined in routine clinical practice.
Methods: Using data from the CRUSADE Initiative, we compared treatment patterns in patients with high-risk non-ST-segment elevation acute coronary syndromes (NSTE ACS) receiving LMWH and UFH at 311 U.S. hospitals with full revascularization capabilities between January 2001 and December 2003. Eligible pts had positive cardiac markers and/or ischemic ST-segment changes. Unadjusted and adjusted in-hospital clinical outcomes were compared in pts treated with LMWH vs. UFH vs. LMWH and UFH.
Results: Of 38,601 pts, 38.4% received LMWH only, 54.4% received UFH only, and 7.3% received both within 24 h of admission. Clinical characteristics were similar among all pt groups. Transfusion rates were lowest in pts treated with LMWH only (Table). These results persisted after adjusting for clinical factors and revascularization.
Conclusions: High-risk NSTE ACS pts in routine clinical practice have lower rates of transfusion when treated with LMWH compared with UFH or both LMWH and UFH in the first 24 h. These results suggest that the safety profile of antithrombin therapies may be different in community practice than those seen in selected trial patients receiving protocol-driven regimens.

Transfusion and Treatment Rates by Antithrombin Use

	LMWH Only (n=14,817)	UFH Only (n=20,987)	LMWH and UFH (n=2,797)	Adjusted OR (95% CI)*
RBC Transfusion Rates				
All pts	13.8%	15.2%	17.0%	0.81 (0.76-0.87)
Non-CABG pts	7.1%	8.5%	8.7%	0.77 (0.70-0.84)
Concomitant Treatment Rates				
GP IIb/IIIa inhibitors	31.7%	45.1%	49.0%	n/a
Clopidogrel <24 h	41.7%	47.0%	52.7%	n/a
Cardiac cath	71.0%	81.0%	82.7%	n/a
PCI	36.8%	49.1%	51.2%	n/a
CABG	13.0%	13.7%	16.3%	n/a

* For LMWH alone versus UFH alone. CABG = coronary artery bypass grafting; GP = glycoprotein; cath = catheterization; PCI = percutaneous coronary intervention.

1119-202 **Approach to Post-Myocardial Infarction Ventricular Septal Defect: Conservative, Percutaneous Device Closure or Surgical Repair**

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Background: Ventricular septal rupture complicating acute myocardial infarction (MI) has extremely poor prognosis. Percutaneous Ventricular Septal Defect (VSD) device closure aims at improving the outcome in this subset of patients.
Methods: Between July 2000 to August 2004, 33 patients (pts) presented to us with acute MI complicated with ventricular septal rupture, mean age 64.18 ± 11.14 years (43-89 years).
Result: Of these 33 patients, 16 were managed conservatively (group A), 12 by percutaneous device closure (group B) and 8 by surgical closure (group C). Both surgical repair and percutaneous device closure was performed in 3 pts. Presentation was with anterior MI in 11 pts in group A, 8 pts in group B and 6 pts in group C. Gross pulmonary edema and or cardiogenic shock was present in 13 pts in group A, 10 pts in group B and 6 pts in group C. Angiographically triple vessel disease and double vessel disease was present in 6 and 4 pts in group A respectively, 4 and 5 pts in group B respectively and 3 and 1 pts in group C respectively . The mean VSD size was 12.9 ± 5.8 millimeters (mm) in group A, 12.3 ± 4.5 mm in group B and 11.7 ± 4.9 mm in group C respectively. The mean left ventricular ejection fraction was 35.3 ± 9.9% in group A, 35.8% ± 8.5% in group B and 35 ± 8.9% in group C. Percutaneous device closure was performed via right internal jugular vein using the Amplatzer VSD (9) or Atrial septal defect(3) closure devices, mean size 22.5 ±3.6 mm (18-30 mm). Mean duration of device implantation after MI was 8.9 ± 18.9 days and for surgical closure was 21.4 ± 12.3 days. Procedural success was achieved in 10 pts in group B and 5 pts in group C. In hospital mortality was 11 in group A, 7 in group B and 1 in group C. At a mean follow up of 2-44 months in 15 discharged pts, survival was 2 in group A, 4 in group B and 4 in group C. Follow up was lost in 2 pts in group A and 3 pts in group C.
Conclusion: Percutaneous device closure of post MI VSD is feasible and is a less invasive modality for treating this sick subset of patients. However a low survival was noted in this group as the patient selection was biased towards inclusion of more acutely sick patients.

1119-233 **Predictors of Death in Patients Treated by Facilitated Percutaneous Coronary Intervention for Acute Myocardial Infarction**

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Background: Facilitated PCI has become the treatment of choice for acute MI. However, the predictors of death after facilitated PCI still need to be investigated .
Objectives: We sought to determine the predictors of in-hospital death after facilitated PCI for acute MI in a large cohort of consecutive patients referred to the cath-lab of our institution.
Methods and results: From 1995 to 2004, a large cohort of > 2000 consecutive patients were referred to the cath-lab of our institution for acute MI. Among them, a total of 553 (28%) underwent facilitated PCI after prompt out-of-hospital management including the administration of thrombolysis and/or IIBIIIA inhibitors.

	In-hospital death N=43	Alive at discharge N=510	*P*
Males	70%	80%	0.16
Age, y-o	65±12	60±14	< 0.05
Diabetes	23%	14%	0.19
Shock on admission	70%	7%	< 0.0001
Pain to admission, minutes	331±202	255±188	< 0.05
Anterior MI	53%	46%	0.27
Initial TIMI-3 flow	19%	38%	< 0.01
Thrombus containing lesion	51%	39%	0.09
Direct stenting	37%	49%	0.07
Ejection fraction, %	39±17%	53±14	< 0.05
PCI success	65%	92%	< 0.01
Re-MI (early IRA reocclusion)	10%	1%	< 0.001
Peak CK, IU/L	3028±2378	2184±2037	< 0.05

By multivariate analysis, shock on admission (0.18, 95%CI [0.00-0.36]) and re-MI (0.41, 95%CI [0.20-0.63]) were independent predictors of death after facilitated PCI for AMI.
Conclusion: Patients who died after facilitated PCI for acute MI had less favourable clinical and angiographic characteristics (older pts with larger infarcts and late coronary re-opening). Shock on admission and early re-MI were independent predictors of death after facilitated PCI for acute MI.

1119-234 **Beneficial Effect of Reperfusion Therapy Beyond Preservation of Left Ventricular Function In Patients With Acute ST Elevation Myocardial Infarction: Support for the Open Artery Hypothesis**

Uwe Zeymer, Anselm Gitt, Ralf Zahn, Rudolf Schiele, Ralph Winkler, Martin Gottwik, Jochen Senges, Herzzentrum Ludwigshafen, Ludwigshafen, Germany

Background: Left ventricular ejection fraction (LVEF) is one of the most important predictors of mortality during follow-up in patients with acute ST elevation myocardial infarction (STEMI). While randomized clinical trials have shown a reduction of mortality by early reperfusion therapy, the effect of fibrinolysis and primary PCI on the preservation of left ventricular function was only modest. Therefore we sought to determine the impact of early reperfusion therapy on 1-year mortality in patients with STEMI and a comparable LVEF before discharge.
Methods: We used data from the prospective MITRA-PLUS registry containing nearly 10.000 patients with STEMI and 1-year follow-up. Results: From a total of 9934 patients 3103 were treated with primary PCI, 3856 with fibrinolysis and 2975 without early reperfusion therapy. The 1-year mortality related to LVEF and reperfusion therapy is given in table 1 and revealed significant differences between patients with and without early reperfusion therapy in the groups with the same LVEF. Reperfusion therapy remained an independent predictor of survival even after adjusting for confounding parameters such as age, gender, prior MI, diabetes, killip class, etc.
Conclusion: Early reperfusion therapy improves mid-term mortality compared to patients without reperfusion therapy despite similar LEVF at discharge. These results support the open-artery hypothesis which suggests a clinical benefit of reperfusion therapy for STEMI beyond preservation of LEVF.

1-Year mortality related to LVEF at discharge

	No reperfusion therapy	Fibrinolysis	Primary PCI	p-value
LVEF > 55%	8.4 %	2.8 %	2.2 %	< 0.0001
LVEF 41-55%	14.1 %	6.6 %	4.4 %	< 0.0001
LVEF < 40%	28.1 %	15.2 %	11.5 %	< 0.0001

POSTER SESSION

1120 Assessing Short- and Long-Term Outcomes After Acute Coronary Syndrome II

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1120-229 **Has the Impact of a Recurrent Acute Myocardial Infarction on Mortality Changed Within the Last Two Decades?**

Pernille Buch, Steen Abildstrom, Søren Rasmussen, Gunnar Gislason, Jeppe Rasmussen, Mette Madsen, Christian Torp-Pedersen, Bispebjerg University Hospital, Copenhagen, Denmark, National Institute of Public Health, Copenhagen, Denmark

Background: Recurrent acute myocardial infarction (re-AMI) has been shown to be a strong predictor of subsequent mortality in the past. But the impact of a re-AMI on prognosis in more recent years is unknown. We therefore analyzed trends in the mortality from a re-AMI during 1985-2002.
Methods: Patients aged 30 years or older with a first acute myocardial infarction (MI) were identified through the Danish National Patients Registry during 1985-2002. International Classification of Diseases was used to identify all re-AMI's within the first month after admission from a first AMI. Estimates of mortality were obtained from the Kaplan Meier method. A time dependent Cox regression model with adjustment for sex and age was used to compare relative risk (RR) of mortality from first re-AMI with patients without an event.
Results: A total of 167,260 patients had a first AMI and 5363 had a re-AMI. One year-mortality was 39% after admission for a first MI and 49% for patients with a re-AMI in 1985-1989. The respective percentages were 34% and 35% in 1990-1994, 29% and 25% in 1995-1999 and 25% and 18% in 2000-2002. A re-AMI carried a poor prognosis in 1985-1989, particularly in relation to the acute event. The RR of mortality declined throughout the period and was no longer of significance 60 days after a re-AMI in 2000-2002 (see Table).
Conclusion: The predictive power of a first re-AMI within 30 days of an infarction has weakened during the last 17 years. After 2 months the subsequent prognosis is as good as for patients without a re-AMI.

Relative risk of mortality within first year after a re-AMI during 1985-2002

	RR (95% CI) of mortality - days after re-AMI*		
Year	**0 - 7 days**	**8 - 60 days**	**61 - 365 days**
1985-1989	34.8 (30.3 - 40.0)	8.7 (7.5 - 10.0)	2.9 (2.4 - 3.5)
1990-1994	26.1 (22.7 - 30.0)	4.8 (4.1 - 5.6)	1.9 (1.6 - 2.3)
1995-1999	13.4 (11.1 - 16.1)	2.8 (2.3 - 3.4)	1.4 (1.2 - 1.7)
2000-2002	5.5 (4.2 - 7.1)	2.2 (1.8 - 2.6)	0.8 (0.6 - 1.0)

*Risks are calculated as lifetime since admission from a first re-AMI. Reference group is patients with a first AMI who did not suffer a re-AMI in the same period.

1120-230 **Prediction of Depressive Disorder Following Myocardial Infarction; Data From the Myocardial Infarction and Depression - Intervention Trial (MIND-IT)**

Joost P. Van Melle, Peter de Jonge, Astrid M. Kuyper, Adriaan Honig, Aart H. Schene, Harry J. Crijns, Maarten P. van den Berg, Johan Ormel, University Hospital Groningen, Groningen, The Netherlands

Background- Depression following myocardial infarction (MI) is associated with complicated cardiac rehabilitation, non-compliance and poor cardiovascular prognosis.

Whether depression following MI can be predicted from variables routinely assessed during hospitalization for MI is unknown.
Methods - Using data from the Myocardial INfarction and Depression - Intervention Trial (MIND-IT), we identified 2177 patients (mean age 63 years; 23% female) who were hospitalized for MI. Patients were randomly divided into a derivation and a validation sample. In the derivation sample, we analyzed, demographic, cardiac, and medical variables potentially associated with the development of post-MI depressive disorder, which were tested in the validation sample.
Results - In the year following MI, 199 patients (18.5%) suffered from depressive disorder according to ICD-10 criteria. In a multivariate model, the factors associated with depressive disorder were younger age (OR 1.94; CI 1.38-2.74), hypercholesterolemia (OR 1.68; CI 1.08-2.61), the use of calcium channel blockers at discharge (OR 1.80; CI 1.20-2.71), and especially left ventricular ejection fraction (LVEF) (OR 4.14 for patients with LVEF<30%; CI (2.42-7.10). The derived predictors were tested in the validation sample. The final model yielded two clinical predictors, i.e. younger age and LVEF<30%, which correctly predicted post discharge depression status in 82.9% of the MI patients. Of note, this model has a high negative predictive value (89%).
Conclusions - During hospitalization for MI and using common clinical variables, i.e. younger age and severe LV-dysfunction, it is possible to identify MI patients with a high risk for subsequent development of a depressive disorder.

1120-231 The Magnitude of ST-Segment Depression at Hospital Admission for a Non-ST Acute Coronary Syndrome Identifies the High-Risk Patients Among Those in Low-Risk Score Categories.

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Background: The prognostic value of the TIMI score has been well validated in non ST-elevation acute coronary syndromes. Although ST-segment shifts are incorporated in the score, their characteristics are not. This study looked at the prognostic value of the direction and magnitude of ST-shifts in perspective with TIMI scores in the PRISM-PLUS patients.
Methods: The pre-randomization 12-lead ECGs were all re-analyzed blindly by a cardiologist, excluding confounding ECGs with pacemaker activity, left ventricular hypertrophy, or left bundle branch block. Of 1299 patients, 806 (62.0%), 225 (17.3%) and 268 (20.6%) showed ST depression (STD), elevation (STE) and no deviation (noST) respectively. Among these patients, TIMI scores were ≤4 in 70.3% and > 4 in 29.6%.
Results: STD and STE were associated with a significantly higher 6-month rate of death/myocardial infarction (MI) with the highest rate of adverse events highest in patients with STD≥2 mm. This was most apparent at TIMI score ≤4; patients with higher (≥2 mm) STD had more events: 17.6% vs 8.5% with STD < 2 mm (p<0.001). Those with a combination of TIMI score>4 and STD ≥2 mm had an OR of 1.83 for 6-month death/MI (95% CI: 1.21-2.76, p=0.004). The c-index of this combination was 0.64 vs 0.61 and 0.59 for TIMI index alone and STD, respectively.
Conclusion: The magnitude of ST-segment depression confers additional prognostic information over the TIMI risk score; a 2 mm ST-segment depression helps identify high-risk individuals from lower-risk score groups.

Six-month death/MI rates (%)					
TIMI score	**NoST**	**STD**		**STE**	
		1 mm	**≥2 mm**	**1 mm**	**≥ 2 mm**
Any	6.3	11.8**	18.5**	4.9*	14.7*
1-4	5.2	9.8*	17.6**	3.4	12.7*
> 4	13.9	17.8	19.9**	8.3	19.0
P-values vs noST: * <0.05, ** <0.0001					

1120-232 Prognostic Importance of Post Procedural Systemic Blood Pressure Following Mechanical Reperfusion For Cardiogenic Shock Complicating Acute Myocardial Infarction

Hassan Kafri, Simon R. Dixon, Amr E. Abbas, James A. Goldstein, Judith A. Boura, William W. O'Neill, William Beaumont Hospital, Royal Oak, MI

Background: Despite the benefit of early mechanical revascularization in cardiogenic shock (CS) in-hospital mortality remains high. Predictors of survival after percutaneous coronary intervention (PCI) for CS have not been well defined.
Methods: From 1995-2002, 110 patients with CS due to left ventricular failure complicating acute myocardial infarction were admitted to William Beaumont Hospital and were selected to undergo early PCI. Reperfusion success was defined as restoration of TIMI-3 flow and < 50% diameter stenosis.Clinical variables were examined to identify predictors of survival after PCI.
Results: The overall in-hospital mortality was 46%. After PCI, 86% of patients had intra-aortic balloon pump (IABP), and 80 % of patients were on intravenous pressors. Revascularization success was achieved in 61/110 (56%) of cases. Patients who died after PCI were more likely to have multi-vessel disease, diabetes, a lower creatinine clearance (CrCl), a lower rate of successful reperfusion and a lower systolic BP (SBP) at the end of PCI. Infarct location, age, stent and use of IIb/IIIa inhibitors did not correlate with in hospital death. Independent clinical predictors of in-hospital death after PCI were: lower SBP (OR 0.84, CI 0.76-0.91, p<0.0001), and multi-vessel disease (OR10.3, CI 1.003-1.02, p=0.008).
Conclusion: Patients with refractory hypotension after mechanical reperfusion have a poor prognosis. New therapeutic strategies are required to improve outcome in this high risk group.

		Survivors N=59	Non-survivors N=51	P value
Pre-PCI (BP at shock onset)	SBP	79±10	76±11	0.23
	DBP	43±17	37±20	0.15
Post-PCI*	SBP	106±21	72±15	<0.0001
	DBP	64±15	42±11	<0.0001
	Augmented DBP	123±27	98±28	0.0001

*In 95 patients, post-PCI SBP and DBP were obtained while on IABP

Table 1: Mean systemic blood pressure before and after PCI

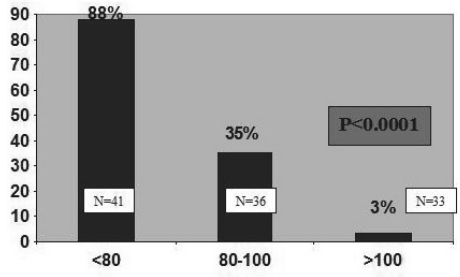

Figure 1: In-hospital mortality according to SBP end of PCI for cardiogenic shock (n=110)

1120-235 Long-Term Outcome of Patients Presenting With Acute Myocardial Infarction And Normal Coronary Arteries Is Just As Bad As Those With Advanced Coronary Artery Disease

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Background: Previous case series and small series reports have described situations in which patients have presented with acute myocardial infarction (AMI) but have normal coronary arteries by angiography. It has been proposed that their long-term clinical outcome is better than AMI patients with significant coronary artery disease (CAD), but this has not been well documented.

Methods: We identified 244 patients who presented to LDS Hospital with AMI (characteristic symptoms and troponin-I [TnI] ≥2.1 ng/ml) but with normal coronary arteries by angiography and compared their clinical presentation and long-term mortality to 3,376 AMI patients with advanced (>50%) angiographic CAD. The two groups were compared with respect to their clinical presentation, demographics, and long-term survival at 3-years follow-up.
Results: AMI patients with normal coronary arteries were younger (54±17 years versus 64±13 years [p<0.001]) and more likely to be female (42% versus 70% [p<0.001]) than those with advanced CAD and had lower peak levels of TnI (53 ng/ml versus 131 ng/ml [p<0.001]). They were also less likely to have hypertension (40% versus 60% [p<0.001], hyperlipidemia (22% versus 57% [p<0.001] and diabetes (13% versus 23% [p<0.001]). Long-term survival did not significantly differ between the two groups (death: 10.9% vs. 15.3% [p=0.06] for normal vs. CAD patients, respectively). When new non-fatal AMI events were also considered in a long-term combined endpoint of death/new AMI, outcomes did differ (25.0% vs. 39.9% [p<0.001]).
Conclusion: Patients presenting with AMI with normal coronary arteries are more often younger women and without traditional CAD risk factors. However, their long-term survival is not significantly different than those with advanced CAD. Whether this similar risk relates to the presence of angiographically silent CAD or other undetermined factors requires further study. In any event, these patients should not be dismissed as being at low future cardiovascular risk.

1120-236 Practice Variations in Treatments and Outcomes of Acute Myocardial Infarction From 1995 to 2000. The PRIAMHO Registries

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Background: To analyse practice variations and their incidence in outcome in patients with acute myocardial infarction (AMI) included in the PRIAMHO I and II Registries, performed in years 1995 and 2000.
Methods: Forty-seven in 1995 and eighty-one in 2000 of the 168 Spanish public hospitals with a coronary care unit participated in the PRIAMHO Registries. Hospitals underwent quality data control.
Results: In PRIAMHO II (n= 6221) compared with I (n=5242), patients were older (65.4 vs 64.4 , p <0.001), more women (25.3% vs 22.6%, p= 0.001), more diabetics (29.4% vs 24.2%, p <0.001), smokers (44.1% vs 37.6%, p <0.001), dyslipemia (40.3% vs 28.6%, p <0.001), hypertension (46.1% vs 42.4%, p <0.001), previous MI (15.7% vs 17.5%, p= 0.013). Drug therapy is given in table 1. Mean time to reperfusion was 12 minutes shorter

in PRIAMHO II (48 vs 60, p<0.001). Patients were followed-up during one year. Mortality at 28-day was 11.3% vs 14.2%, p <0.001 and at one-year 16.4% vs 18.5%, p<0.001, respectively.The adjusted odds ratio of death at one year for patients included in the PRIAMHO II compared with those in PRIAMHO I was 0.71 (95% CI 0.63-0.81) p=0.003 (adjusted for patients characteristics and clinical parameters).
Conclusions: In Spain within a 5 year-interval, there has been a 29% reduction on one-year mortality in patients with an AMI, despite patients admitted in year 2000 were a higher risk group. More and quicker reperfusion and a better use of antithrombotic, betablockers and ACE-inhibitors account for this improvement.

Table 1

	PRIAMHO I N=5242	PRIAMHO II N= 6221	P
Reperfusion	41.9%	45.7%	<0.001
Antiplatelet	89.1%	96.1%	<0.001
Heparin	65.4%	86.9%	<0.001
Betablockers	30.1%	51.1%	<0.001
ACE-inhibitors	24.9%	41.6%	<0.001

POSTER SESSION

1121 Chronic Ischemic Heart Disease: Evaluation and Management

Tuesday, March 08, 2005, 9:00 a.m.-12:30 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 9:00 a.m.-10:00 a.m.

1121-223 Sustained One Year Benefit of Enhanced External Counterpulsation in Relieving Mild Angina in Patients with End Stage Coronary Disease

William E. Lawson, Elizabeth D. Kennard, John CK Hui, Sheryl F. Kelsey, State University of New York, StonyBrook, Stony Brook, NY, University of Pittsburgh, Pittsburgh, PA

Background: Most enhanced external counterpulsation (EECP) patients have disabling angina refractory to medical therapy and are poor CABG or PCI candidates. The success of EECP in relieving angina and freedom from adverse events at 1 year in the end stage CAD patient with mild versus severe angina has not been reported.
Methods: Data of 1,989 consecutive pts with refractory angina not amenable to PCI/CABG in the International EECP Registry were divided into 2 groups: CCS angina Class I/II (Mild) and CCS Class III/IV (Severe). Patient demographics, immediate and 1 year outcomes, freedom from MACE (death/MI/CABG/PCI) were compared. Significant differences by students t test and on Kaplan Meier survival plots were defined by $p < 0.05$.
Results: Mild and Severe angina groups were similar in age, race, gender, hyperlipidemia, smoking, diabetes, prior MI or revascularization. Mild and Severe groups differed significantly in HBP [66.1 vs 72.4 %], non-cardiac vascular disease [23.9 vs 32.8 %], CAD duration [9.5 vs 11.5 years], multivessel CAD [72.4 vs 80.4%], EF [48.8 vs 45.9%]. Baseline angina [11.9 vs 4.1 times/week] and Ntg use were significantly greater in the Severe group. After comparable EECP [33.8 ± 9.0 vs 33.2 ± 10.0 hours], angina was reduced by ≥ 1 class in 57.8% of Mild and 77.2% of Severe pts with similar decreases in angina [2.9 and 8.6 times/week] and Ntg use. Post EECP 31.5% of Mild and 14.3% of Severe pts were angina free. Angina reduction was preserved in both Mild and Severe groups at 1 year [44.7 vs 24.1 % with no angina; 21.8 vs 18.2 % with Class I angina] with parallel reductions in angina and Ntg use. MACE at 1 year in Mild vs Severe groups differed significantly: death [3.1 vs 6.9%], MI [2.7 vs 7.2%], overall MACE [11.9 vs 21.4 %]. CABG [4.1 vs 3.2%] and PCI [4.9 vs 8.4 %] rates were similar.
Conclusions: End stage non-revascularizable CAD pts with severe angina have more "room for improvement" and were more likely to have an immediate reduction in angina. However, pts with mild angina initially were more likely to be angina and event free one year following EECP. Mild, but limiting angina, in the pt with end-stage CAD may be effectively treated with EECP.

1121-224 Low-Dose Pioglitazone Safely Provides Clinical Antiatherosclerotic Effects For Patients With Coronary Artery Disease and Metabolic Syndrome

Tatsuaki Murakami, Sumio Mizuno, Fukui Cardiovascular Center, Fukui, Japan

Background: Thiazolidinedione is one of potential agents to treat patients with coronary artery disease and metabolic syndrome, but the concern about its safety and cost hesitates clinical administration. We assessed hypothesis that low-dose pioglitazone provides both effectiveness and safety for patients with coronary artery disease and metabolic syndrome.
Methods: Twenty-six patients with coronary artery disease and metabolic syndrome were randomized to group-L where they received low-dose pioglitazone (7.5mg/day, a quarter dose of standard dose) for 4 months, or to group-C where they continued therapy without thiazolidinedione. We evaluated serum lipid and glycemic variables. We noninvasively ultrasonic quantified flow mediated endothelium-dependent dilation of brachial artery after 5 minutes forearm occlusion (FMD) and quantified brachial-to-ankle pulse wave velocity (PWV). Changes in serum variables and FMD were compared between the 2 groups.
Results: Patients in group-L (n=13) manifested good compliance to the treatment without adverse events such as edema and liver dysfunction and improvements in some of serum variables (mg/dL) associated with insulin resistance while those in group-C showed no improvement (group-L versus group-C: triglycerides: from 205±75 to 151±62, p=0.01, versus, from 198±89 to 194±91, p=ns, HDL: from 42±11 to 50±9, p<0.01, versus, from 41±12 to 40±11, p=ns). They manifested improvements in high sensitive CRP (high sensitive CRP: from 0.14±0.07 to 0.08±0.04, p=0.04, versus, from 0.13±0.08 to 0.14±0.09, p=ns). FMD (%) improved after medication in group-L (4.1±1.6 to 6.5±2.8, p<0.01) but not in group-C (4.1±1.8 to 4.2±1.5, p=ns). PWV also improved after medication in group-L (1727±269cm/sec. to 1664±234cm/sec., p=0.03) but not in group-C (1711±284cm/sec. to 1714±294cm/sec., p=ns).
Conclusion: Low-dose pioglitazone use in patients with coronary artery disease and metabolic syndrome safely improves serum insulin resistant variables and vascular function, which may have beneficial potentials for management of atherosclerosis.

1121-225 Racial Determinants Of Premature Coronary Artery Disease And Predictors Of Early Mortality In Young, Inner-city Patients Undergoing Coronary Angiography - Results Of An Open Cohort Study

Sandeep Nathan, Amit Amin, Steve Attanasio, Vijay Mehta, Russell F. Kelly, Rush University Medical Center, Chicago, IL, Cook County Hospital, IL

Background: The epidemiology of premature CAD (PCAD) is poorly defined in the inner-city population. We investigated the relationship between race, cardiac risk factors (CRFs), and PCAD risk and assessed predictors of early mortality in these patients.
Methods: Data from 416 pts ≤ 40 yrs of age, undergoing coronary angiography at Cook County Hospital (1993-2001) were compiled prospectively and analyzed as an open, retrospective cohort. The primary outcome measure was mortality analyzed via Kaplan-Meier analysis. Risk of CAD (defined as ≥ 50% stenosis in ≥1 coronary artery) by race and CRFs was estimated via stepwise logistic regression. Angiographic data was adjudicated by blinded film review.
Results: 1,444 pt-yrs of follow-up were attained. Of 416 pts, 33% (136) had PCAD, of which 96% (131) had severe CAD (≥ 70% stenosis). White and Indian pts, dyslipidemics, smokers, diabetics and older pts all evidenced increased PCAD risk (Fig. 1). Total mortality at 3.47 yrs mean follow-up was 5.8% and was higher with severe CAD (9.2% if CAD vs 4.2% if no CAD, p=0.044). Diabetes mellitus (DM) (OR 3.71 [1.13-12.2], p=0.031) and systolic dysfunction (OR 3.13 [1.0-9.81], p=0.05) independently predicted mortality.
Conclusions: This data suggests a previously unrecognized risk associated with certain ethnic subgroups of the inner-city population, independent of that conferred by traditional CRFs, with CAD linked to higher mortality. DM and systolic dysfunction were predictive of early mortality, independent of CAD.

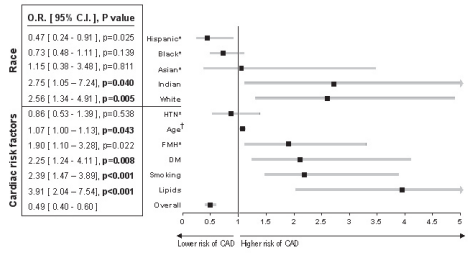


Figure1: Risk of premature CAD by race and traditional cardiac risk factors
* Univariate odds, excluded from final multivariate logistic regression model
† Per incremental year of life

1121-226 The Prevalence of Impaired Functional Status in Unrecognized Myocardial Infarction: A Population Based Study

Khawaja A. Ammar, Ravindrakumar Makwana, Barbara Yawn, Jan Kors, Margaret M. Redfield, Steven J. Jacobsen, Richard Rodeheffer, Mayo Clinic, Rochester, MN, Olmsted Medical Center, Rochester, MN

Background: Unrecognized Myocardial Infarction (UMI), diagnosed by a surveillance ECG, has a poor prognosis equal to that of recognized myocardial infarction (RMI). The impact of UMI on quality of life, functional status and cardiac symptoms other than angina has not been evaluated.
Methods: A population based random sample of 2042 Olmsted County residents, age >=45 years, were studied by self-administered questionnaire, chart review, ECG and echocardiogram. UMI (n=81) were diagnosed if ECG-MI criteria were met without the history of a documented myocardial infarction. RMI (n=101) were diagnosed if Gillum criteria were met. Functional Status was measured by Goldman Specific Activity Scale (SAS) and 6 minute walk test.
Results: In the No MI/UMI/RMI groups, there was a stepwise increase in the prevalence of cardiac symptoms and abnormal functional status. The relationship of UMI with abnormal functional status persisted after stratification for age, sex, obesity, smoking and pulmonary disease, but became insignificant after stratifying for wall motion abnormalities, and left ventricular systolic or diastolic dysfunction.
Conclusion: UMI subjects have a significantly higher prevalence of cardiac symptoms, resulting in an abnormal functional status. These symptoms may be mediated via structural damage demonstrable on echocardiography. These findings signify the impact of an ECG based diagnosis of UMI in adults with otherwise unexplained cardiac symptoms and abnromal functional status.

	No MI	UMI	RMI
Dyspnea on exertion (%)*	29	49	53
Paroxysmal Nocturnal Dyspnea (%)*	4	6	11
History of fluid overload (%)*	1	6	8
Angina (%)*	9	24	78
Palpitations (%)*	15	20	31
Abnormal Functional Status by SAS (%)*	11	22	39
Average Distance Covered in 6 Minute Walk Test(meters)*	526	476	446

*p <0.001

1121-227 N-Terminal Pro-BNP Predicts Coronary Stenosis

Thomas Wolber, Micha Maeder, Ramin Atefy, Walter Riesen, Peter Ammann, Hans Rickli, Kantonsspital St. Gallen, St. Gallen, Switzerland

Background: B-Type Natriuretic Peptide (BNP) and its precursor, N-terminal proBNP (NT-ProBNP), are released from cardiac myocytes in response to various stimuli. In acute coronary syndromes, BNP is a strong predictor of mortality independent of ventricular function. Recent data suggest that BNP elevations can be attributed to myocardial ischemia in the absence of heart failure. The use of BNP to predict coronary stenosis could improve non-invasive diagnosis of coronary heart disease. We tested the hypothesis, that elevated levels of NT-ProBNP are associated with significant coronary disease in patients with normal systolic left ventricular function.
Methods: We measured plasma NT-ProBNP levels in 62 consecutive patients (30% female) with stable angina pectoris referred for coronary angiography. Patients with valvular heart disease or abnormal systolic left ventricular function (ejection fraction < 60%) were excluded.
Results: Coronary angiography showed relevant coronary artery disease (CAD) with at least one ≥50% stenosis in 43 (69%) patients. NT-ProBNP levels were significantly increased in patients with CAD compared to patients without CAD (plasma NT-ProBNP 251 ± 215 ng/L vs. 126 ± 88 ng/L, p=0.026). Receiver operating curve analysis showed an area under the curve of 0.68. NT-ProBNP levels above 300 ng/L had a specificity of 90% for CAD. Systolic left ventricular function was similar in both groups (ejection fraction 0.69 ± 0.6 vs. 0.72 ± 0.6, p=0.10). Patients requiring percutaneous coronary interventions (PCI) (n=13) or bypass surgery (CABG) (n=13) had significantly higher NT-ProBNP levels than patients (n=35) who were managed with medical treatment only (plasma NT-ProBNP 167 ± 149 ng/L vs. 276 ± 230 ng/L, p=0.05).
Conclusions: Coronary artery disease is associated with elevated levels of NT-ProBNP in patients with stable angina pectoris and normal systolic left ventricular function. NT-ProBNP may play an important role in non-invasive assessment of patients with suspected coronary disease. As elevated NT-ProBNP levels are predictive of significant coronary stenosis and of the need for PCI and CABG, invasive testing might be warranted in these patients.

1121-228 Resting Magnetocardiographic Imaging Can Accurately Detect ObstructiveCoronary Artery Disease in Patients with Chronic Ischemia

Yuanlu Chen, Xiaocheng Liu, Xiangqian Qi, Kirsten Tolstrup, Yi Lian, Fang Liu, Yu Song, Jian Zhang, TEDA International Cardiovascular Hospital, Tianjin, People's Republic of China, Cedars-Sinai Medical Center, Los Angeles, CA

Background: Magnetocardiographic (MCG) imaging is a new noninvasive mapping technique that measures and records cardiac electric activity. It has been suggested that the MCG provides independent information for the detection of myocardial ischemia. We evaluated the utility of MCG for the diagnosis of coronary artery disease (CAD) in patients with chronic ischemic heart disease.
Methods: We studied 77 patients (56 men,21 women, mean age 58 ±9.4 years old) with CAD confirmed by coronary angiography (≥70% stenosis in ≥ one branch of main coronary arteries). Patients with concomitant hypertension, left ventricular hypertrophy, bundle branch block, complex rhythm disturbances and NYHA functional class III and IV were excluded. The control group consisted of 36 healthy subjects (12 men, 24 women, mean age 31.5 ± 8.9 years) who all underwent 12-lead ECG, stress testing,transthoracic echocardiography, and Electron Beam-CT. All MCG images were acquired with a 9-channel MCG system (CardioMag Imaging, Schenectady, New York), in an unshielded location. The scans were performed at rest with an acquisition time of 6 minutes. Ventricular repolarization was analyzed using 7 parameters set by an automated software program, and scores for normal and abnormal were obtained.
Results: All 7 interrogated parameters demonstrated significant differences between CAD group and control group (p<0.001 and <0.002 for all). The sensitivity of each of the parameters for the diagnosis of CAD was 71.1%, 71.4%, 71.1%, 50.6%, 20.7%,29.9% and 46.7%, respectively.The corresponding specificities were 91.6%, 86.1%, 97.2%, 97.2%, 97.2%,94.4% and 100%, respectively. The accuracy of the scan was 51% to79% depending on the chosen parameter. With ≥ 3 parameters positive, the specificity of the test was ≥ 97% and the accuracy was 85%-88%.
Conclusion: Resting magnetocardiographic imaging is an accurate and rapid test for the detection of obstructive coronary artery disease in patients with chronic ischemic heart disease.

ORAL CONTRIBUTIONS

846FO Featured Oral Session... Cellular-Based Therapy for Myocardial Infarction

Tuesday, March 08, 2005, 10:30 a.m.-Noon
Orange County Convention Center, Room 231A

10:45 a.m.

846-4 Dose Timing Dependent Effects of GCSF administration on Left Ventricular Remodeling and Global Function

Nirat Beohar, Jayesh Mehta, Charles J. Davidson, Seema Singhal, Daniel Lee, James D. Flaherty, Mladen Vidovich, Jonathan Rapp, Adam Brodsky, Chad Rammohan, Francis J. Klocke, Edwin Wu, Robert O. Bonow, Northwestern University, Chicago, IL

Background: We evaluated the effect of immediate or delayed administration of IM granulocyte colony stimulating factor (G-CSF) on LV performance and remodeling in a porcine model of acute MI and reperfusion. Two administration regimens were assessed: 1) immediately after MI and reperfusion or 2) delayed until 5 days.
Methods: MI was induced percutaneously (n=35) with 90 min proximal LCX balloon occlusion followed by reperfusion. Controls (C): n=11. Early treatment (ET): n=17, G-CSF 300 µg IM QOD for 20 days immediately after reperfusion; Delayed treatment (DT): n=7, G-CSF 300 µg IM QD for 10 days starting day 5 post MI. Cine and contrast MR were performed at 5 (MR1) and 56 (MR2) days post MI. EDV, ESV, LVEF, Expansion Index (EI), Systolic and Diastolic Sphericity Index (SI) were calculated.
Results: EDV, ESV and LVEF were similar between groups at MR1. Mean infarct size was similar: (Infarct mass/LV mass) 6.5 ± 2.6% (C), 7.0 ± 2.8% (ET), 7.2 ± 2.5% (DT) (p= NS, C vs ET, C vs DT, ET vs DT). Systolic and diastolic SI were similar at baseline and followup between groups.

	Control	Early	Control vs Early (P)	Delayed	Control vs Delayed (P)
Δ EDV ml	17± 9	8±7	0.005	21±10	NS
Δ ESV ml	10.6±7	10.1±7	NS	16.8±7	NS
LVEF% (MR2)	47±7	44±7	NS	38±6	0.008
Expansion Index (MR2)	0.32±0.15	0.37±0.2	NS	0.62±0.2	0.003

Conclusions: While early treatment with GCSF after myocardial infarction does not improve overall left ventricular ejection fraction, it favorably affects LV remodeling by decreasing post MI ventricular dilatation. However, delayed treatment appears to have a deleterious effect on LV remodeling by causing infarct expansion and decreased LVEF. These important timing dependent treatment effects should be considered in designing clinical trials with GCSF.

11:00 a.m.

846-5 Extravasation Of Intracoronary Administered Bone-marrow Derived Cd34+ Stem Cells In Patients With Acute Myocardial Infarction Evidenced By In111 Cell Labelling

Tomasz Siminiak, Rafal Czepczynski, Dorota Fiszer, Olga Jerzykowska, Olga Jerzykowska, Grygielska Beata, Sowinski Jerzy, Kurpisz Maciej, Kalmucki Piotr, District Hospital, Department of Cardiology, Poznan, Poland

Background. Increasing experimental and initial in-man experience indicate that autologous bone marrow stem cells (AMB) do have a potential for myocardial regeneration. The protocols of currently ongoing clinical phase 2/3 trials evaluating functional benefits of AMB do involve their intracoronary administration, although a direct evidence of AMB cells extravasation and tissue migration after intracoronary administration is missing.
Aim. To evaluate the extravasation and tissue migration of autologous CD34+ stem cells after intracoronary administration in patients with acute myocardial infarction (AMI).
Material and methods. 8 patients that underwent AMI treated with primary PTCA were included into the study. In all patients, at day 2-6 after AMI onset, under local anesthesia, ca 30 ml of bone marrow aspirate was obtained by sternal puncture. CD34+ cells were isolated from bone marrow aspirate by magnetic cell sorting using the Dynal® CD34 Progenitor Cell Selection System. Cells were subsequently labeled with 0.4-0.8mCi (15-30MBq) of 111-Indium-oxinate (Mallinkrodt). Cell suspension was administered sub-selectively intracoronary into the infarct-related artery at the time of a brief coronary flow decrease. An over-the-wire balloon was inflated for 120 seconds and cells were delivered via the internal catheter lumen. Whole-body scans using a double-head Varicam gamma camera were performed in each patient after 24 hours.
Results. Main regions of uptake were detected over liver, spleen and heart. Based on evaluation of tissue activity in the regions of interest, we estimated that 1-11% of injected activity was concentrated in the heart, whereas uptake in the spleen and the liver was 3-17% and 12-45% of total injected activity, respectively.
Conclusion. Our preliminary data provide evidence for stem cell extravasation and tissue migration after intracoronary administration in patients with AMI. Detailed studies evaluating possible correlations of stem cell tissue migration with cell administration protocol used as well with clinical data, including the time of primary PTCA after AMI onset and timing of cell administration, are needed.

11:15 a.m.

846-6 **Granulocyte-Colony Stimulating Factor in the Acute Myocardial Infarction (The Rigenera Study)**

Antonio Maria Leone, Leonarda Galiuto, Giovanna Liuzzo, Alessandro Giordano, Maria Lucia Calcagni, Barbara Garramone, Maria Benedetta Giannico, Fiammetta Cirillo, Luigi M. Biasucci, Antonio G. Rebuzzi, Filippo Crea, Università Cattolica del Sacro Cuore Institute of Cardiology, Rome, Italy, Università Cattolica del Sacro Cuore Institute of Nuclear Medicine, Rome, Italy

Background: recent data suggest that of bone marrow derived stem cells (BMSC) can improve post-infarction LV function. The Granulocyte-Colony Stimulating Factor (G-CSF) induces mobilization of transplantable BMSC and its administration could improve LV function.
Methods: we enrolled in a pilot open label study 12 patients with a large anterior AMI as first manifestation of IHD and a LVEF <45% after 5 days from a successfully performed revascularization. Nine patients (8 males, 54±11 yrs) were treated with G-CSF (250 mcg s.c./b.i.d.+ enoxaparin 80Ui/Kg s.c/b.i.d) and compared to 3 patients (3 males; 57±3) treated with conventional therapy. LV function was evaluated by Gated-SPECT scan during hospitalization and after 3 and 6 months.
Results: during hospitalization none of the 9 G-CSF patients experienced major adverse events, two reported mild bone pain and one 2 episodes of nocturnal dyspnea. Eight patients underwent 3 months follow up (6 in the G-CSF group and 2 in the control group) and 5 underwent 6 months follow up (all in the G-CSF group). None of the patients had any cardiac recurrence. One G-CSF patient preferred to drop out from the study after completed administration of G-CSF, however she's alive and came back to her normal life.
After G-CSF the CD34+ BMSC increased from 5.36±3.57 to 47.71±31.02 cell/µl. After 5 days from the end of the G-CSF therapy CD34+ cells' concentration came back to 4.32±2.71 cellule/µl. At 3 months LV function was improved in the group of patients treated with G-CSF, in terms of LVEDV (from 207±47 to 180±58 ml, p=0.06), LVESV (from 150±46 to 115±45 ml, p=0.03), LVEF (from 28±8 to 38±8 %, p=0.03), summed motion score (SMS) (from 43±13 to 28±11 p=0.03) and summed thickening score (STS) (from 34±10 to 22±12, p=0.03). At 6 months LV function parameters remained substantially unchanged (LVEDV 184±55 ml, LVESV 115±45 ml, LVEF 39±9 %, SMS 24±10, STS 22±10). No significant improvement in LV function was observed in the 2 patients treated with conventional therapy at 3 months FU.
Conclusions: in our initial experience G-CSF therapy in patients with large anterior AMI seems to be safe and well-tolerated and potentially able to improve post-infarction left ventricular function.

11:30 a.m.

846-7 **Feasibility, Safety And Efficacy Of Bone Marrow-derived Cell Mobilization With G-csf And Gm-csf In Patients With Acute Myocardial Infarction: A Pilot Study**

Sebastiano Marra, Paolo Scacciatella, Corrado Tarella, Giacomo Tamponi, Tullio Usmiani, Maurizio D'Amico, Giorgio Millesimo, Marco Sicuro, Mauro Giorgi, Luca Checco, Pierluigi Sbarra, Massimo Baccega, Mario Campana, Irene Ricca, Paola Omedè, Fiorella Sanavio, Mario Boccadoro, Michele Casaccia, Azienda Ospedaliera San Giovanni Battista, Torino, Italy

Background. Myocardial regeneration and neovascularization of the ischemic myocardium may be obtained either in animal models or in human by intracoronary or intramyocardiac injection of growth factor-mobilized peripheral blood stem cells (PBSC) and growth factor PBSC only. Aims of this pilot study were: i) to verify feasibility and safety of PBSC mobilization in patients (pt) with acute myocardial infarction (AMI); ii) to monitor clinical effects of PBSC mobilization in terms of myocardial perfusion and function.
Methods. Eight male pt (mean age: 51,7±5,6 years) were enrolled. All were treated with a primary PTCA for an anterior (5 pt) or an inferior (3 pt) AMI. The mobilization regimen consisted of G-CSF 5 g/kg/12h from day 1 to day 3 and GM-CSF 2.5 g/kg/24h from day 1 to day 5 (starting within 24 hours from PTCA).All pt underwent coronary angiography, intracoronary doppler flow study, echocardiography, and nuclear Thallium scan before treatment and at 6 months apart.
Results. WBC and PBSC peaked during the 3th day of mobilization. Mean WBC and PBSC peaks were 34960±10794 leukocytes/ L and 29.71±30.8 CD34+/ L. Five in hospital adverse events were recorded: severe hypotension in 3 pt, atrial fybrillation in 1 pt, recurrent ischemia in 1 pt. No death was observed. At present 7 pt completed a 6-months follow-up evaluation: target lesion revascularization rate was 14,3% (1 patient) and target vessel revascularization rate was 42,8% (3 pt). Angiographic mean ejection fraction increased from 49,8±11,9 to57,1±8,9 (p=NS), and mean coronary flow reserve raised from 1,63±0,42 to 2,45±0,36 (p=0,005). Perfusion improvement was observed by nuclear study in 66% of pt.
Conclusion. We conclude that: a) cytokine-induced stem cell mobilization is feasible in AMI pt; b) myocardial perfusion clearly improved within the first six months of follow-up; c) even if not statistical significant we observed a global myocardial function improvement; d) the 3 cases of progressive coronary disease give a concern about a potential negative effect of hematopoietic cytokines (particularly GM-CSF) on silent coronary lesions. However, PBSC mobilization is worthwhile of further investigation.

11:45 a.m.

846-8 **Bone-Marrow Stem Cell Mobilization Induced By Granulocyte-Colony Stimulating Factor In Patients Undergoing Delayed Revascularisation For ST Segment Elevation Myocardial Infarction: Early Results From The G-CSF In STEMI Trial**

Markus G. Engelmann, Hans D. Theiss, Christine Hennig, Bernd J. Wintersperger, Armin Huber, Stefan O. Schoenberg, Gerhard Steinbeck, Wolfgang M. Franz, Ludwig Maximilian University, Klinikum Grosshadern, Munich, Germany

Background: Recently, adult human stem cells were considered to improve regional and global contractility after ST elevation myocardial infarction (STEMI). This interim analysis of an investigator driven, prospective, randomized, double-blinded, Placebo-controlled Phase II study compares the effects of G-CSF on the improvement of myocardial function in patients undergoing delayed percutaneous coronary intervention (PCI) for STEMI.
Methods: Eighteen patients (CK_{peak} 3260±450 U/L) with late revascularised STEMI (angina to PCI interval 42±16 hours) were treated either with G-CSF (n=12) or Placebo (n=6) over 5 days after successful PCI. Inflammatory and safety parameters were monitored and mobilized stem cell populations characterized using flow cytometry. Primary endpoints were global and regional myocardial function assessed by magnetic resonance imaging.
Results: G-CSF was generally well tolerated, with no significantly higher rate of in-stent restenosis when compared to Placebo. G-CSF treatment led to mobilization of several stem cell populations ($CD34^+/CD31^+$, $CD34^+/CD133^+$, $CD34^+/c\text{-}kit^+$). Expression of CXCR4, which is essential for stem cell homing in target tissue, was slightly increased onto $CD34^+$ cells. Left ventricular ejection fraction was not significantly changed from baseline over 3 months of follow-up in both treatment groups. However, regional wall thickening of the main infarct segment was improved in G-CSF treated patients in comparison to Placebo (p=0.05).
Conclusion: G-CSF treatment in STEMI patients is safe following PCI with no increased rate of in-stent restenosis. G-CSF mobilizes several stem cell populations considered to improve myocardial regeneration via homing by CXCR4. The more rapid recovery of regional function in late revascularised STEMI patients treated with G-CSF encourages conduction of clinical multi-center trials.

POSTER SESSION

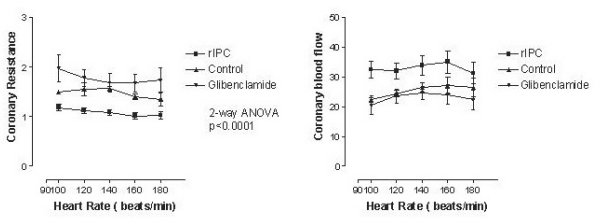
1145 Protecting the Ischemic Myocardium II

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1145-203 **Remote Ischemic Preconditioning modifies Coronary flow and Resistance Via Katp-dependent Mechanism**

Mikiko Shimizu, Igor Konstantinov, Jia Li, Rajesh Kharbanda, Andrew Redington, Hospital for Sick Children, Toronto, ON, Canada

Introduction: Ischemic preconditioning (IPC) is an innate protective mechanism that attenuates myocardial ischemia-reperfusion injury. Remote IPC (rIPC) may be more clinically relevant. It being induced by transient ischemia of distant tissue such as a limb.
Objective: To assess whether rIPC can modify coronary circulation.
Methods: Nineteen pigs were randomized to control group (n=5), rIPC group (n=8) or glibenclamide pretreated rIPC group (n=6). rIPC was induced by four 5 minutes cycles of lower limb ischemia. Mean arterial pressure (MAP) and coronary sinus pressure (CS) were measured via indwelling cannulae. Left anterior descending (LAD) artery flows were monitored by transonic flow probe placed on proximal portion of LAD. Coronary resistance was calculated as: Coronary resistance = MAP- CS / LAD flow All pressure and flow data were collected at baseline and during incremental pacing between 100 -180bpm.
Result: There were no differences in MAP between three groups. Coronary resistance was significantly lower (p<0.0001, 2-way ANOVA) and LAD flow was significantly higher in the rIPC group (p=0.0008). In the Glibenclamide pretreated group, coronary resistance was higher and LAD flow was lower compared to rIPC group (p<0.0001, p<0.0001).
Conclusion: rIPC increases coronary flow and lowers coronary resistance via a Katp channel-dependent mechanism. This may be an important factor in the protective effect of rIPC against subsequent IR injury.



1145-204 Brief Ischemia Before Sustained Ischemia Attenuates The Deterioration Of Cardiac Sympathetic Neuronal Function In The Remote Period After The Ischemic Insult

Teruo Nakadate, Takashi Nozawa, Akira Matsuki, Makoto Nonomura, Norio Igarashi, Bun-ichi Kato, Nozomu Fujii, Akihiko Igawa, Hidetsugu Asanoi, Hiroshi Inoue, Toyama Medical & pharmaceutical University, Toyama, Japan

Background: Recent studies demonstrated that a brief episode of transient myocardial ischemia reduced cardiac norepinephrine (NE) release from the sympathetic nerve terminals during the subsequent sustained ischemia. However, the influence of brief ischemia on sympathetic neuronal function in the remote period after the sustained ischemia remains unclear.
Methods: In rats with (group I) and without (group II) 5-min left coronary occlusion and 5-min reperfusion preceding the 30-min prolonged occlusion, cardiac interstitial NE (iNE) during 30-min ischemia and early after reperfusion was determined using microdialysis method. In rats without preconditioning, K-channel opener, nicorandil (group III) was administered at rate of 50μg/kg/min from 20-min before 30-min coronary occlusion to the release of ischemia. In separate animals, the NE uptake function at cardiac sympathetic nerve terminals was assessed by quantitative autoradiography using ^{131}I-metaiodobenzylguanidine (MIBG), an analogue of NE, 3 days after the 30-min ischemia produced in the same method as in group II.
Results: Thirty-min coronary occlusion increased levels of iNE more than 200 times in group II, as compared to that before ischemia. However, the levels of iNE were less in group I (n=8) and group III (n=7) than in group II (n=7) at the latter half of 30-min ischemia (6.3±2.3, 4.9±3.0 vs 19.4±5.9 ng/ml, respectively, p<0.01) and just after the reperfusion (1.5±0.9, 2.3±1.8 vs 8.4±3.6 ng/ml, respectively, p<0.01). MIBG uptake in ischemic region was greater in group I (n=8) than in group II (n=9) (0.062±0.030 vs 0.031±0.011 %kg dose/g, p<0.05) and its uptake ratio of ischemic region to the remote region was greater in group I than in group II (37.4±7.4 vs 24.6±8.1%, p<0.05).
Conclusion: A brief episode of ischemia before sustained ischemia attenuated sympathetic neuronal dysfunction in the remote period after the ischemic insult, i.e., the phenomenon of neural preconditioning, in association with marked reduction in iNE during ischemia. Suppression of increasing iNE during ischemia induced by nicorandil suggests that K-channel may be involved in the mechanism of neural preconditioning.

1145-205 Exogenous Nitric Oxide Inhibits AMP-activated Protein Kinase (AMPK) Phosphorylation and GLUT4 Translocation to Sarcolemma in Ischemic Myocardium

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Background: NO donors such as nitroglycerin (NG) have been used for about a century to treat cardiac ischemia (ISC) and are commonly believed to indirectly reduce myocardial metabolic demand by lowering left ventricular preload, however we hypothesized that exogenous NO directly limits the increase in glucose uptake that normally occurs in the ischemic heart.
Methods: In 18 open-chest dogs, the left anterior descending coronary artery (LAD) was artificially blood-perfused in a flow-controlled mode. Paired blood samples were withdrawn from the perfusion line and from the left anterior cardiac vein at baseline and during ISC induced by 66% reduction in LAD flow. 9 dogs received 0.5 μg/kg/min of NG in LAD during ISC and 9 served as control. Isotopic tracers were infused i.v. After 45 min of ISC, portions of ischemic and non-ischemic ventricular tissue were harvested and fractionated to measure the translocation of the glucose transporter GLUT4 to sarcolemma.
Results: NG did not cause any change in LAD myocardial flow distribution and systemic hemodynamics. At 45 min of ISC, myocardial O_2 consumption, free fatty acid and glucose oxidation were significantly decreased vs baseline by the same amount in both groups. However, myocardial glucose uptake increased significantly less in ISC+NG compared to ISC (0.38±0.03 vs 0.54±0.05 μmol/min/g), which corresponded to significantly less translocation/activation of GLUT4 (73.7±6.9% vs 164.8±16.9%). GLUT4 translocation is stimulated by phosphorylated AMPK and in fact we found that AMPK phosphorylation was inhibited in ISC+NG compared to ISC (76.7±11.8% vs 167.1±17.0%). An important consequence of these effects of NG was the significant reduction in net myocardial lactate production (0.04±0.03 vs 0.28±0.05 μmol/min/g) and the limited depression of regional contractile function (fractional shortening: -6.2±1.4% vs -11.2±1.9%) in ISC+NG vs ISC.
Conclusion: Exogenous NO, a molecule employed in the treatment of angina, causes a direct reduction of glucose transport/uptake in severely ischemic myocardium, likely due to inhibition of AMPK phosphorylation. This metabolic effect is beneficial, since it limits lactate production and contractile depression.

1145-206 Intermittent Limb Ischemia During Myocardial Ischemia Preserves Cardiac Function in the Reperfusion Phase

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Background: Remote ischemic preconditioning (rIPC) by intermittent limb ischemia reduces myocardial infarction in animal models. We hypothesized that systemic protection induced by rIPC may be effective when administered ***during*** ischemia, prior to reperfusion.
Methods: Fourteen 15-kg pigs were randomized (7 in each group) to a 40-minute period of left anterior descending artery (LAD) occlusion with (rIPC group) or without (control group) four 5-minute cycles of limb ischemia ***during*** LAD occlusion followed by120-minutes reperfusion. Left ventricular (LV) function was assessed using a conductance catheter.
Results: The extent of myocardial infarction compared to area at risk did not differ between rIPC and control groups (43.6±13.0% vs. 52.2±16.4%, p=0.30). There were no differences in indices of LV systolic (preload-recruitable stroke-work (PRSW) and dP/dt$_{max}$) or diastolic (tau) function at baseline. However, systolic and diastolic function was significantly better in the rIPC group at 30-minutes and 120-minutes reperfusion. There was no significant difference between the two groups in absolute dP/dt$_{max}$-values at 120-minutes reperfusion, but the results reflect a 46.8±6.7% reduction from baseline in controls compared to 24.3±13.1% reduction in the rIPC group (p<0.001).
Conclusion: Intermittent limb ischemia ***during*** myocardial ischemia preserves global cardiac function during reperfusion. This novel observation has potential implications for reducing LV dysfunction after reperfusion

		Baseline		30 min reperfusion		120 min reperfusion	
PRSW (mmHg)	rIPC	33.5 ± 5.6	p=ns	26.7 ± 8.5	p=0.07	33.1 ± 6.0	p=0.007
	Controls	38.1 ± 10.6		17.7 ± 8.8		21.8 ± 6.9	
dP/dt$_{max}$ (mmHg/s)	rIPC	1511 ± 318	p=ns	1281 ± 368	p=0.03	1158.0 ± 383.4	p=0.16
	Controls	1687 ± 428		826 ± 342		896.2 ± 247.2	
tau (ms)	rIPC	32.4 ± 1.8	p=ns	35.5 ± 2.1	p=0.04	36.2 ± 3.4	p<0.001
	Controls	32.5 ± 1.4		44.3 ± 10.0		44.1 ± 1.8	

1145-207 Either Pretreatment or Treatment at Reperfusion With Pyrroloquinoline Quinone Reduces Lipid Peroxidation and Is Cardioprotective in a Rat Model of Ischemia/ Reperfusion

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Background: The essential nutrient pyrroloquinoline quinone (PQQ) has been newly identified as a redox cofactor vitamin for mammals. As PQQ has shown neuroprotective effects in vitro and vivo, we asked if PQQ is cardioprotective in a rat model of ischemia/reperfusion.
Methods: Intact rats were subjected to 30 min of LAD occlusion and 2 hours of reperfusion with LV hemodynamic monitoring. PQQ (15 mg/kg) was given either 30 min before LAD occlusion by i.p. injection (Pretreatment) or by i.v. injection at the onset of reperfusion (Treatment). Controls received vehicle (2% NaHCO3).
Results: Either Pretreatment or Treatment with PQQ resulted in reduced infarct size (infarct mass/risk area). PQQ protected against ischemia-induced LV dysfunction after 1-2 hours of reperfusion and resulted in fewer episodes of ventricular fibrillation (VF). In separate experiments, PQQ 5-20 mg/kg given as Pretreatment was inversely related to infarct size (r=0.96, P<0.01). In ischemic tissue, levels of malondialdehyde (MDA), a measure of lipid peroxidation, were reduced by PQQ. Additional rats received PQQ (5, 10, 15 mg/kg, 4 rats each dose). Renal and liver functions after 4 and 10 days of treatment remained normal.
Conclusions: PQQ given as pretreatment before ischemia or as treatment at the onset of reperfusion following ischemia is highly effective in reducing myocardial infarct size and improving cardiac function in a dose-related manner in intact rats. PQQ appears to act as a free radical scavenger in ischemic myocardium.

* P<0.05, ** P<0.01, *** P<0.001 versus Ischemia/Reperfusion (I/R)

Groups	Infarct size(%)	LV developed pressure (mmHg)	LV (+) dP/dt (mmHg/sec)	LV (-) dP/dt (mmHg/sec)	VF (%)	MDA (nmol/g)
I/R	38±3	84±5	4415±349	-3415±306	71	316±88
Pretreatment	18±2***	115±3**	6300±311*	-4750±150*	31**	99±14**
Treatment	26±4**	108±2**	5571±268*	-4429±156*	42*	123±17*

1145-208 Gp91-Phox Expression Increases in the Remote Noninfarcted Myocardium After Myocardial Infarction in Rabbits: Association With Myocyte Apoptosis

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Background: NADPH oxidase subunit gp91-phox expression is increased in the infarct site 1 week after myocardial infarction (MI). In this study, we proposed to test whether gp91-phox expression was increased in the remote non-infarcted myocardium (RM) late after MI and whether the change was associated with myocyte apoptosis.
Methods: Rabbits were randomly assigned to MI or sham operation. The animals were sacrificed 4 weeks after MI. We measured cardiac function, hemodynamics, infarct size, gp91-phox protein and mRNA expression by Western blot and RT-PCR, oxidative stress by examining the ratio of reduced to oxidized glutathione (GSH/GSSG), myocyte apoptosis by TUNEL assay and p38 mitogen-mediated protein kinase (p38 MAPK) activity.
Results: MI rabbits exhibited an increase of left ventricular (LV) end-diastolic dimension (EDD) and a decrease of LV dP/dt. The infarct size was 29.0±2.5 %. Gp91-phox protein and mRNA expression was increased in RM after MI. Immunolabeling revealed that gp91-phox was present in myocytes. We also found a decrease in GSH/GSSG ratio and increases in p38 MAPK activity and myocyte apoptosis after MI.
Conclusion: Gp91-phox expression was increased in RM late after MI. The change was associated with increased oxidative stress, p38 MAPK activation and myocyte apoptosis. The findings suggest that increased gp91-phox expression may play a role in myocyte apoptosis and LV remodeling by contributing to increased oxidative stress.

Group	gp91-phox protein (arbitrary unit)	GSH/GSSG	P38 MAPK (arbitrary unit)	Apoptotic cells (per 10000 myocytes)	LV EDD (mm)	dP/dt (mmHg)
Sham	1.03±0.03	133±10	1.01±0.02	4.6±0.7	15.2±0.1	4554±181
MI-4W	1.92±0.22*	64±9*	1.35±0.05*	20.4±2.7*	16.8±0.6*	3845±180*

n=8-12. Values are mean±SE. *P<0.05 vs Sham. W: week.

POSTER SESSION

1146 Inflammation, Infection, and Novel Observations and Acute Ischemic Syndrome

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1146-215 Association Between Systemic Inflammation and 10-Year Risk for Coronary Heart Disease Among Healthy U.S. Adults

Hee-Yeol Kim, Don D. Sin, Jae-Hyung Kim, St Paul's Hospital, The Catholic University of Korea, Seoul, South Korea, St Paul's Hospital, University of British Columbia, Vancouver, BC, Canada

Background: The association between estimated 10-year risk for coronary heart disease (CHD) and systemic inflammation, which is a known risk factor for cardiovascular events, remain largely unknown. We sought to determine whether the distribution of the 10-year risk in a dose-dependent way is associated with novel inflammatory markers among U.S. adults.
Methods: We applied the risk prediction algorithm used by the National Cholesterol Education Program Adult Treatment Panel III guidelines to data from 6,371 participants (age 40 to 79 years) without self-reported heart attack, stroke, peripheral vascular disease, and diabetes in NHANES III.
Results: After adjustments for age, sex, BMI, race, and various co-morbidities, participants with high risk had circulating leukocyte, platelet, fibrinogen and homocysteine levels that were 914/μL (95% confidence interval [CI], 672 to 1,156/μL), 10,222/μL (95% CI, 2,837 to 17,607/μL), 21.9 mg/dl (95% CI, 12.5 to 29.4 mg/dl) and 1.5 μmol/L (95% CI 0.8 to 2.3 μmol/L) higher, respectively, than in those with low risk. They were also more likely to have elevated levels of CRP, fibrinogen and homocysteine (Table). There were dose-dependent increases in circulating levels of markers across 3 risk groups.
Conclusions: These findings indicate that low-grade systemic inflammation and hyperhomocysteinemia were present in participants with high 10-year risk for CHD. These observations may in part explain the high rates of cardiovascular events in a high-risk population.

Relative odds(95% CI) of having elevated level of circulating markers

	Intermediate risk	High risk
CRP >0.21 mg/dl	1.12 (1.00, 1.26)	1.61 (1.30, 2.01) **
CRP >1.00 mg/dl	1.07 (0.89, 1.30)	1.41 (1.03, 1.93) *
Fibrinogen ≥377 mg/dl	0.97 (0.83, 1.14)	1.36 (1.05, 1.78) *
Homocysteine ≥13.3 μmol/L	1.11 (0.89, 1.38)	2.11 (1.48, 3.01) **
Elevated fibrinogen and homocysteine levels were defined as ≥85th percentile of either variable. *P<0.05, **P<0.0001 compared with low risk group, adjusted for confounding factors		

1146-216 Elevated Wbc Count Not Associated With Obstructing Coronary Lesions In Patients Presenting With Non-st Elevation Acute Coronary Syndromes.

Maliha Zahid, Ali F. Sonel, Lauren Wall, Chester Bernie Good, Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, Pittsburgh, PA, Cardiovascular Institute, University of Pittsburgh, Pittsburgh, PA

Background: Elevated peripheral white blood cell (WBC) count has been shown to predict adverse events in patients presenting with unstable angina or non-ST segment elevation MI. The value of elevated WBC in predicting degree of coronary artery disease (CAD) is unknown.
Methods: To determine the relationship between WBC count and degree of coronary artery disease on catheterization, we prospectively studied 251 consecutive patients without ST elevation, admitted with suspicion of MI and who subsequently underwent coronary angiography during hospitalization. Clinical information was determined by medical record abstraction. All patients had a WBC count determined at time of admission. Elevated WBC count was defined as >10K/mm^3. Significant CAD was defined as any stenosis of >70% and/or left main stenosis >50%. Univariate logistic regression modeling was performed to analyze the relationship between different parameters and presence of significant CAD.
Results: Mean age was 63 years, with majority of patients being male (99.2%). 26.3% had significant CAD. Patients with elevated WBC count were less likely to have significant CAD (OR=0.40, 95% CI=0.18-0.91, p=0.029). This relationship persisted and in fact was stronger after correcting for presence of diabetes, hypertension, hypercholesterolemia and tobacco use (OR=0.36, 95% CI=0.16-0.84, p=0.018).
Conclusion: Patients presenting with acute coronary syndromes and elevated WBC count were much less likely to have obstructing CAD on catheterization. These results suggest that ruptured plaque rather than severity of coronary stenoses may be responsible for poor outcomes in patients with non-ST elevation acute coronary syndromes and elevated WBC counts. Further research is needed to clarify the value of WBC count as a predictor of plaque stability and inflammation.

1146-217 Infiltration of Neutrophils Directly Relates to the Clinical Severity in Patients with Unstable Angina Pectoris

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Background: Neutrophils in unstable atherosclerotic lesions have not received much consideration, despite accumulating evidence suggesting a link between systemic inflammation and acute coronary syndromes. We have recently demonstrated that neutrophils play a role in mediating destabilization of atherosclerotic plaques (Naruko T et al, *Circulation* 106, 2002). However, the relationship of neutrophil infiltration to clinical severity of unstable angina pectoris (UAP) has not been adequately explored. For this reason, we immunohistochemically studied the infiltration of neutrophils in coronary atherectomy specimens obtained from patients with stable angina pectoris (SAP) and patients with diverse clinical presentation of UAP.
Methods: All patients underwent atherectomy at primary atherosclerotic lesions responsible for SAP(n=30) and UAP(n=25). Based on Braunwald's class, the patients with UAP were divided into two groups: Braunwald's IB+IIB and Braunwald's IIIB. Frozen samples were studied with antibodies against smooth muscle cells, macrophages, endothelial cells, and neutrophils (CD66b, CD11b, myeloperoxidase, and elastase). The presence of macrophage and neutrophil immunoreactivity was quantified, respectively, using computer-aided planimetry.
Results: Quantitative analysis demonstrated that macrophage positive area and the number of neutrophils in UAP patients was significantly (P<0.001) higher than in SAP patients. Furthermore in culprit lesions obtained from UAP patients, the number of infiltrated neutrophils was significantly (P<0.001) higher in the Braunwald's IIIB group than in the Braunwald's IB+IIB group.
Conclusions: These findings strongly suggest a correlation between the magnitude of neutrophil infiltration and the clinical severity of UAP.

1146-218 Levels of Inflammatory Markers at the Site of Plaque Rupture in Acute Myocardial Infarction Depend on Preceding Symptoms

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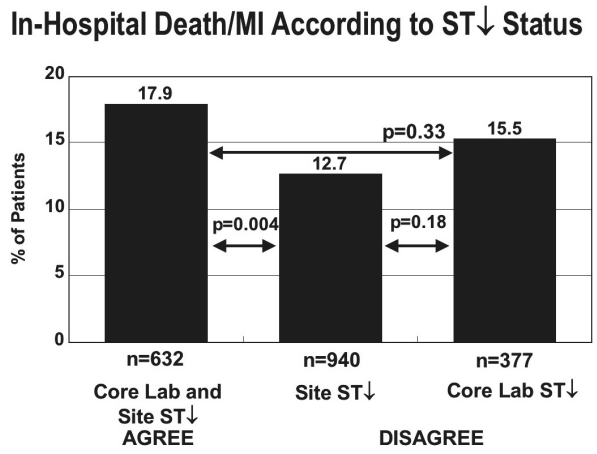
Background: Clinical practice experiences two groups of patients with acute myocardial infarction (AMI): those with preceding, intermittent symptoms over a longer period of time prior to the event, and those without any previous warning signs (sudden onset). Since evidence is accumulating that inflammation plays an important role in the pathogenesis of AMI, we analyzed inflammatory markers in the local and the systemic circulation during PCI for AMI with respect to the onset characteristics (more versus less than 24 hours).
Methods: In sixty-one patients undergoing primary percutaneous coronary intervention (PCI), the acute phase reactants C-reactive protein (hs-CRP), interleukin 6 (IL-6), and serum amyloid A (SAA) were assessed in the aorta and at the immediate site of the culprit lesion with occlusion of the distal part of the artery by means of a protection device (PercuSurge GuardWire) for prevention of distal embolization. Patients with preceding symptoms (n=26, 43%) were compared to those without (n=35, 57%). The Mann-Whitney rank test was applied, since inflammatory markers were not normally distributed.
Results: The systemic inflammatory markers were significantly higher in patients with preceding symptoms. These differences prevailed at the site of plaque rupture (medians [IQR] in AMI with preceding symptoms versus sudden onset): IL-6 was 11.1[7.8-38.3] versus 5.0 [5.0-14.4] ng/L, SAA was 26.8 [22.8-324.3] versus 23.3 [14.6-34.3] mg/L, and CRP was 5.5 [1.8-15.5] versus 1.7 [0.8-3.6] mg/L, all p<0.05.
Conclusion: In patients with AMI and preceding symptoms, not only systemic, but also local levels of inflammatory markers at the site of plaque rupture were significantly elevated compared with sudden onset AMI. This difference in inflammatory activation might reflect two different mechanisms of disease: one primarily inflammation-driven, and another with spasm and thrombus formation as primary trigger.

1146-219 Disagreement in the Interpretation of the Admission Electrocardiogram in Acute Coronary Syndromes and Association With Clinical Outcome: Real-World Insights From GRACE

Shaun G. Goodman, Andrew T. Yan, Jeanna Allegrone, Jose Lopez-Sendon, Christopher B. Granger, Joel M. Gore, Andrzej Budaj, Alina A. Georgescu, Quamrul Hassan, Janna Luchansky, Frans Van de Werf, for the GRACE ECG Substudy Investigators, Canadian Heart Research Centre, Toronto, ON, Canada, St. Michael's Hospital, Toronto, ON, Canada

Background Clinically relevant differences in ECG interpretation between site and central core laboratory have been demonstrated in clinical trials but the extent and impact of this variability in a "real-world" setting is unclear.
Methods Pts in a prospective substudy (n=7900, 39 hospitals, 7 countries) of the GRACE registry were stratified according to admission ECG findings in the following hierarchy: left bundle branch block (LBBB), ST-segment elevation (ST↑)*, ST-depression (ST↓)*, T-wave inversion (T↓)*, and other changes/normal (*≥0.1 mV, ≥2 contiguous leads). The proportion of potential agreement achieved between the site and core lab (noncardiologist physician readers) categorization beyond chance was calculated (kappa [κ]).
Results Overall agreement between the sites and core lab was moderate (κ=0.48); agreement was good in pts with LBBB (κ=0.70), moderate in ST↑ (κ=0.55), and fair in ST↓ (κ=0.40) and T↓ (κ=0.38). In-hospital death/MI was high in core lab-categorized pts with LBBB (19.3%), ST↑ (16.1%), ST↓ (17%), T↓ (10.3%), and others (11.4%). In-hospital death/MI was higher in the ST↓ subgroup identified by both sites and core lab vs those categorized by the sites but not confirmed by the core lab.



Conclusions Only moderate agreement was evident when comparing site and core lab interpretations of the admission ECG in ACS. Consistent with clinical trial settings, important differences in even a simple categorization of the admission ECG findings may be associated with different outcomes.

1146-220 **Hypertensive Patients Have Increased Sensitivity To Meteorological Parameters For Myocardial Infarction Occurrence. Analysis From Rico Database**

Clothilde Royer, Jean-Claude Beer, Marianne Zeller, Jean-Pierre Besancenot, Jack Ravisy, Isabelle L'Huillier, Michel Vincent-Martin, Yves Laurent, Alexandra Oudot, Jean-Eric Wolf, Hamib Makki, Yves Cottin, on behalf of RICO survey working group, University of Burgundy, Dijon, France

Background: Cold temperatures are known to be associated with an increase in vascular resistance. However, the seasonal distribution of acute myocardial infarction (MI) occurrence in hypertensive patients is unknown.
Methods: RICO is a French regional survey for patients hospitalized with acute MI. From 01 January 2001 to 31 December 2002, date of MI onset, hypertensive (HT) status of each patient, and daily mean climatic parameters (atmospheric pressure, temperature and passage of weather cold or warm fronts) obtained from Meteo-France for the region corresponding to RICO covering area were collected. Non parametric Mann-Whitney rank sum test was performed to assess the relationship between daily occurrence of MI and climatic variables in HT and normotensive (NT) patients.
Results: Among the 748 patients included during the study period, 373 (50%) were HT. A peak in MI onset was observed in overall population at lowest temperatures (-6.9 to -4.0°C) vs warmer (-3.9 to 27°C), which was nearly exclusively due to HT patients (respectively 1.20 vs 0.51 MI/day, p<0.023, increased risk = 96%). In contrast, MI onset was similar for temperatures for NT patients (respectively 0.80 vs 0.52 MI/day, ns). Also, HT patients have increased risk (+62%) of MI when the difference in temperature between the day before and the day of MI onset was >5°C (0.81 vs 0.5 MI/day, p=0.04), while NT patients had similar occurrence of MI (0.58 vs 0.53 MI/day, ns). Mean pressure gap > 8 hPa between the day before and the day of MI onset had no influence on NT patients (0.56 vs 0.50 MI/day, ns) but induced an increased risk of MI in HT patients (+54%, 0.74 vs 0.49 MI/day, p=0.039). Moreover, increased MI onset observed at the passage of cold fronts in overall population was mainly due to HT patients (0.79 vs 0.46 MI/day, p<0.03) with no influence of this variable in NT patients (0.57 vs 0.50 MI/day, ns). Inversely, no significant deviation from chance expectation was observed between HT and NT after warm fronts.
Conclusion: Our results show for the first time the increased sensitivity of hypertensive patients to several climatic parameters for myocardial infarction triggering, when compared to normotensive patients.

1146-221 **Human Immunodeficiency Virus (HIV) Infection as an Independent Risk Factor for the Development of Severe Coronary Artery Disease**

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Background: The use of Highly Active Anti-Retroviral Therapy (HAART) has significantly reduced the morbidity and mortality associated with HIV infection. However, the limited angiographic data in several studies questions whether HIV positivity is independently associated with an increased risk for the development of angiographically severe coronary artery disease (CAD).
Methods: All patients who had undergone cardiac catheterization at Grady Memorial Hospital, Atlanta, Georgia between January 2001 and December 2001 for evaluation of an acute coronary syndrome or an abnormal cardiac stress test were studied. Patients were evaluated for the presence or absence of HIV infection, common cardiac risk factors, HAART, and findings on coronary angiography. Multivariate analyses were conducted to determine the relationship between HIV status and angiographically severe CAD (major epicardial coronary artery stenosis ≥70%).
Results: 525 patients were enrolled in the study; the average age was 55.7 ± 10.9 years; 304 (58%) were male; 462 (88%) had hypertension; 237 (45%) had diabetes mellitus; 333 (63%) had dyslipidemia; 178 (34%) used tobacco; 27 (5%) were HIV positive; and 111 (21%) were admitted with a myocardial infarction. Of the latter group, only 7 (1.4%) were HIV positive. Cardiac catheterization revealed that 213 patients (45%) had ≥ 70% stenosis of a major epicardial coronary artery; of these, 14 patients were HIV positive. On unadjusted analysis, HIV status was found to be significantly associated with angiographically severe CAD (p = 0.05). However, after adjusting for age, gender, hypertension, diabetes, hyperlipidemia, and tobacco use, HIV status was no longer associated with severe CAD (OR 1.88, 95% CI 0.86 - 4.11; p = 0.12). Furthermore, there was no significant relationship between angiographically significant CAD and HAART, CD4 count, or viral load.
Conclusions: Although HIV infection was common in an urban population referred for cardiac catheterization, it was not a significant risk factor for the development of angiographically severe CAD. This suggests that other factors play a significant role in the pathogenesis of severe CAD in patients who are HIV positive.

1146-222 **Opposite Effects of CX3CR1 Receptor Mutants I249 and M280 on the Development of Acute Coronary Syndrome: A Possible Implication of Fractalkine in Inflammatory Activation**

Alexander Niessner, Rodrig Marculescu, Arvand Haschemi, Georg Endler, Gerlinde Zorn, Cornelia M. Weyand, Gerald Maurer, Christine Mannhalter, Johann Wojta, Oswald Wagner, Kurt Huber, Medical University of Vienna, Vienna, Austria, Wilhelminen-Hospital, Vienna, Austria

Background: Several lines of evidence suggest that the chemokine fractalkine (FKN) and its receptor CX3CR1 contribute to the accumulation of leukocytes in the atherosclerotic plaque. The CX3CR1 mutation M280 modulates leukocyte recruitment and is associated with lower prevalence of cardiovascular disease. The effect of I249, another CX3CR1 mutation, is discussed controversially. We investigated the association of the mutations M280 and I249 of CX3CR1 with coronary artery disease (CAD) and with acute coronary syndrome (ACS). Furthermore, we examined the relationship of the receptor mutations to the concentrations of soluble ligand FKN and high-sensitivity C-reactive protein (hsCRP).
Methods: 1152 patients with suspected CAD were genotyped for M280 and I249. We applied multivariate logistic regression analysis to assess the independent effect of mutations on CAD and ACS while adjusting for age, sex and cardiovascular risk factors. Circulating FKN and hsCRP were measured in a subgroup of 67 subjects during ACS. Due to non-normal distribution continuous variables were expressed as median [interquartile range] and analyzed using the Mann-Withney U test.
Results: 63% of individuals (n = 720) showed significant CAD (stenosis ≥ 60%) with an ACS life-time prevalence of 59% (n = 427). We found a harmful influence of I249 (adjusted odds ratio 1.8, 95% confidence interval [CI]: 1.1-3, P = 0.023) and a protective effect of M280 (adjusted odds ratio 0.6, 95% CI: 0.3-1, P = 0.037) on the occurrence of ACS in patients with CAD. Correspondingly, patients with CAD carrying I249 but not M280 (17%) were at elevated risk of ACS (odds ratio 1.6, 95% CI: 1-2.5, P = 0.039) compared to those lacking both mutations. During ACS these patients (carrying only I249) had higher concentrations of FKN (997 [659-2047] vs. 532 [374-960] pg/mL, P = 0.033) and hsCRP (14.2 [9.8-36.1] vs. 8.6 [2.6-14.2] mg/L, P = 0.042). We found no effect of M280 and I249 on the occurrence of CAD.
Conclusion: I249 and M280 have opposite independent effects on the occurrence of ACS. The presence of I249 "unbalanced" by M280 confers an elevated risk of ACS in patients with CAD. A FKN-mediated enhanced inflammatory activation may in part explain this increased risk.

POSTER SESSION

1147 Adjunctive Therapy for Acute Myocardial Infarction

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1147-197 **Protection of LV Remodeling by Intravenous Infusion of Human Atrial Natrieuretic Polypeptide in the Patients with Acute Anteroseptal Myocardial Infarction. - Prospective Randomized Trial Assessed by Quantitative Gated Spect Imaging-**

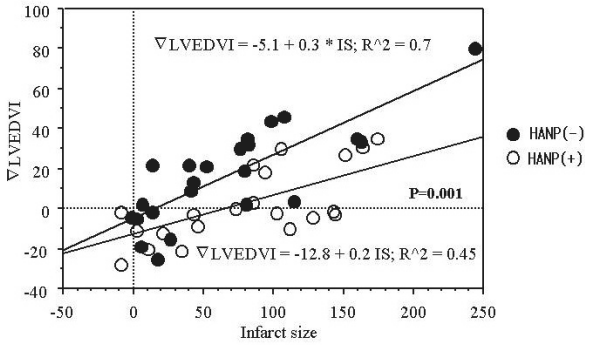
Hitoshi Matsuo, Tomonori Segawa, Takatomo Watanabe, Shunichiro Warita, Shunichiro Warita, Tai Kojima, Takeru Shiraki, Takeshi Hirose, Makoto Iwama, Kouji Ono, Masahiko Kouda, Haruki Takahashi, Yukihiko Matsuno, Sachiro Watanabe, Gifu Prefectural Gifu Hospital, Gifu, Japan

Purpose: The aim of this study is to demonstrate HANP administration combined with acute revascularization prevent LV remodeling independent of myocardial salvage.
Methods: Consecutive 44 patients with acute anteroseptal myocardial infarction were randomly assigned to either continuous infusion of HANP at a dose of 0.025 μg/kg/min for 3 days, or control. Myocardial salvage, infarct size, and LV volume was assessed by ^{99m}Tc-tetrofosmin imaging.
Results: No differences in patients backgrounds were observed. HANP suppressed LVEDVI increase in comparison with placebo (HANP:3.2±16.8 control:16.0±23.4 p<0.05) with no difference in salvage index (HANP:55.6±24.9% control:55.5±34.1%). A close correlation was observed between delta LVEDVI and infarct size in both group as shown in figure. This relationship means the linear correlation between the severity of infarct size and the degree of LV remodeling. The regression line is steeper and shifted to upward in control group than HANP infusion group, suggesting supprsive effect of HANP for LV volume expansion. Multilinear regression analysis to test the significance of HANP

infusion independent of infarct image severity score yielded a significant relationship between delta-LVEDVI and infusion of hANP ($p<0.05$) as well as infarct severity score ($p<0.001$).

Conclusion : This study clearly demonstrate that HANP can suppress LV volume expansion despite no difference of infarct size.

LV remodeling vs infarct size (Randomized trial of HANP)



Myocardial Ischemia and Infarction

1147-198 Effects Of Early Ace-inhibition In Patients With Non-STEMI Acute Myocardial Infarction.

Claudio Borghi, Stefano Bacchelli, Daniela Degli Esposti, Ettore Ambrosioni, University of Bologna, St.Orsola-Malpighi Hospital, Bologna, Italy, Menarini Research S.p.A., Firenze, Italy

Background. The early use of ACE-inhibitors is among the recommended treatments in patients with ST-elevated acute myocardial infarction (AMI) where it improves the clinical outcome.

Objective and methods. The aim of the present study is to evaluate the effects of the early administration of an ACE-inhibitor in a population of 526 non-STEMI patients enrolled in the SMILE study and randomly allocated to the treatment with zofenopril (30-60 mg/day) or matched placebo within 24 hours from the onset of symptoms of acute MI.

Results. The two populations were comparable for demography, baseline clinical characteristics and concomitant pharmacological treatment, and none of them underwent thrombolysis. Blood pressure decreases in a similar fashion in response to treatment with zofenopril or placebo. The primary end-point (6-week death+severe CHF) occurred in 10.3% of patients treated with placebo and in 3.6% of those allocated to ACE-inhibition (adjusted 2p=0.003). The 6-week rate of severe CHF was reduced from 4.0% to 0.4% (p=0.006) whereas 1 year mortality was significantly lower in patients treated with zofenopril (7.9% vs.13.9%: 2p=0.036) with a relative risk reduction of over 43.1%. Kaplan-Meier estimate of survival showed a reduced mortality in patients treated with zofenopril with an affect that was already evident after 6-weeks of treatment and increased after 12 months of follow-up (p=0.013). The benefit of early ACE-inhibition was confirmed in both males and females and in the different age groups and infarct locations.

Conclusions. The results of the present study clearly confirm the extensive role of ACE-inhibitors in patients with MI and support their primary role in patients with non-STEMI where they could interfere with the angiotensin II-mediated mechanisms responsible for coronary vasoconstriction and myocardial ischemia.

1147-229 Aqueous Oxygen Therapy for ST Segment Elevation Myocardial Infarction; Final Results and One Year Follow Up of the AMIHOT Trial

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Background: Although rapid reperfusion in ST segment elevation myocardial infarction (STEMI) reduces mortality, epicardial vessel patency does not insure full restoration of nutrient flow at the tissue level. Animal and Phase I testing of the TherOx® Aqueous Oxygen (AO) System suggest that percutaneous coronary infusion of autologous blood mixed with hyperoxemic saline may overcome the downstream barrier to oxygen delivery and improve myocardial salvage after percutaneous coronary intervention (PCI) for STEMI.

Methods: A Phase II randomized trial to evaluate the efficacy of regional AO therapy in STEMI. A sub-selective catheter positioned in the infarct artery delivers AO for 90 minutes at 75 ml/minute. Contrast echocardiography performed after PCI and before randomization is repeated at 24 hours, and days 30 and 90. Primary endpoints include regional wall motion scores, ST segment resolution and day 14 SPECT defects.

Results: Patients with anterior MI (n=144) had significantly less resolution of ST elevation after PCI alone than those with non-anterior (n=125) MI (57.8 ± 22.7 vs 75.4 ± 2.3 %, p< 0.05). Anterior MI patients randomized to AO therapy (n=70) after PCI demonstrated more complete resolution and less marked (area >5000) persistence (47 vs 35% and 9 vs 21%, p= 0.023). Core laboratory data demonstrates more improvement in regional wall motion scores at 3 months in the anterior MI group assigned to AO therapy (0.78 ± 0.56 vs 0.57 ± 0.49, p< 0.03) particularly those (n=40) treated <6 hours from symptom onset (8.1 ± 0.58 vs 0.56 ± 0.48, p=0.01). There is a trend to 6% smaller SPECT defects (p=ns). Twelve-month follow up will be available by 3/05.

Conclusion: AO after PCI for anterior MI significantly improves ST segment resolution suggesting enhanced reversal of ischemia at the tissue level. This is associated with improved convalescent regional wall motion.

1147-230 Caldaret (MCC-135) Lowers the Frequency of Severe Systolic Left Ventricular Dysfunction in STEMI patients undergoing PCI

Mark Hibberd, Dan Tzivoni, Fritz Bar, Johannes Brachmann, Hans Reiber, Mitchell Krucoff, Martin Davies, Jun Tatsuno, on behalf of the (CASTEMI) Study Group, Shaare Zedek Medical Centre, Jerusalem, Israel

Background: Recently we demonstrated that caldaret, a novel compound that modulates myocardial calcium handling, given before PCI for STEMI lowered infarct size and increased early LVEF in anterior MI. We investigated whether the frequency of severe LV dysfunction (LVD) (LVEF ≤30%) will be reduced in caldaret-treated STEMI patients.

Methods: CASTEMI enrolled 387 patients with STEMI and ≥10 mm total summed ST elevation (12 leads) undergoing primary PCI, receiving 48hr IV caldaret 57.5 mg (LD), 172.5mg caldaret (HD) or placebo (PL). Global LVEF was assessed by resting gated SPECT on Day 7/discharge and Day 30 post MI. Populations were analyzed by infarct location and pre-PCI TIMI flow.

Results: HD caldaret produced modest reductions in frequency of patients with LVD at day 7 with any TIMI flow and any MI location(Table 1). However, in anterior MI patients significant dose-dependent lowering of LVD was seen at Day 7 and 30 compared with PL.

Table 1: Percentage of patients in each treatment group with severe LVEF ≤30%, by location of index MI and pre-PCI TIMI flow

		Placebo PL		Caldaret 57.5mg LD		Caldaret 172.5mg HD	
		TIMI Flow		TIMI Flow		TIMI Flow	
Location of MI	Day of SPECT	All %(n)	0/1 % (n)	All %(n)	0/1 %(n)	All %(n)	0/1 %(n)
All MI Locations	D 7	19.4 (98)	25.7 (70)	18.8 (96)	25.0 (64)	15.5 (84)	19.2 (52)
Anterior MI	D 30	17.4 (86)	22.6 (62)	9.5 (95)	13.6 (66)	7.7 (78)	9.6 (52) p=0.080
	D 7	34.5 (55)	48.6 (37)	28.3 (53)	36.1 (36)	19.7 (61) p=0.093	23.7 (38) p=0.031
	D 30	29.8 (47)	41.9 (31)	13.7 (51) p=0.083	20.0 (35) p=0.065	10.5 (57) p=0.023	12.5 (40) p=0.006

Conclusions: Pre-PCI caldaret in STEMI patients lowered the frequency of severe LVD and could help reduce high mortality in patients with large infarcts.

1147-231 Intracoronary Hyperbaric Oxygen Administered During Primary Percutaneous Coronary Intervention Prevents One Month Left Ventricular Remodeling

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Background: Initial experience with the TherOx® Aqueous oxygen (Ao) system (TherOx Inc) in AMI patients (pts) post primary PCI shows rapid recovery of LVEF and improvement of wall motion primarily due to functional recovery within the infarct zone. We tested whether hyperbaric Ao infusion (Ao) prevents unfavorable LV remodeling.

Methods: We studied 42 pts presenting within 6 hours of onset of an anterior AMI. Angiographic inclusion criteria were initial TIMI 0-1 flow in the IRA and TIMI flow 2-3 post PCI. Pts were randomized to either treatment group (Ao group, n = 20) or control group (Non-Ao, n = 22). Ao group patients received Ao infusion for 90 minutes through a selective catheter positioned in the stent. Myocardial contrast echo was performed after 24 hours and at 1 month follow up (FU).

Results: Patients did not show any differences in baseline clinical characteristics. In the non-Ao group, EDV and ESV were significantly increased at 1 month FU demonstrating clear remodeling (p=0.004 for EDV and p=0.017 for ESV). In the Ao-group group, EDV and ESV did not significantly change at 1 month FU (p=0.600 and 0.196 respectively). In addition, ejection fraction significantly increased in the treatment group (p=0.041) but remained relatively constant in the non-Ao group (p=0.433) (see table).

Conclusion: Intracoronary hyperbaric oxygen as an adjunct to primary PCI prevents LVED dilatation and preserves LVES volume at 1 month follow up. Also, patients with Ao therapy showed improved ejection fraction at 1 month follow up.

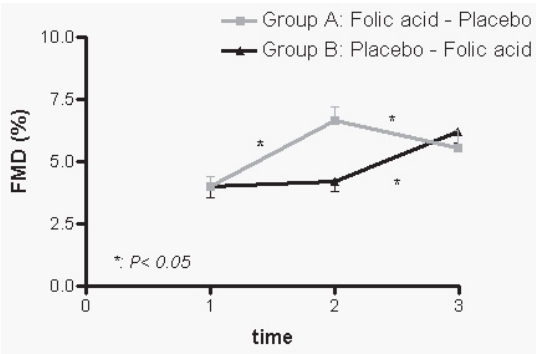
LV volumes (ml) at 24h and 1 mo

	24 hours	1 month	Delta	P value
EDV non Ao	114.2 ± 25.0	129.6 ± 31.4	15.4 ± 22.6	**0.004**
EDV Ao	119.6 ± 28.0	116.5 ± 34.2	-3.1 ± 25.8	0.600
Delta EDV Ao vs nonAo				**0.018**
ESV non Ao	56.0 ± 15.9	65.8 ± 22.6	9.8 ± 17.6	0.017
ESV Ao	62.6 ± 24.6	55.9 ± 27.3	-6.7 ± 22.3	0.196
Delta ESVAo vs nonAo				**0.011**
EF non Ao	50.5 ± 10.1	19.5 ± 9.2	-1.0 ± 5.9	0.433
EF Ao	48.8 ± 10.6	53.7 ± 11.3	5.1 ± 10.1	**0.041**
Delta EFAo vs nonAo				**0.023**

1147-232 **Beneficial Effect Of Folic Acid On Endothelial Dysfunction In Patients With Normo- And Hyperhomocysteinemia After An Acute Myocardial Infarction.**

An L. Moens, Marc J. Claeys, Inge Goovaerts, Christiaan J. Vrints, University of Antwerp, Antwerp, Belgium

Background: Folic acid (FA) has multiple mechanisms of action. It not only lowers homocysteine (HCY), e.g. it also enhances the bioavailability of tetrahydrobiopterin and it directly interacts with eNOS. In this study, we investigated the effect of folic acid on endothelial dysfunction after an acute myocardial infarction (AMI).
Material en methods: A randomized, double-blind crossover study was performed in 35 patients with AMI. In group A, FA(10mg/d) was administered for 6 w, followed by a washout period (2 w) and by a placebo period (6w). Group B received first the placebo, thereafter FA. Endothelial function was assessed by flow-mediated dilation (FMD), using high-resolution ultrasound at t1(basal), t2(week 6) and t3(week 14). All subforms of homocysteine were determined using HPLC.
Results: FMD values at t1, t2 and t3 for group A and B are shown in fig1. This effect significantly decreases after stopping folic acid administration.
The basal levels of all HCY forms were comparable between the groups. There was no correlation between all forms of HCY (baseline and Δ) and FMD (baseline and Δ).
Repeated measures ANOVA indicated a interaction effect (p=0.003).Using the different forms of HCY (baseline and Δ) as covariates in this analysis didn't abolish the interaction-effect, indicating that the beneficial effect of FA on FMD in AMI is independent of HCY.
Conclusion: Folic acid has a beneficial effect on endothelial dysfunction in patients with normo- and hyperhomocysteinemia after an AMI.



1147-233 **Efficacy of Eplerenone in Killip Class II-III Post AMI Patients: Results from EPHESUS**

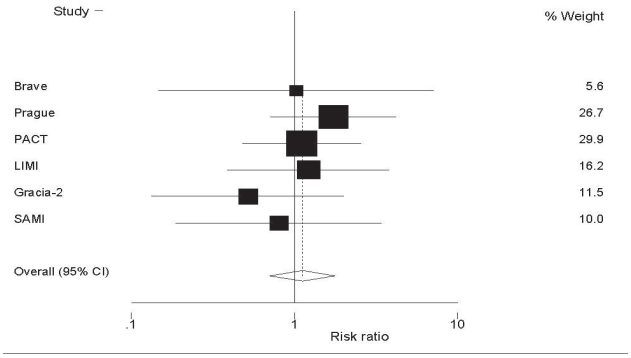
Jeffrey Anderson, Faiez Zannad, Henry Solomon, Robin Mukherjee, Rajiv Patni, Bertram Pitt, LDS Hospital, Salt Lake City, UT

Introduction: The risks of adverse outcomes following acute myocardial infarction (AMI) are believed to be associated with the presence of heart failure (HF) (Wu et al. *J Am Coll Cardiol.* 2002;40:1389), but the relationship is incompletely defined. Thus, we performed a post-hoc analysis of the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) to evaluate the efficacy of eplerenone in patients who were Killip Class II or Killip Class III.
Methods: Patients with clinical HF (Killip II or III) and left ventricular systolic dysfunction (ejection fraction ≤40%) were randomized 3-14 days after index AMI to eplerenone (25 mg titrated to 50 mg QD; N=3319) or placebo (N=3313) used with standard therapy, and followed for up to 2.5 years. Study endpoints included all-cause mortality (ACM), cardiovascular (CV) mortality (CVM), CV hospitalization (CVH), CVM/CVH, and sudden cardiac death (SCD).
Results: Among the total intent-to-treat EPHESUS population, 81% were classified as Killip Class II (64.6%) or Killip Class III (16.5%). In these patients, eplerenone reduced the risk of ACM by 19% (*P*=0.002), CVM by 20% (*P*=0.002), CVH by 9% (*P*=0.116), CVM/CVH by 14% (*P*=0.003), and SCD by 26% (*P*=0.009).
Conclusions: When compared with placebo, eplerenone reduced the risk of these endpoints in post-AMI patients who were Killip class II or III at presentation.

1147-234 **Does Facilitated Percutaneous Coronary Intervention Improve Angiographic and Clinical Outcomes in ST Elevation Myocardial Infarction? A Quantitative Review**

Thomas T. Tsai, Brahmajee K. Nallamothu, P. Michael Grossman, Debabrata Mukherjee, Stanley Chetcuti, Mauro Moscucci, Eric R. Bates, University of Michigan, Ann Arbor, MI

Background: Facilitated percutaneous coronary intervention (PCI) combines the rapidity and availability of fibrinolysis with the infarct-artery stabilization of PCI in STEMI. Randomized clinical trials (RCTs) comparing this strategy to primary PCI alone have yielded inconsistent results. We performed a quantitative review to evaluate the efficacy of facilitated PCI on early TIMI-3 flow and short-term mortality in STEMI.
Methods: We searched MEDLINE, PREMEDLINE, Current Contents and recent scientific session databases to identify relevant RCTs. A RCT was included if it: 1) involved fibrinolysis with planned PCI versus primary PCI for STEMI; and 2) reported "early" TIMI-3 flow (i.e., prior to PCI) and/or short-term mortality.
Results: Six studies with 1809 patients met the above criteria. The likelihood of TIMI-3 flow was significantly higher in patients receiving facilitated PCI (41.1% versus 12.8%; pooled relative risk-ratio [RR], 3.0; 95% CI, 2.2-4.0). However, facilitated PCI was not associated with a lower risk for short-term mortality (5.5% versus 5.1%; RR, 1.1; 95%, CI 0.7-1.8) (**Figure**). In the 4 studies reporting the outcome, major bleeding was not significantly increased with facilitated PCI (RR, 1.6; 95% CI, 0.7-3.9)
Conclusions: Facilitated PCI results in higher rates of early TIMI-3 flow when compared to primary PCI, but this advantage has not yet been associated with improved clinical outcomes. Larger trials are needed to evaluate this strategy more definitively.



1147-235 **Single High-Dose BoluS TiRofibAn and Sirolimus Eluting STEnt Versus Abiciximab and Bare Metal Stent in Acute MYocardial Infarction (STRATEGY) Study**

Marco Valgimigli, Gianfranco Percoco, Giordano Cicchitelli, Patrizia Malagutti, Gianluca Campo, Fabrizio Ferrari, Dario Barbieri, Lucia Ansani, Roberto Ferrari, University of Ferrara, Ferrara, Italy

Background: Primary bare metal stenting and abciximab infusion are currently considered the best available reperfusion strategy for acute ST-segment elevation myocardial infarction (STEMI). Sirolimus eluting stents (SES), compared to bare metal stent (BMS), greatly reduce the incidence of binary restenosis and target vessel revascularisation (TVR), but their use on a routine basis results in a significant increase in medical costs. With current European list prices, the use of tirofiban instead of abciximab would save enough money to absorb the difference between SES and BMS.
Aim: To assess whether in patients with STEMI the combination of SES with a single high dose bolus (SHDB) tirofiban regimen results in a similar incidence of death and myocardial infarction (MI) but in a lower rate of TVR and binary restenosis (BR) after six months compared to BMS and abciximab.

Methods and Results: 175 patients (mean age: 63 ± 12; 128 M) with STEMI have been randomised to a SHDB tirofiban regimen (bolus of 25 µg/Kg/3-min, followed by an infusion of 0.15 µg/Kg/min for 18-24 h) plus SES (n=87) vs. standard dosing of abciximab and BMS (n=88). Seventy-five patients in the SHDB tirofiban-SES and 77 patients in the abciximab-BMS group ultimately received the prespecified treatment combination (n=152). Analysis is based on the intention-to-treat principle. At 6 months, 115 patients underwent clinical and angiographic follow-up. The rate of major cardiovascular events (MACE) and BR were both lower in the in the tirofiban-SES (15% and 9.6%, respectively) than in the abciximab-BMS group (26% and 40%, p<0.04 and p<0.001, respectively). Cumulatively, the primary end-point, which included the summation of death, myocardial infarction and BR, occurred in 24 (41%) patients randomized to abciximab-BMS compared to 13 (23%) patients randomized to the SHDB tirofiban regimen-SES (p=0.03). In the tirofiban group, there were 1 major and 7 minor bleeds, while they were 2 and 8 in the abciximab group, respectively.
Conclusions: The combination of the SHDB regimen of tirofiban and SES is a new promising strategy for STEMI, resulting in similar cost but lower MACE and BR when compared to abciximab and BMS.

1147-236 **Transport for Abciximab Facilitated PCI Versus Onsite Thrombolysis With a Liberal Rescue Policy: A Randomized Trial in Large ST-Elevation MI Presenting Early in a Referral Hospital: The Holland Infarction Study (HIS)**

Hendrik-Jan Dieker, Elvira V. van Horssen, Ferry M.K.J. Hersbach, Marc A. Brouwer, Arnoud W. van 't Hof, Ad J. van Boven, Wim R.M. Aengevaeren, Freek W.A. Verheugt, Frits W.H.M. Bär, University Medical Center, Nijmegen, The Netherlands, University Hospital, Maastricht, The Netherlands

Introduction: HIS studied transport for abciximab facilitated primary PCI versus on-site fibrin-specific thrombolysis in patients presenting in a referral hospital. In contrast to DANAMI-2, a liberal protocol-driven rescue PCI policy was advocated in case of failed thrombolysis.
Method and Results: Patients presented with ST-elevation in a referral center having < 4.5 hrs of chest pain and ≥12 mm ST-segment shift. These patients were randomized to transport for abciximab facilitated primary PCI (FP) or to on-site thrombolysis (TT) with advocated rescue angioplasty in case of failed reperfusion (< 50% ST-resolution at 60 min. after start TT). Of the originally planned 900 patients only 48 were included, due to suspension of financial funding.

	transport for FP n=25	on-site TT n=23	p-value
time to randomization, min, median, (IQR)	130 (81 - 146)	150 (115 - 181)	0.15
time to treatment, min, median, (IQR)	230 (195 - 250)	170 (123 - 191)	< 0.01
complete ST-segment resolution (>70%)	58%	35%	0.10
CK-peak, U/l, median, (IQR)	2091 (914 - 3005)	2582 (1327 - 3370)	n.s

In the FP-group all patients received abciximab pretreatment for a median duration of 85 min. The rate of preprocedural TIMI-3 flow was 17% (TIMI 2+3, 35%) and postprocedural TIMI-3 flow was 85%. In the TT-group 48% underwent urgent catheterization of which 58% had TIMI-3 flow at angiography and 55% underwent immediate PCI.
At 30 days 1 patient (4%) died in the FP-group, in the TT-group 2 (9%) patients died and one (4%) had non-fatal MI.
Conclusion: Patients treated with abciximab facilitated primary PCI tended to have more complete ST-resolution and smaller infarctions than thrombolytic treated patients with a liberal rescue strategy. Larger studies should address the optimal treatment strategy for patients presenting in hospitals without intervention facilities.

POSTER SESSION

1148 Chronic Stable Angina: Evaluation and Management

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1148-223 Risk of First Coronary Ischemic Events Following First Atrial Fibrillation: Data from 2 Decades (1980-2000)

Yoko Miyasaka, Marion E. Barnes, Stephen S. Cha, Kent R. Bailey, James B. Seward, Walter P. Abhayaratna, Bernard J. Gersh, Teresa S.M Tsang, Mayo Clinic, Rochester, MN

Background: Although coronary artery disease (CAD) is known to be a risk factor of AF, the risks of symptomatic CAD following first AF are not well characterized.
Methods: The medical records for residents of Olmsted County, MN, with an ECG-confirmed diagnosis of first AF between 1980 and 2000 were reviewed. Cox proportional hazards modeling was used to assess overall and sex-specific incidence of new symptomatic CAD following incident AF. Time dependent Cox modeling was used to assess prognosis following coronary events.
Results: Of 4618 residents (mean age 73 ± 14 years, 51% men) who developed first AF in 1980-2000, 1771 (38%) had prior CAD, and 180 (4%) diagnosis of first ischemic coronary event and first AF was made on the same day. Of the remaining 2667 patients without CAD at the time of AF onset, 818 (30%) developed a first coronary ischemic event during a mean follow up of 6 ± 5 years, and1580 died. Age (P<0.0001), but not sex, and multiple other factors were independently predictive of ischemic coronary events within 5 years (Table). The Kaplan-Meier estimate of cumulative probability of the development of a first coronary ischemic event was 25% and 41% at 5 and 10 years, respectively. The occurrence of post-AF ischemic coronary events was associated with significantly increased mortality risk (HR=11.20, p<0.001).
Conclusions: Symptomatic CAD developed in a significant proportion of patients following first AF, which conferred substantial mortality risk. Age, but not sex, was predictive of such events.

Table:

Variable	HazardRatio	Lower95% CI	Upper 95% CI	*P-value*
Calendar Year	1.03	1.022	1.038	<.0001
BMI (kg/m^2)	1.014	0.998	1.029	0.0797
History of ASO	1.522	1.103	2.101	0.0106
History of diabetes mellitus	1.451	1.077	1.955	0.0144
History of dyslipidemia	1.139	0.92	1.411	0.2316
History of hypertension	1.982	1.545	2.544	<.0001
Current and past smoker	0.947	0.779	1.151	0.583
1 / Creatinine (dl/mg)	0.868	0.62	1.215	0.408
Log glucose	0.991	0.642	1.53	0.9669

1148-224 Creatinine Clearence Independently Predicts Extent And Severity Of Coronary Atherosclerosis In Patients With Stable Coronary Artery Disease

Johann Auer, Thomas Weber, Gudrun Lamm, Robert Berent, Elisabeth Lassnig, Michael Porodko, Edwin Maurer, Bernd Eber, General Hospital Wels, Wels, Austria

Background: Although there is accumulating evidence that renal insufficiency is associated with an increased risk for cardiovascular events in patients with coronary artery disease (CAD), it is not known whether creatinine clearence rates a the time of hospital admission is associated with the extent and severity of coronary atherosclerosis assessed angiographically.
Patients and Methods: We studied 1062 consecutive white subjects (336 women and 726 men; mean age 65.6 +/- 18.8 years) undergoing coronary angiography for stable CAD at a single referral center. In addition to conventional risk factors and clinical characteristics as predictors of extent and severity of coronary atherosclerosis, we assessed creatinine clearence rates at the time of admission. Two experienced cardiologists blinded to the clinical and laboratory data reviewed the angiographic films and defined severity of CAD on the basis of the sum of three scoring systems, whose total score could range from 0 to 27.
Results Patients were devided into three groups according to CAD severity score. Creatinine clearence rates were 67.5±12.8, 60.1±15.9, and 57±18.3 mL/min for group I (410 patients; CAD score 0 to 3), group II (316 patients; CAD score 4-8), and group III (336 patients; CAD score >8), respectively (p<0.05). Significant renal dysfunction, as defined by the National Kidney Foundation as an estimated glomerular filtration rate of <60 ml/min/1.73 m^2, was significantly more common in groups II and III compared to group I (p<0.01). When grouped according to levels of creatinine clearence (group A: >75 mL/min; group B: ≤75 to >68; group C: ≤68 to >58; group 4: ≤58), scores of the angiographic CAD severity were 5.0±3.7, 5.64±3.6, 6.63±4.1, and 7.35±4.0, respectively (p for trend <0.0001). After adjustment for baseline characteristics including age, gender, and CAD risk factors, patients in groups C and D had significantly higher scores of CAD severity as compared to group A and B patients (p<0.01).
Conclusion: Creatinine clearence on admission independently predicts extent and severity of coronary atherosclerosis in patients with stable CAD. Thus, increased serum creatinine may be a marker for non-traditional proatherogenic factors.

1148-225 Evaluation of Patients with Dyspnea Without Chest Pain: Prevalence and Predictors of Coronary Artery Disease (CAD) Using Myocardial Perfusion Imaging (SPECT) and Coronary Angiogram (CATH)

Su Min Chang, Regina Chu, Douglas Russell, Timothy F. Christian, University of Wisconsin, Madison, WI

Background: Dyspnea could precede angina as manifestation of CAD.
Objectives: In dyspneic patients (pts) with no chest pain (CP) , examine the prevalence and predictors of CAD as myocardial perfusion abnormality (MPA) by SPECT and angiographic coronary stenosis (> 50 %) (CAS).
Method: SPECT was performed in 915 pts with dyspnea alone and 1357 pts with CP alone . CATH was done in 238 and 452 pts respectively. High risk MPA was defined as >15 % LV perfusion defect size(LVPDS) , multivessel or LAD distribution and Severe CAS as left main, 3 VD or 2VD involving LAD.
Results: Compared to pts with CP, dyspneic pts were older (65 +-12 vs 61+-12 y/o) , had less MI (17 % vs 24 %), similar risk factors but less likely to exercise (35 % vs 48 %) (all p < 0.01). Prevalence of MPA (44% vs 45 % p =0.8) , high risk MPA (27 % vs 29 % p =0.6) and LVPDS (18.8+-14 % of LV vs 19.8 +- 15 % p =0.7) were about equal. No statistical significance on CATH finding : 73 % of dyspneic pts had CAS vs 79 % of pts with CP and 33 % vs 37% were severe.(p= ns). Both groups had similar univariate predictors of MPA : age > 65, male, h/o MI, diabetes (DM), abnormal ECG, inability to exercise and positive stress ECG. Of CAS were DM, hyperlipidemia and MPA for dyspneic pts , and DM, positive stress ECG and MPA for pts with CP. Independent predictors of severe CAD were shown on table.
Conclusion: In dyspneic pts referred for SPECT/CATH, the prevalence and predictors of CAD appeared similar to pts with CP alone. Inability to exercise, positive stress ECG and high risk MPA identified pts at high risk for severe CAS.

all p< 0.05

Pts with Dyspnea alone	Odds Ratio (95% CI)	**Pts with CP alone**	Odds Ratio (95% CI)
Severe CAS Inability to exercise	2.24 (1.03 - 4.9)	**Severe CAS** Diabetes	1.96 (1.14-3.4)
Positive stress ECG	5.5 (2.1 - 14.3)	Positive stress ECG	1.85 (1.02-3.3)
MPA	3 (1.2 - 7.2)	MPA	3.2 (1.7 -6)
High risk MPA	2.6 (1.3 - 5.2)	High risk MPA	3.1 (1.8 -5.1)
High Risk MPA Male	2.4 (1.7 - 3.5)	**High Risk MPA** Male	2.05 (1.5-2.8)
h/o MI	4.1 (2.8 - 6.2)	h/o MI	1.55 (1.08-2.2)
Diabetes	2 (1.36 - 2.9)	Diabetes	1.64 (1.16-2.3)
Inability to exercise	2 (1.34 - 3)	Inability to exercise	1.96 (1.4-2.7)
Positive stress ECG	2.4 (1.4 - 4.2)	Positive stress ECG	2.5 (1.6 -3.8)

1148-226 Should Erectile Dysfunction Be Considered as a Sign of Occult Coronary Artery Disease?

Charalambos Vlachopoulos, Nikolaos Ioakeimidis, Konstantinos Rokkas, Konstantina Aggeli, Andreas Michaelides, Konstantinos Aznaouridis, Athanassios Askitis, Christodoulos Stefanadis, Athens Medical School, Athens, Greece

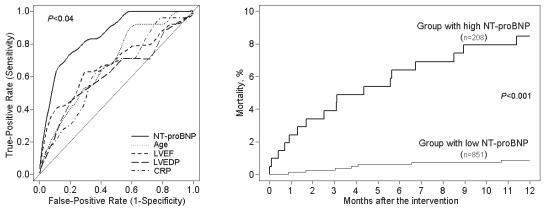
Background: Erectile dysfunction (ED) shares many risk factors with coronary disease (CAD) and in most of the cases of ED the underlying abnormality is endothelial dysfunction in the penile arteries. The aim of this prospective study was to evaluate the incidence of asymptomatic CAD in men with ED of vascular origin.
Methods: Twenty-six consecutive asymptomatic men, aged 40-70 years, with non-psychogenic and non-hormonal ED were compehensively evaluated using medical history, exercise teadmill test and stress echocardiography. Patients who had positive one or both of the two non-invasive procedures were referred for coronary arteriography in order to document CAD and evaluate the severity of the disease.
Results: The mean time interval between the onset of ED and cardiological assessment was 14 months (range 2-36). Smoking (17 pts/65%), hypertension (15 pts/58%) and hyperlipidemia (13 pts/50 %) were the most common risk factors, followed by diabetes mellitus (5 pts/20 %) and family history (3 pts/11%). Moreover, 19 (73 %) men had two or more risk factors. One patient presented with myocardial infarction before he completed the non-invasive investigation and coronary arteriography was performed during hospitalization. In addition, eight (32 %) patients with ED had positive one or both of the two non-invasive procedures. Coronary arteriography performed in 6 patients with positive one or both of the two non-invasive procedures and in the patient with myocardial infarction demostrated that 5 patients had single-vessel disease (1 pt LAD, 3 pts LCx, 1 RCA) and 1 patient had coronary artery ectasia.

Conclusions: A considerable proportion (23%) of patients with ED of vascular origin have angiographically documented CAD. These findings support the strategy that patients with ED should undergo further cardiovascular evaluation.

1148-227 Prognostic Value of N-Terminal Pro-Brain Natriuretic Peptide in Patients with Chronic Stable Angina

Gjin Ndrepepa, Siegmund Braun, Kathrin Niemöller, Julinda Mehilli, Nicolas von Beckerath, Olga Gorchakova, Wolfgang Vogt, Albert Schömig, Adnan Kastrati, Deutsches Herzzentrum, Munich, Germany

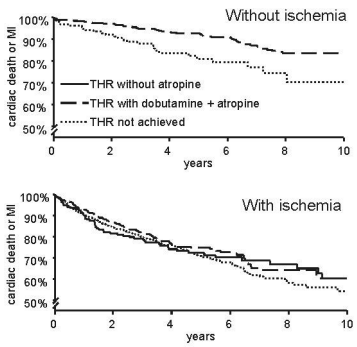
Background: Patients with stable angina are poorly characterized in terms of biomarkers that may help in the assessment of prognosis. We investigated whether N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) may be used as a prognostic marker in patients with stable angina treated with coronary stenting.
Methods: Plasma NT-proBNP was measured in 1059 patients with stable angina and angiographic confirmation of significant coronary artery disease. The primary end point was mortality at one year.
Results: Using receiver operating characteristic curve analysis, the best cutoff value of NT-proBNP maximizing sensitivity and specificity for prediction of one-year mortality was 1048 pg/ml. Patients were divided into 2 groups: the group with NT-proBNPgreater than 1048 pg/ml (the high NT-proBNP group, 208 patients) and the group with NT-proBNP less than1048 pg/ml (the low NT-proBNP group, 851 patients). At one year there were 17 deaths (8.2%) among the patients in the high NT-proBNP group and 7 deaths (0.8%) among the patients in the low NT-proBNP group (odds ratio 10.4, 95% confidence interval [CI] 5.1 - 21.1, *P*<0.001). Plasma NT-proBNP was the strongest independent correlate of one year mortality (adjusted hazard ratio [HR] 1.4, 95% CI 1.07 - 1.22, *P*<0.001) followed by left ventricular ejection fraction (HR 0.52, 95% CI 0.31 - 0.88, *P*=0.01) and age (HR 2.23, 95% CI 1.11 - 4.51, *P*=0.024).
Conclusions NT-proBNP is a strong prognostic biomarker in patients with chronic stable angina.



1148-228 Long-term Prognosis Of Dobutamine-atropine Stress Echocardiography: The Impact Of Heart Rate Response

Boudewijn J. Krenning, Jeroen J. Bax, Elena Biagini, Vittoria Rizzello, Arend F.L. Schinkel, Ron T. van Domburg, Maarten L. Simoons, Don Poldermans, Thoraxcenter, Rotterdam, The Netherlands

Background: During dobutamine-atropine stress echocardiography (DSE) atropine is frequently added to overcome the negative chronotropic effect of concomitant anti-ischemic therapy. The aim of this study was to assess the long-term prognostic value of atropine addition and a sub-maximal DSE.
Methods and results: 3,800 patients undergoing DSE between 1989 and 2002 were evaluated for heart rate response, test results, and long-term cardiac events (cardiac death and myocardial infarction). Patients were followed for 6±4 years; 217 underwent revascularization within 3 months and were excluded, 50 patients were lost-to follow-up. Patients were divided into three groups; group 1 THR using dobutamine (n=1917); group 2 THR achieved after the addition of atropine (n=1247), and group 3 THR not achieved (n=419). Test end-points in group 3 were: maximum dose (47%), severe ischemia (21%), and side effects (32%). The 5-year cardiac event rate in patients in group 1 and 2 with and without new wall motion abnormalities (NWMA) was comparable, 5.6% vs 4.8%, and 1.5% vs 1.5%, respectively, p=NS. However, a sub-maximal test had a 5-year cardiac event rate of 18% in the absence of NWMA, while in the presence of ischemia the prognosis was poor (5-year cardiac event rate 30%).
Conclusion: A completed DSE has an excellent prognostic accuracy, irrespective of the addition of atropine. A sub-maximal DSE carries a high risk for cardiac events despite a normal test outcome, while patients with severe ischemia have a poor prognosis.



POSTER SESSION

1149 Novel Methods in CABG Outcomes

Tuesday, March 08, 2005, 1:30 p.m.-5:00 p.m.
Orange County Convention Center, Hall E1
Presentation Hour: 1:30 p.m.-2:30 p.m.

1149-195 Effectiveness of N-3 Fatty Acids for the Prevention of Atrial Fibrillation After Coronary Artery Bypass Surgery

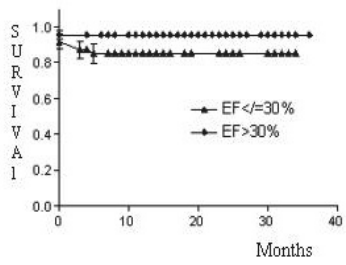
Leonardo Calo', Leopoldo Bianconi, Antonella Meo, Filippo Lamberti, Maria Luisa Loricchio, Ermenegildo de Ruvo, Furio Colivicchi, Claudio Pandozi, Massimo Santini, San Filippo Neri Hospital, Rome, Italy

Background: Postoperative atrial fibrillation (AF) is a common complication of coronary artery bypass surgery (CABG) and several studies have explored the effectiveness of pharmacological and non-pharmacological interventions for prevention of AF. Recently, there is growing clinical evidence that n-3 polyunsaturated fatty acids (PUFA) have cardiac antiarrhythmic effects. Aim of this study was to assess the efficacy of preoperative and postoperative treatment with n-3 PUFA in preventing the occurrence of AF after CABG.
Methods: A total of 150 patients were prospectively randomized to control group (76 patients, 13 female, 65 ± 9 years) or PUFA 2 g/day (74 patients, 11 female, 66 ± 8 years) for a minimum of 7 days before elective CABG and until the day of discharge from the hospital. Exclusion criteria included prior AF, concurrent therapy with class I or III antiarrhythmic drugs, or concomitant valve surgery. The primary endpoint was the development of AF in the postoperative period.
Results: The clinical characteristics of the patients in the 2 groups were similar. Postoperative AF developed in 27 patients of control group (35.5%) and in 11 patients of PUFA group (14.9%) (P=0.006). Non fatal postoperative complications occurred in 5 patients who received n-3 PUFA (6.8%) and in 6 controls (7.9%, P=NS). Postoperative mortality was not significantly different in n-3 PUFA-treated patients (1 patient, 1.4%) versus controls (1 patient, 1.3%). After CABG, the patients in the n-3 PUFA group were hospitalized for significantly fewer days than those in the placebo group (7.2 ± 1.9 days versus 8.3 ± 3.2 days, P < 0.05).
Conclusions: This study first demonstrates that the preoperative and postoperative administration of n-3 PUFA (2g/day) was associated with a significant decrease (58%) in postoperative AF in patients undergoing CABG without side effects.

1149-196 Mid-Term Clinical and Hemodynamic Outcome Following Surgical Ventricular Restoration in Patients with Ischemic Cardiomyopathy

Marisa Di Donato, Serenella Castelvecchio, Alessandro Frigiola, Lorenzo Menicanti, San Donato Hospital, San Donato Milanese, Milano, Italy

Background. Pts with ischemic cardiomyopathy and EF =/< 30% are at high risk of death, mostly of arrhythmic origin. We followed-up (FUP)122 pts (65±10 yrs,20F) operated by surgical ventricular restoration (SVR) for post-anterior infarction and symptoms of angina and/or heart failure.
Aim: to assess survival and the rate of events following SVR at mid term follow-up (18±8 months,min 3 max 33).
Patients: Group 1(G) with pre-op EF=/<30% , median 24% (n=53) and Group 2 with pre-op EF>30%, median 36%(n=69). All had SVR with the use of a shaper device and coronary graftings.All pts had pre and post-op echocardiogram and 46 had late echo at 18±8 m. On telephone interview we assessed: functional status,death,rate of hospitalization,cardiac procedures,cardiac events.
Results: FUP was completed in 88% of pts. NYHA class from 2.4±0.6 to 1.2±0.6 p=0.0001. EF from 24+/-4 to 35+/-4 in G 1 and from 38±6 to 45±8 % in G 2 (p 0.0001). Two operative cardiac deaths in G1 (3.6%) and 3 in G 2 (4.3%). Two late deaths in G1 (at 3 and 5 months; 1 for sudden death). No late deaths occurred in G 2. In G 1 seven pts (13.5%) had cardiac hospitalization: 3 pts had implantable defibrillator for ventricular arrhythmias (5.8% of survivors); 1 pt had biventricular pacing (2%) and 1 had stroke. Seven pts in G 2 required cardiac hospitalization (10.6%): 1 pts had PTCA for myocardial infarction (1.5%) and one had pace maker (1.5%).
Conclusions: SVR improves pump function and functional status. Survival is excellent and the rate of events is low even in pts with </=30 EF% .



1149-199 Sustained Regional Improvement in Myocardial Perfusion One Year After Transplantation of Autologous Bone Marrow Cells in Patients With Diffuse Coronary Artery Disease

Luis Henrique W. Gowdak, Isolmar T. Schettert, Carlos Eduardo Rochitte, Luiz Antonio M. Cesar, Protasio L. da Luz, Jose Eduardo Krieger, Jose Antonio Ramires, Sergio A. de Oliveira, Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil

Background: Adult bone marrow cells (BMC) have recently been tested as a novel therapeutic option for patients (pt) with severe coronary artery disease (CAD). However, little data is available regarding the duration of the angiogenic effect shortly seen after the cell injections. The aim of this study was to verify whether the increase in myocardial perfusion after intramyocardial injection of autologous BMC could be sustained in the long-term.
Methods: 10 pt (8 men), 59±6 years-old, with limiting angina and 3-vessel CAD, not amenable to complete CABG due to the diffuseness of the disease were enrolled. BMC were obtained immediately prior to surgery, and the lymphomonocytic fraction separated by density gradient centrifugation. During surgery, 4mL containing $13\pm3x10^7$ BMC (CD34+ = 1.3±0.4%) were delivered by multiple injections in the ischemic non-grafted myocardium. Before (B), 1 (1M), 3 (3M), 6 (6M) and 12 (12M) months after surgery, myocardial perfusion (at rest and after pharmacological stress with adenosine) was assessed in 17 segments by magnetic resonance imaging (MRI). Each segment was blindly graded as normal (0), or having mild (1) or severe (2) perfusional defect. An ischemic score (IS) comprising all 17 segments (*total IS*) or only those injected non-grafted segments (*regional IS*) was calculated.
Results: Injected myocardial segments (n=12) included the inferior (n=7), anterior (n=2), septal (n=1), apical (n=1) and lateral (n=1) walls. No complications or deaths occurred. As expected, MRI showed a sustained reduction in total IS (B=0.65±0.14, 1M=0.15±0.08, 3M=0.24±0.10, 6M=0.11±0.06 and 12M=0.17±0.05; P=0.002) but more interestingly also in the regional IS (B=1.11±0.20, 1M=0.28±0.21, 3M=0.51±0.25, 6M=0.35±0.18, and 12M=0.34±0.13; P=0.0009).
Conclusions: In this small series of pt, one-year after a single procedure of intramyocardial injection of autologous BMC combined to CABG, a sustained increase in myocardial perfusion could be verified. Provided the angiogenic effect seen in this trial is confirmed in a larger randomized trial, this strategy could be used for myocardial angiogenesis in pt with a more advanced CAD not suitable for complete surgical revascularization.

1149-200 Electrocardiographic Left Ventricular Mass and Conduction and Long-Term Survival Following Coronary Bypass Surgery

Derlis Martino, Eugene Blackstone, Ken Baker, Michael Lauer, Cleveland Clinic Foundation, Cleveland, OH

Objective: Electrocardiographic left ventricular (LV) mass and QRS duration predict adverse outcomes in healthy populations. We sought to determine if QRS duration and ECG LV mass predict survival in patients undergoing primary isolated CABG.
Methods: Digital data on preoperative ECGs on 13,427 patients undergoing primary isolated CABG between 1991 and 2002 were analyzed for QRS duration and the Cornell voltage criteria for LV mass (sum of R wave in avL and S wave in V3). Excluded were patients with pacemakers and Wolff-Parkinson-White syndrome. The primary endpoint was all-cause mortality during a median of 6.3 years of follow-up.
Results: There were 2,749 deaths. Increased QRS duration was strongly associated with death (Figure 1).

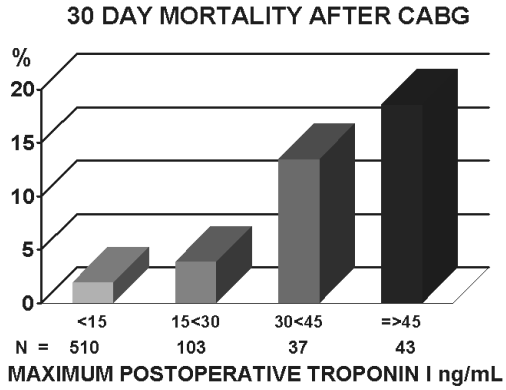
Figure 1

After adjusting for demographics, cardiovascular risk factors, surgical characteristics, LV function, severity of coronary disease, renal function, and other ECG findings (including heart rate, Q waves, and bundle branch block), QRS duration remained a strong predictor of risk (P<0.0001). Cornell voltage also provided additional prognostic information to QRS duration.
Conclusions: The finding that increasing QRS duration is a strong independent risk factor for late mortality in patients undergoing CABG has not previously been reported. This effect was seen even at the low end of the spectrum of QRS durations, and was not dependent on left or right bundle branch blocks or evidence of myocardial infarction. The Cornell criteria were also predictive of mortality, but less so.

1149-201 Postoperative Troponin I is a Better Predictor of 30 Day Mortality Following Coronary Artery Bypass Compared to the Postoperative Electrocardiogram.

Henry S. Loeb, Donald Depinto, Donald D. Thomas, II, William P. Gunnar, Edward Hines Jr. Veteran's Administration Hospital, Hines, IL, Loyola University Stritch School of Medicine, Maywood, IL

Background: The EKG is routinely used after coronary artery bypass (CABG) to identify patients with perioperative myocardial infarction (MI) for whom closer monitering might be indicated. After CABG however the EKG often is difficult to interpret due to non specific changes. Elevation of troponin i (TROP) is a highly specific and sensitive marker for myocardial damage and therefore could be useful in identifying patients at risk for an adverse outcome following CABG.
Methods: We studied 693 consecutive patients undergoing isolated elective CABG in whom at least one postoperative TROP was obtained. The sensitivity of TROP and of postoperative EKG changes for prediction of 30 day mortality were compared.
Results: Of the 693 patients undergoing CABG, 27 patients (3.9%) expired within 30 days of surgery. Maximum postoperative TROP was =>15ng/mL in 17 of these patients (63%) where as only 6 of these patients (22%) had an EKG diagnosis of perioperative MI. Of the 666 survivors 25% had a post operative TROP =>15ng/mL and 8.6% had perioperative MI by EKG.
Thirty day mortality was directly related to the maximum postoperative value of TROP .



Conclusions: Elevation of TROP =>15ng/mL following CABG is a much better predictor of 30 day mortality than is the postoperative diagnosis of perioperative MI by EKG. The direct relationship between the extent to which TROP increases following surgery and 30 day mortality suggests that such patients have significant myocardial damage not identified by postoperative EKG changes.

1149-202 A Novel C5-Binding Nucleic Acid Aptamer That Protects Isolated, Perfused Mouse Hearts From Human Complement-Mediated Damage and Inhibits Primate C5 Activity In Vivo

James Rottman, Claude Benedict, Jeffrey Kurz, David M. Epstein, Archemix, Cambridge, MA

Background and Aims: Activation of the complement (C') cascade during coronary artery bypass (CABG) surgery causes morbidity and mortality mediated by C5 cleavage products C5a and C5b-9. We synthesized a nucleic acid aptamer that binds human and primate C5 with high affinity (human K_D = 600 +/- 100 pM) and inhibits zymosan-mediated C5 cleavage and C'-mediated lysis of sheep erythrocytes. We studied the ability of this aptamer to inhibit human C5-mediated damage of isolated, perfused mouse hearts and to inhibit primate C5 activity in vivo.
Methods: Mouse hearts were perfused with Krebs-Heinseleit buffer containing 6% human plasma + / - aptamer. During each experiment, hearts were observed for myocardial dysfunction (increased end-diastolic pressure, and asystole). Heart sections were examined by immunohistochemistry (IHC) for deposition of C5b, and the heart buffer effluent was assessed for C3a, C5a and C5b-9 levels by ELISA.The aptamer was then administered to macaques by bolus and C5 inhibition assessed by zymosan activation of serial plasma samples.
Results: When the C5 aptamer was added to the heart perfusate in a 50-fold or 10-fold molar excess over plasma C5 (25 μM or 10 μM), myocardial dysfunction and C5b deposition were observed in 0/5 and 0/4 hearts, respectively. At C5 aptamer concentrations equivalent to plasma C5 levels (0.5 μM), or with irrelevant aptamer (25 μM) or in the absence of any aptamer, C5b deposition and myocardial dysfunction were observed in 3/3, 3/3 and 5/5 mice, respectively. The heart perfusion effluent contained equivalent amounts of C3a in all groups, but the C5 aptamer inhibited C5a and C5b-9 generation in a dose-dependent manner. The aptamer completely inhibited zymosan-mediated activation of primate plasma C5.
Conclusion: The C5-aptamer may be useful to protect human CABG patients from complications of complement activation.

ORAL CONTRIBUTIONS

850 Treatment Approaches in Acute Ischemic Syndrome

Tuesday, March 08, 2005, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Room 414A

2:00 p.m.

850-3 Intensive Statin Therapy Reduces CRP in Acute Cornonary Syndrome Patients With Metabolic Abnormalities and Adverse Lifestyle Features: An Analysis From PROVE IT-TIMI 22

Kausik K. Ray, Christopher P. Cannon, Richard Cairns, Ajay J. Kirtane, David A. Morrow, Carolyn Hoss McCabe, C. Michael Gibson, Paul M. Ridker, Eugene Braunwald, Brigham and Women's Hospital, Boston, MA, Harvard Medical School, Boston, MA

Background and Aims: CRP is an important prognostic indicator of cardiovascular risk and statin therapy has been shown to reduce CRP. A number of factors such as adverse lifestyle and components of the metabolic syndrome are associated with an elevated CRP. We sought to investigate whether intensive statin therapy reduced CRP in these subgroups, more than standard dose statin therapy within the PROVE IT-TIMI 22 study.
Methods: The effect of intensive (atorvastatin 80mg) vs standard (pravastatin 40 mg) statin therapy on CRP (n=3507) at 4 months after an ACS in smokers, diabetics and among individuals with components of the metabolic syndrome was assessed.
Results: Intensive statin therapy was associated with a lower CRP in each group (see table). In a multivariable model after accounting for treatment groups, a number of clinical factors remained associated with CRP: age (p<0.0001), female sex (p<0.0001), smoking (p<0.0001), BMI>25(p<0.0001), Triglyceride >150mg/dl (p=0.0005), HDL<50 mg/dl (p=0.001), glucose (p=0.009), on treatment LDL (p<0.0001), % change in LDL from baseline (p=0.02) and intensive statin therapy (p<0.0001).
Conclusion: Our data demonstrates that intensive statin therapy is effective at reducing CRP across many high-risk subgroups of ACS patients. Potential therapeutic areas to target for further reductions in CRP are control of non-LDL metabolic abnormalities and lifestyle modification.

The effect of intensive statin therapy on 4 month CRP
(median IQR)

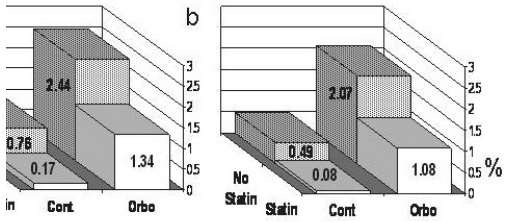
Sub-Groups	Standard Therapy (pravastatin 40mg)	Intensive therapy (atorvastatin 80mg)	p
Age >65	2.12 (1,4.6)	1.41 (0.7,3)	<0.001
Female	3.44 (1.4,7.2)	2.22 (1,5.1)	<0.001
BMI >25 (Baseline)	2.2 (1.1,4.8)	1.42 (0.7,3.1)	<0.001
Current Smokers	2.4 (1.2,5.6)	1.77 (0.8,3.6)	<0.001
Diabetes (baseline)	2.74 (1.3,5.5)	1.51 (0.7,3.5)	<0.001
Glucose>110mg/dl (on Tx 4 mth)	2.89 (1.2,6)	1.44 (0.7,3)	<0.001
HDL <50mg/dl (on Tx 4 mth)	2.15 (1,4.5)	1.34 (0.7,3.1)	<0.001
Triglyceride >150 mg/dl (on Tx 4 mth)	2.39 (1.2,5.1)	1.68 (0.8,3.6)	<0.001
BP >130/85 (On Tx at 4 mth)	2.56 (1.2,4.8)	1.39 (0.7,3.2)	<0.001

2:15 p.m.

850-4 Use of Statins Is Associated With Decreased Risk of Bleeding in Patients With Unstable Coronary Syndromes Treated with Antiplatelet Therapy

Yochai Birnbaum, Salvatore Rosanio, Sabina Murphy, Mohammad Saeed, Atiar M. Rahman, Christopher P. Cannon, University of Texas Medical Branch, Galveston, Brigham and Women's Hospital, Boston, MA

Background: Antiplatelet therapy improves outcome in patients with acute coronary syndrome (ACS), but increases bleeding rates. Independent of their lipid-lowering mechanism, statins upregulate the production of PGE_2 and PGI_2 which may protect the gastrointestinal (GI) tract. We studied whether statins reduce the risk of bleeding associated with antiplatelet therapy.
Methods: Retrospective analysis of the Orbofiban in Patients with Unstable coronary Syndromes (OPUS-TIMI-16) trial that compared orbofiban (ORBO) and placebo in 10,288 patients with ACS. All patients received ASA 162 mg/d.
Results: GI bleeding occurred in 1.89% and 0.94% of the patient -/+ statins (p<.001). Statins were associated with less overall bleeding in both the ORBO (p=.001) and placebo (p=.017) groups (Fig. 1a). Severe and major GI bleeding occurred in 1.55% and 0.74% of the patients -/+ statins (p<.001). Statins were associated with less severe and major bleeding in both the ORBO (p=.001) and placebo (p=.043) groups (Fig. 1b). Logistic regression analysis showed that the use of statins (OR 0.57; 95% CI 0.38-0.85; p=.005), age >65 y (5.27; 3.53-7.87; p<.001), ORBO treatment (4.07; 2.45-6.77; p<.001), Killip ≥2 (1.61; 1.05-2.51; p=.030), history of cardiovascular disease (1.99; 1.04-3.79; p=.036), and the use of calcium channel blocker (1.47; 1.05-2.07; p=.027) were independently associated with the risk of GI bleeding.
Conclusions: Statins may protect against gastrointestinal bleeding in patients with ACS.



2:30 p.m.

850-5 Predictors of Major Bleeding and Transfusion in SYNERGY: Effects of Pretreatment Variables and Treatment Assignment

Sunil V. Rao, Kenneth W. Mahaffey, Elliott Antman, Neal S. Kleiman, James J. Ferguson, Robert M. Califf, Richard C. Becker, Shaun G. Goodman, Philip E. Aylward, Duke Clinical Research Institute, Durham, NC

Background: In the SYNERGY trial (N=9978), enoxaparin was noninferior to unfractionated heparin in patients with acute coronary syndromes, but was associated with a modest increase in bleeding. We determined predictors of bleeding and transfusion among patients treated with enoxaparin or unfractionated heparin.
Methods: Predictive models for GUSTO severe bleeding, TIMI major bleeding, and transfusions were developed from baseline characteristics. Stepwise logistic regression was used to determine independent predictors of the three outcomes. Interactions between treatment arm and candidate predictors were considered.
Results: Independent predictors of the three outcomes are shown. Enoxaparin was not an independent predictor of bleeding in any model. No significant interaction between treatment and other variables for GUSTO severe bleeding or transfusions was seen. However, for TIMI major bleeding there was a significant interaction between creatinine and treatment such that patients with elevated creatinine treated with enoxaparin were more likely to have a TIMI major bleed.

Conclusions: Treatment with enoxaparin is not associated with GUSTO severe bleeding or transfusions, but is associated with TIMI major bleeding in patients with renal insufficiency. This emphasizes the need for careful dosing of enoxaparin in patients with abnormal renal function.

Independent predictors of bleeding and transfusions

GUSTO severe bleeding		TIMI major bleeding		Blood transfusion	
Predictor	Odds ratio (95% CI)	Predictor	Odds ratio (95% CI)	Predictor	Odds ratio (95% CI)
ST-segment depression	1.52 (1.16-1.98)	Region (Americas vs. others)	2.23 (1.78-2.78)	Region (Americas vs. others)	1.93 (1.66-2.25)
Age (per 10 yr increase)	1.22 (1.03-1.46)	ST-segment depression	1.62 (1.39-1.89)	ST-segment depression	1.58 (1.40-1.78)
Renal function (per 5 mL/hr increase in creatinine clearance)	0.91 (0.85-0.97)	Baseline hematocrit	1.38 (1.27 - 1.5)	Baseline hemoglobin	0.75 (0.72-0.78)
Prior CABG	0.51 (0.34-0.77)	Age (per 10 yr increase)	1.33 (1.21-1.48)	Prior CABG	0.48 (0.40-0.57)
Region (Europe vs. others)	0.47 (0.31-0.71)	Renal function (per 10 mg/dL increase in creatinine) and enoxaparin treatment	1.09 (1.05-1.13)		
		Prior CABG	0.48 (0.38-0.61)		

2:45 p.m.

850-6 Enoxaparin Versus Unfractionated Heparin: Consequences of Treatment Duration on Efficacy and Safety in SYNERGY

James J. Ferguson, Kenneth W. Mahaffey, Yao Huang, Paul Armstrong, Glenn Levine, Neal S. Kleiman, Shaun G. Goodman, Marc Cohen, Elliott Antman, Robert M. Califf, for the SYNERGY Investigators, Texas Heart Institute, Houston, TX, Duke Clinical Research Institute, Durham, NC

Background: SYNERGY randomized 9978 patients with non-ST-segment elevation acute coronary syndromes (NSTE ACS) managed with an early invasive strategy to enoxaparin or unfractionated heparin (UFH). Questions remain as to the effect of treatment duration on outcomes in patients coming rapidly to the catheterization laboratory.
Methods: We evaluated death/myocardial infarction (MI) and TIMI major bleeding as functions of treatment duration for enoxaparin and UFH. Since 75% of patients received antithrombin treatment prior to enrollment and 12% received nonrandomized treatment after randomization (crossovers), only patients with consistent therapy (no prerandomization therapy or prerandomization therapy same as randomized and no postrandomization crossover) were included to avoid the confounding influences of changing therapy.
Results: 4718 patients (47%) had consistent therapy during the entire hospitalization or before experiencing death/MI; 4700 (47%) had consistent therapy during the entire hospitalization or before experiencing a major TIMI bleed. The median time from randomization to catheterization was 22 hours; the median duration of therapy was 33.67

hours with UFH and 46.21 hours with enoxaparin. The incidence of death or MI at 30 days was 12.4% with enoxaparin and 14.2% with UFH (p=0.064), with no significant effect of duration of therapy on outcome for either enoxaparin (p=0.249) or UFH (p=0.068). The incidence of TIMI major bleeding was 6.3% with enoxaparin and 5.8% with UFH (p=0.477). In patients assigned to enoxaparin, bleeding did not vary with duration of treatment (p=0.536); however, in UFH-assigned patients there was a significant association between bleeding and duration of treatment (p=0.003), with bleeding rates tending to increase after approximately 3-4 days of therapy.

Conclusions: Enoxaparin and UFH have similar treatment effects regardless of the duration of treatment; longer duration with UFH (but not enoxaparin) is associated with an increased risk of bleeding. Enoxaparin is a safe and effective antithrombotic agent for both short and long durations of therapy in patients with NSTE ACS.

3:00 p.m.

850-7 **Safety of Single Versus Multi Vessel Angioplasty for Patients with Unstable Angina and Multi Vessel Coronary Disease: a Report from the New York State Angioplasty Registry**

James A. Kong, Robert Minutello, Steve S. Kim, Atul Sharma, Srhihari Naidu, Manish Parikh, Geoffrey Bergman, Shing C. Wong, Mun K. Hong, New York Hospital-Weill Cornell Medical Center, New York, NY

Background: Recent clinical trials support an early invasive management strategy for patients with unstable angina (UA). Many of these patients may have significant lesions in multiple coronary arteries. However, the safety of multi vessel versus single vessel percutaneous coronary intervention (PCI) as a treatment strategy in UA has not been studied.

Methods: Using the 2000/2001 New York State Angioplasty Registry, we compared the in-hospital clinical outcomes in patients with multivessel disease (>70% stenosis) who underwent either single versus multi vessel PCI for class III or IV UA without evidence of acute myocardial infarction (MI). Patients with previous MI, PCI, or coronary artery bypass surgery (CABG), and those presenting with hemodynamic instability or shock were excluded.

Results: Patients in the multi vessel PCI group were less likely to have peripheral vascular disease, renal insufficiency, and diabetes. There was no difference in the total number of lesions with >70% stenosis. A chronic total occlusion (CTO) was present more often in the single vessel PCI group, though a CTO was more likely to be treated in the multi vessel PCI group. There was no difference in death, CABG, stroke, renal failure, or stent thrombosis.

Conclusion: Despite the added complexity of multivessel PCI, there was no increase in adverse in-hospital outcomes in this group. In patients undergoing percutaneous revascularization for UA, multi vessel PCI is likely to be safe compared to single vessel PCI in selected cases.

	Single vessel PCI (n=2441 patients)	Multi vessel PCI (n=1805 patients)	*P*
Patient characteristics			
Age (years)	66.1 +/- 12.0	64.8 +/- 12.3	0.002
Male sex (%)	63.7	64.3	NS
History of stroke (%)	5.4	4.2	NS
Peripheral vascular disease (%)	13.4	11.1	0.024
Diabetes mellitus (%)	29.0	25.4	0.010
Renal insufficiency (%)[1]	2.0	1.2	0.038
Congestive failure on admission (%)	5.2	5.2	NS
Angiographic and procedural characteristics			
Ejection fraction (%)	54.5 +/- 10.8	55.4 +/- 10.4	0.008
Lesions >70% (per patient)	3.2	3.2	NS
GPIIb/IIIa inhibitor use (%)	58.5	63.5	0.001
CTO present (%)	37.9	17.5	<0.001
PCI for CTO (%)	8.2	10.4	0.015
Outcomes			
Renal failure with dialysis (%)	0.1	0.2	NS
Stroke (%)	0.2	0.1	NS
Emergency CABG (%)	0.5	0.2	NS
Stent thrombosis (%)	0.6	0.2	NS
Death (%)	0.4	0.7	NS
MACE[2] (%)	1.2	0.8	NS

[1]Renal insufficiency: serum creatinine >2.5 mg/dL, [2]MACE: Major Adverse Cardiac Event (stroke, CABG, and death)

p value compared to placebo

3:15 p.m.

850-8 **Intensity of Lipid Lowering With Statins and Brachial Artery Vascular Endothelium Reactivity After Acute Coronary Syndromes: The BRAVER Trial**

Jocelyn Dupuis, Jean-Claude Tardif, Jean-Lucien Rouleau, Joseph Ricci, Malcolm Arnold, Eva Lonn, René Roux, Lawrence Title, Jean Diodati, Nickie Bonafede, Anna Woo, Christopher P. Cannon, Montreal Heart Institute, Montreal, PQ, Canada

Background. The time course and the differential effects of statin regimens on endothelial function after acute coronary syndromes (ACS) are unknown and could contribute to the superiority of a more intense strategy.

Methods. Subjects enrolled in the PROVE IT-TIMI 22 trial (n=50) underwent serial evaluation of vascular reactivity by high-resolution brachial ultrasound. Endothelium-dependent flow-mediated dilatation (FMD) was measured after reactive hyperemia while endothelium-independent dilatation was measured after 0.4 mg sublingual nitroglycerin (NMD). Evaluations were performed at baseline and at 48 hours, 1 month and 4 months after the initiation of pravastatin 40 mg (n=26) or atorvastatin 80 mg (n=24).

Results. Baseline lipid profiles and C-reactive protein were similar except for mildly higher LDL cholesterol in the atorvastatin group (104 ± 26 mg/dL vs. 90 ± 27 mg/dL, p<0.05). After 4 months, atorvastatin therapy reduced total cholesterol by 22% and LDL cholesterol by 32% while pravastatin had no significant effect. C-reactive protein decreased similarly in both groups. Brachial artery diameters prior to the determination of FMD and NMD were similar in both groups and at each time point of the trial. Both FMD and NMD increased significantly after 4 months only by 27% and 24% respectively, with no difference between groups. There was no correlation between the change in FMD and the change in lipids or C-reactive protein.

Conclusion. Statin therapy soon after ACS is associated with improvement of both endothelium-dependent and-independent vascular reactivity after 4 months. The improvement is unrelated to the reduction of lipids and is thus unlikely to contribute to the superiority of a more intense regimen.

ORAL CONTRIBUTIONS

858 Stable Cardiac Ischemic Syndromes: Novel Risk Stratification Methods

Tuesday, March 08, 2005, 4:00 p.m.-5:00 p.m.
Orange County Convention Center, Room 414A

4:00 p.m.

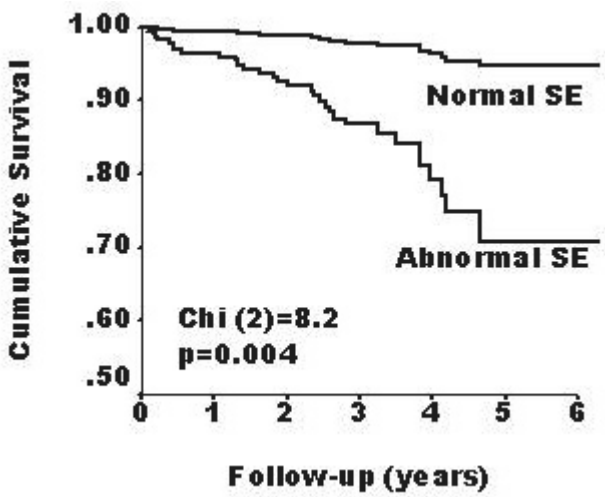
858-3 **Prognostic Implications in Patients With Angiographically Flow Limiting Coronary Artery Disease but a Normal Stress Echocardiogram: Incremental Value of Stress Echocardiography Over Coronary Angiography**

Sripal Bangalore, Devi Gopinath, Ajay Shah, Utpal Patel, Nilo Ayuyao, Mutahir Khan, James Wilentz, Siu-Sun Yao, Farooq A. Chaudhry, St Luke's-Roosevelt Hospital Center, New York, NY

Background: Data on the importance of normal stress echocardiogram in the presence of angiographically significant CAD is limited.

Methods: We evaluated 290 patients (62 ± 11 years; 67% males) undergoing stress echocardiography (22% treadmill, 78% dobutamine) within a 3-month period of angiography without an intervening intervention. All patients had significant CAD as defined by coronary stenosis ≥70% in major epicardial vessels or its branches. Abnormal stress echocardiography was defined as those with stress-induced ischemia (increase in wall-motion score of ≥1 grade). Followup (2.9 ± 1.3 years) for cardiac death (n = 21) and total mortality (n = 33) was obtained.

Results: Stress echocardiography effectively risk stratified normal vs. abnormal subgroups for endpoints of both cardiac death (Event rate 0.0%/year vs. 3.4%/year; p = 0.003) and total mortality (Event rate 0.9%/year vs. 5.1%/year; p = 0.004; OR = 6.7; 95% CI = 1.6-28.9)(graph). Cox proportional hazard model showed incremental value of stress echocardiography over angiography (Global chi^2 increased from 5.8 to 24.2 , p <0.0001 for cardiac death and from 7.1 to 23.1, p <0.0001 for total mortality).



Conclusions: A normal stress echocardiography *even* in the presence of angiographically determined coronary stenosis is associated with benign prognosis (<1%event rate/year) and provides incremental value over angiography. Physiology (function) may be a better predictor of mortality rather than anatomical coronary stenosis.

4:15 p.m.

858-4 **Usefulness of N-Terminal Pro-Brain Natriuretic Peptide for Predicting Moderate-to-Severe Myocardial Perfusion Defects in Patients With Stable Coronary Artery Disease**

Gerald Vanzetto, Peggy Jacon, Alex Calizzano, Yannick Neuder, Malik Zine, Patrice Faure, Daniel Fagret, Jacques Machecourt, University Hospital of Grenoble, Grenoble, France

BACKGROUND: The prognostic value of NT-pro-brain natriuretic peptide (NTBNP) is demonstrated in patients (pts) with acute coronary syndromes but not in pts with stable coronary artery disease (SCAD). We determined the relationship between NTBNP and the extent of myocardial perfusion defects on exercise (EST) Tl201 SPECT in SCAD pts with normal ejection fraction (EF > 45%).
METHODS: 88 pts (79 men, 61±8 years) with known SCAD and no history of heart failure were included. Mean EF was 62+11%. NTBNP was measured at baseline, peak-EST, and 3 hours post-EST.
RESULTS: SPECT was normal in 33 pts (37%, group 1) and abnormal in 55 (63%, group 2 - fixed defects n=33, reversible defects n=49). Group 2 pts had higher baseline, peak-EST and post-EST NTBNP values than group 1 (Table below). NTBNP baseline vs. post-EST variations were also higher in group 2. Post-EST NTBNP was predictive of perfusion abnormalities and moderate-to-severe ischemia (areas under the ROC curves = 0.71 and 0.61 respectively). A post-EST NTBNP <190 pmol/ml ruled-out moderate-to-severe myocardial ischemia with a negative predictive value of 85%. The accuracy of combined EST and post-stress NTBNP was 74% for identifying the presence or absence of significant ischemia.
CONCLUSION: A single post-EST NTBNP measure accurately predicts the presence or absence of significant myocardial ischemia in SCAD and can be useful in centers without on site nuclear facilities for selecting pts requiring perfusion imaging as second line diagnostic or prognostic tool.

	Group 1	Group 2
Baseline	107 (52-172)	183 (100-274)*
Peak-EST	119 (56-182)	201 (110-311)*
Post-EST	122 (59-195)	213 (108-326)*
Baseline- Post EST	+ 16 (6-25)	+ 23 (7-66)*
Value are medians (interquartile range). * p < 0.05 versus Group 1		

4:30 p.m.

858-5 **Brain Natriuretic peptide (BNP) Provides Incremental Data for Risk Stratification of Diabetics: A Stress Echocardiography Study**

Shrikanth P. Upadya, Sripal Bangalore, Tariqshah Syed, Asif Malik, Deborah Cantales, Amandeep Kalra, Lubna Rashid, Veerana Merla, Ranju Soni, Joseph Schappert, Farooq A. Chaudhry, St. Luke's-Roosevelt Hospital, New York, NY

Background: In the absence of heart failure, Brain natriuretic peptide (BNP) is elevated in patients with coronary artery disease (CAD). Diabetics (DM) are known to have accelerated CAD and non invasive stress testing is commonly used for prognosticating and risk stratifying DM's. We evaluated the effect of a pre stress BNP in DM's referred for a stress echocardiogram (SE).
Methods: We measured BNP pre SE in 74 diabetic patients (mean age 63 ±14 yrs; 54% males). Dobutamine stress echocardiogram was performed in 78% and exercise echocardiogram in 22% of patients. Echocardiogram readings were blinded to BNP levels. LV was divided as per the standard 16-segment model. Ischemia was defined as new reversible wall motion abnormality and/or biphasic response. BNP levels were analyzed at Biosite Inc.
Results: Significant variables are presented in the Table. Ischemia by SE was seen in 37 patients (50%). Mean pre-stress BNP was higher in ischemics compared to non-ischemics (254.4 ± 451.4 vs. 37±62.2, p =0.006). When pre stress BNP was added to clinical risk factors (age, gender, race, body mass index, hypertension, hypercholesterolemia, family history of premature CAD, smoking) global chi square increased from 5.9 to 15.5 (p<0.001) in predicting ischemia on SE.
Conclusions: Pre stress BNP has incremental value to clinical risk factors in predicting ischemia during SE in DM. An elevated baseline BNP in DM suggests the presence of CAD, requiring SE for risk stratifiaction and prognostification.

Table

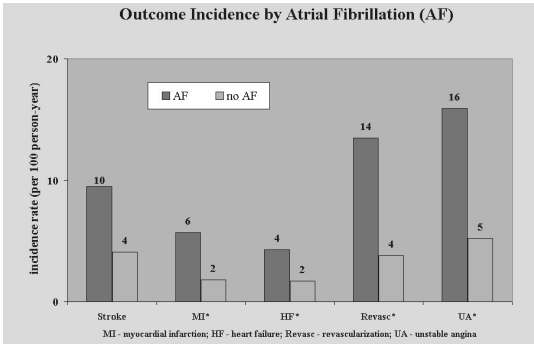
	Ischemics	Non ischemics	P value
Age	66 ± 12	59 ± 14	0.016
History of heart failure (%)	19	5	0.075
Hypertension (%)	87	81	NS
Prior myocardial infarction (%)	19	19	NS
LVEF (%)	49 ± 15	58 ± 4	0.002
Resting Wall Motion Index	1.5 ± 0.7	1.0 ± 0.2	<0.001
Stress Wall Motion Index	1.5 ± 0.9	1.1 ± 0.3	0.006
Pre Stress BNP	254.4 ± 451.4	37 ± 62.2	0.006

4:45 p.m.

858-6 **Occurrence of Atrial Fibrillation in Chronic Stable CAD Patients Is Common and Predictable of Unfavorable Outcome**

Yinong Young-Xu, Shmuel Ravid, Lown Cardiovascular Foundation, Brookline, MA

Background: Atrial Fibrillation (AF) is associated with increased risk of morbidity and mortality. Coronary artery disease (CAD) is a known risk factor for AF. We studied the long-term incidence and the development of associated outcomes of AF in patients with chronic stable CAD.
Methods: The study cohort included patients with stable CAD followed prospectively. Episodes of AF were documented throughout the study. The outcomes of interest were cardiac death, nonfatal myocardial infarction (MI), heart failure (HF), unstable angina (UA), revascularization and stroke. We calculated incidence rate and estimated the odds ratios (ORs) and 95% confidence intervals (CI).
Results: 449 subjects with a mean follow-up of four years were included in the analysis.. A total of 52 patients developed AF during follow-up (12%). In multivariate analysis the occurrence of AF was not predictable by prior MI, HF, ischemia, or left ventricular ejection fraction. Compared with those who did not develop AF, patients with AF were at significantly higher risk for having stroke (OR, 5.7), HF (OR, 6.9), revascularization (OR, 11.2), UA (OR, 6.8), and nonfatal MI (OR, 8.7), even after adjustment for potential confounders such as age, hypertension, diabetes, drug usage, and medical treatments.
Conclusion: Development of AF in patients with CAD is relatively common and is associated with a significant increase in the risk of HF, UA, nonfatal MI and revascularization in addition to the predictable higher risk of stroke.



ORAL CONTRIBUTIONS

862 Coronary Artery Bypass Surgery: Still the Underutilized Therapy for Multivessel Disease in Diabetics

Tuesday, March 08, 2005, 4:00 p.m.-5:00 p.m.
Orange County Convention Center, Room 231A

4:00 p.m.

862-3 **Differential Impact of Coronary Artery Bypass Graft Surgery and Diabetes on Cause of Death, a Long-Term Report from the BARI Study**

David R. Holmes, Jr., Lauren Kim, Maria M. Brooks, Katherine M. Detre, Robert L. Frye, Mandeep Singh, Mayo Clinic, Rochester, MN, University of Pittsburgh, Pttisburgh, PA

Background: Evaluation of the cause of death may have implications for developing treatment strategies in patients with coronary artery disease (CAD).
Purpose: Evaluate cause of death in patients in the BARI study during long-term follow-up and the effect of revascularization treatment and diabetes on cause of death.
Population: Of 3610 patients who received revascularization (PTCA or CABG) in the BARI trial and registry, 642 (18%) had diabetes. 621 patients (17%) had died at a mean follow-up of 7.8 years. All deaths were classified by an independent mortality and morbidity committee.
Results: Forty six percent (46%) of the deaths were due to cardiac causes; 17% were sudden cardiac deaths, 18% secondary to myocardial infarction, and 11% related to congestive heart failure or other cardiac causes. Of 642 diabetics in the study, 32% died compared to 14% of the 2968 patients who were not diabetic (p<.01). Death was more often due to cardiac causes among patients with diabetes compared to those without diabetes (51% versus 43%, p=.08), and the primary cause of death was more frequently congestive heart failure/other (16% versus 9%, p=.01). Using competing risks Cox proportional hazards models, diabetes was associated with higher rates of death for all causes, but the effect of diabetes on CHF/other cardiac death was significantly greater compared to the effect of diabetes on other causes of death (RR=3.73 for CHF death vs RR=1.85 for the all other causes, p=.01). In these multivariate models, receiving CABG (time dependent variable) was associated with a significant reduction in sudden cardiac death but was not significantly associated with other causes of death (RR=0.61

for sudden cardiac death vs RR=0.97 for all other causes, p=.03).
Conclusion: Over a mean follow-up of 7.8 years, mortality was 17% in patients with established multivessel coronary artery disease who received revascularization. Death was due to cardiac causes in 46% of cases. Diabetes was associated with higher death rates for all causes of death, but the relative difference was most pronounced for death from congestive heart failure/other cardiac causes. Receiving CABG was associated with lower sudden death rates for all patients.

4:15 p.m.

862-4 **Clinical Outcomes of Patients with Multivessel Disease Treated With Three or More Sirolimus-eluting Stents**

Seung-Woon Rha, Awefork GebreEyesus, Pramod Kuchulakanti, Daniel A. Canos, George Aggrey, Jana Fournadjiev, Augusto D. Pichard, William O. Suddath, Kenneth M. Kent, Lowell F. Satler, Ron Waksman, Washington Hospital Center, Washington, DC

Background: Sirolimus-eluting stent (SES; Cypher™) implantation for single vessels is proven to be effective and durable. This study aimed to compare the clinical outcomes of 3 or more SES implantations for multivessels to those of single SES implantation.
Methods: From our SES registry, we identified 31 patients (pts) with 71 lesions that were treated with 3 or more SES and 1013 pts that were treated with a single SES for various coronary lesions. The in-hospital, 30-day, and 6-month clinical outcomes of both groups were compared.
Results: Baseline characteristics were similar except for more history of diabetes mellitus (53.1% vs. 33.1%, P=0.02), renal insufficiency (22.6% vs. 8.4%, P=0.006), and restenotic lesions (14.1% vs. 7.2%, p=0.03) in the multiple SES group. The multiple SES group had a higher incidence of periprocedural CK-MB elevation (p=<0.02), abrupt closure, dissection, and renal failure. At 30 days and 6 months, the multiple SES group had a higher incidence of Q-wave and non-Q-wave myocardial infarction (MI) and TLR-MACE, TVR-MACE compared to the single SES group. (Table)
Conclusions: Patients with multivessel disease, requiring 3 or more SES, experience increased periprocedural and in-hospital complications and worse adverse clinical outcomes at 30 days and 6 months when compared to pts with single vessel that require single SES. Therefore, when 3 or more SES are needed for pts with multivessel disease, CABG should be considered as a revascularization alternative.

Clinical Outcomes at 30 Days and 6 Months			
Variables, %	**Multiple SES (n=31 pts)**	**Single SES (n=1013 pts)**	**p Value**
At 30 days			
Death	3.6	0.6	0.07
Q-wave MI	7.1	0.4	<0.001
Non-Q-wave MI	21.4	9.1	0.04
TVR-MACE	7.1	1.0	0.002
TLR-MACE	7.1	0.9	0.001
Subacute stent thrombosis	0.3	0.0	0.03
At 6 months			
Death	6.7	1.9	0.18
Q-wave MI	23.5	1.6	<0.001
Non-Q-wave MI	31.6	10.8	0.004
TVR-MACE	23.5	5.6	0.002
TLR-MACE	23.5	2.9	<0.001
TLR	6.7	1.1	0.04
TVR	6.7	2.8	0.37

4:30 p.m.

862-5 **The Medicine Angioplasty Or Surgery Study (MASS Registry): Impact Of Diabetes On Long-term Prognosis In Patients With Single Or Multivesel Coronary Artery Disease. Five Years Of Follow-up.**

Whady Hueb, Fernando Costa, Bernard J. Gerh, Neuza Lopes, Aecio Gois, Paulo Dutra, Desiderio Favarato, Jose R L Luces, Sergio A. Oliveira, Jose Ramires, Heart Institute (InCor) University of Sao Paulo, Sao Paulo, Brazil, Mayo Clinic, Rochester, MN

Background: Diabetes mellitus is a major cause of coronary artery disease (CAD). Despite improvement in the management of patients with stable CAD diabetes remains a major adverse risk factor for increased morbidity and mortality. Although the frequent use of Coronary Artery Bypass Surgery (CABG) and Percutaneous Coronary Intervention (PCI), there is no conclusive evidence that either treatment modality is better then Medical Therapy (MT) alone for the treatment of single or multivessel in patients with diabetes.
Methods: We compared MT, PCI and CABG in patients with single and multivessel disease in diabetic (399) and non-diabetic subjects (930). The composite primary end point was defined as cardiac mortality; Q-wave myocardial infarction (MI); or refractory angina requiring revascularization.
Results: A total of 1329 patients were assigned to either CABG (n=519), PCI (n= 414) or MT (n= 396). The five year survival rates were 88.2 % for CABG; 73.4 % for PCI and 74.5 % for MT (p<0.0001) for diabetes and non diabetes patients. There was a significant higher mortality in diabetic subjects compared to non-diabetics regardless of the tree therapeutic options (p <0.001). When stratified by the number of vessels disease, there was a significant benefit for CABG in patients with diabetes and multivessel disease versus single vessel (p=0.001).
Conclusion: All three therapeutic regimens resulted in a high rate of cardiac related death in diabetic comparing with non diabetic patients. However, we observed better outcome in the multivessel CAD diabetic patients undergoing to surgery regarding the primary end points in the 5 years of follow-up study..

4:45 p.m.

862-6 **A Double-Blind, Placebo-Controlled, Crossover Study of the Safety of Intravenous Glyceryl Trinitrate After Administration of Sildenafil Citrate to Men With Coronary Artery Disease**

John D. Parker, Bradley A. Bart, David Webb, Michael J. Koren, Richard L. Siegel, Susan Nicholas, Mount Sinai and University Health Network Hospitals, Toronto, ON, Canada, Hennepin County Medical Center, Minneapolis, MN

Background: Nitrate and sildenafil coadministration is contraindicated, and the ACC/AHA Expert Consensus Document does not recommend coadministration within 24 hours unless benefits far outweigh risks. This double-blind study assessed intravenous (IV) glyceryl trinitrate (GTN) in men with coronary artery disease (CAD) who had taken sildenafil.
Methods: 34 men (≥35 years) with a history of angina pectoris and CAD (>50% stenosis of ≥1 coronary artery) were randomized to a single dose of sildenafil 100 mg or placebo (with crossover after 3-7 days) followed in 45 min by escalating doses of IV GTN.
Results: After sildenafil, 2 men were discontinued following GTN 5 µg/min for asymptomatic hypotension and 1 for nausea. The maximum infusion rate at discontinuation for sildenafil versus placebo was: median (range), 80 (0-160) versus 160 (20-160) µg/min; adjusted mean ± SE, 77±7 versus 127±7 (*P*<0.0001; ANOVA). GTN 160 µg/min was tolerated by 8 (sildenafil) and 19 (placebo) men. Maximum decreases in supine blood pressure (BP) and increases in supine heart rate (HR) were slightly greater for sildenafil than placebo at most GTN doses (**Table**). Adverse events were mostly mild or moderate hypotension, headache, dizziness, and paresthesia. These events were not unexpected and are often associated with GTN alone.
Conclusions: Most men with CAD who have taken sildenafil tolerate a low dose of IV GTN with gradual upward titration, while BP and HR are monitored closely.

	Difference in Adjusted Mean ± SE Changes From Baseline: Sildenafil - Placebo (Number of Subjects: Sildenafil, Placebo)*						
GTN dose, µg/min†	**5 (29, 32)**	**10 (28, 32)**	**20 (23, 32)**	**40 (21, 30)**	**80 (19, 28)**	**120 (10, 24)**	**160 (8, 19)**
SBP, mmHg	-4±2	-6±3‡	-4±3	-5±2	-6±2**	0.5±2	-7±4
DBP, mmHg	-1±2	-2±2	-2±2	-3±2	-2±2	-2±3	-0.7±3
HR, bpm	0.5±2	0.1±0.7	-0.3±1	1±2	0.9±2	9±4‡	5±4

*32 men completed the study; the other 2 had SBP below protocol cutoff after sildenafil.
†GTN dose was escalated every 10 min. Infusion was stopped when systolic BP (SBP) decreased either by >35 mm Hg from the pre-GTN measurement, or decreased to <100 mm Hg and was sustained for 1 min; or HR increased >25 bpm from the pre-GTN measurement, or increased to >100 bpm and was sustained for 1 min; or if the subject, in the opinion of the investigator, suffered significant hypotensive symptoms.
‡*P*<0.05, *******P*<0.01 (ANOVA); DBP=diastolic BP; bpm=beats/min.

ORAL CONTRIBUTIONS

872FO Featured Oral Session... Antiplatelet Therapy in ST-Segment Elevation Myocardial Infarction

Wednesday, March 09, 2005, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 231A

8:45 a.m.

872-4 **Upstream Administration of Abciximab Prior to Primary Angioplasty Improves Epicardial Patency and Myocardial Tissue Perfusion - Results From a Meta-Analysis of 602 Cases**

Jochen Goedicke, Marcus Denis Flather, Hans-Richard Arntz, Henrique Mesquita Gabriel, Lars Grip, Kurt Huber, Marko Noc, Gilles Montalescot, Eli Lilly, Critical Care Europe, Geneva, Switzerland, Clinical Trials and Evaluation Unit, Royal Brompton Hospital, London, United Kingdom

Background: The 2004 ACC/AHA guidelines on STEMI state that it is reasonable to start treatment with Abciximab (ABC) as early as possible before primary PCI. While there is ample evidence for peri-procedural (=late) application of ABC, data on upstream application (=early) is limited to several but small studies. This meta-analysis was performed to provide more robust information on surrogate parameters as well as estimates for potential benefit on clinical outcomes.
Methods: 6 prospective studies that compared early and late start of ABC were identified. The investigators from ADMIRAL, BRIDGING, ERAMI, REOMOBILE, SWEDES and Zorman et al provided individual patient data to the co-ordinating center. Analyses were performed on the composite of death, reinfarction (re-MI) and target vessel revascularisation (TVR) at 30 days (primary outcome), death alone, major bleeding, TIMI flow and ST-resolution (ST-RES) after PCI. Planned subgroup analyses were performed for PCI<3hrs or >=3hrs from symptom onset.

Results:

	Early	Late	p / OR (95% CI)
Median ABC to Angio (min, IQR)	50 (32 to 73) (246/260)	5 (-9 to 30) (267/342)	p=<0.001
Pre-PCI TIMI 2/3	42% (107/255)	29% (98/337)	p=0.001
Pre-PCI TIMI 2/3 (PCI<3hrs)	52% (50/97)	29% (31/107)	p=0.001
ST-RES >=70%	59% (95/160)	41% (75/182)	p=0.003
ST-RES >=70% (PCI>=3hrs)	62% (53/85)	36% (27/74)	p=0.005
Death, re-MI, TVR	7.3% (19/260)	9.7% (33/340)	OR 0.73 (0.41 - 1.32)
Death, re-MI, TVR (PCI>=3hrs)	5.5% (8/146)	9.9% (15/151)	OR 0.53 (0.21-1.29)
Death only	2.7% (7/260)	4.7% (15/340)	OR 0.56 (0.23-1.39)
Major Bleeding	3.5% (9/260)	3.8% (13/342)	OR 0.91 (0.38-2.16)

Conclusions: Starting ABC early for primary PCI is feasible and appears safe. The incidence of death and the composite of death, re-MI and TVR appears lower with ABC started early. Early ABC improves epicardial patency prior to PCI, which is predominantly present in PCIs performed <3hrs from symptom onset. In delayed PCIs (>=3hrs from symptom onset) early ABC can restore myocardial tissue perfusion as assessed by post-PCI ST-RES to a similar level to that observed with PCI <3hrs.

9:00 a.m.

872-5 Safety of Glycoprotein 2b/3a Inhibitors in Patients with Acute Myocardial Infarction requiring Percutaneous Coronary Intervention after Thrombolytic Therapy: A Report From The New York State Angioplasty Registry

Alexander J. Slotwiner, Robert M. Minutello, Atul Sharma, James A. Kong, Steve S. Kim, Mun K. Hong, Manish Parikh, Geoffrey Bergman, S. Chiu Wong, New York Presbyterian Hosp.-Weill Med. College of Cornell Univ., New York, NY

Background: Few studies have examined glycoprotein 2b/3a inhibitor (GPI) use in patients with acute myocardial infarction (AMI) who received antecedent thrombolytic therapy. Therefore, we sought to ascertain in-hospital outcomes in this patient cohort.
Methods: Using the 2000-2001 New York State PCI Database, we identified patients with AMI treated with thrombolytic therapy who subsequently underwent PCI with and without GPIs (N=1,053). All patients identified received thrombolytic therapy within 6 hours of PCI.
Results: Of 1,053 patients who underwent rescue angioplasty for AMI, 686 (65%) patients received GPI and 367 (35%) had not. There was no significant difference in baseline characteristics. Similarly, there was no difference in inpatient clinical outcomes between the two groups with respect to death, emergent CABG, access site injury requiring surgical treatment, renal failure requiring dialysis, stent thrombosis, or length of hospital stay. Importantly, only 9 patients in the GPI group (1.3%) experienced a stroke post PCI, in comparison to 5 (1.4%) in the non-GPI group (p= NS).
Conclusion: The use of peri-procedural PCI GPIs after recent thrombolytic therapy does not pose an increased risk of major inpatient clinical adverse events, including stroke. It therefore appears safe to use a GPI during PCI in the setting of an AMI in a patient who received thrombolytics.

In - Hospital Outcomes

	GPI N=686	No GPI N=367	P value
Death (%)	4.5	5.4	NS
Emergent CABG (%)	0.4	0.3	NS
Length of stay (days)	5.4 +/- 6.5	5.8 +/- 8.0	NS
Access site injury (%)	0.3	0.3	NS
Renal failure requiring dialysis (%)	0.4	0.5	NS
Stent thrombosis (%)	0.9	0.5	NS
Stroke (%)	1.3	1.3	NS

9:15 a.m.

872-6 CLARITY-TIMI 28: Primary Results

Marc S. Sabatine, Christopher P. Cannon, C. Michael Gibson, Jose Lopez-Sendon, Gilles Montalescot, Marc Claeys, Frank Cools, Carolyn H. McCabe, Eugene Braunwald, Brigham and Women's Hospital, Boston, MA

Background: Although fibrinolysis is effective in improving outcomes in ST-elevation myocardial infarction (STEMI), failure to achieve reperfusion and/or reocclusion of the infarct-related artery occur in substantial proportions of patients and are associated with a significant increase in morbidity and mortality. We hypothesized that the addition of the oral antiplatelet agent clopidogrel, an adenosine diphosphate (ADP)-receptor antagonist, to standard fibrinolytic therapy in patients with STEMI will improve reperfusion.
Methods: CLopidogrel as Adjunctive ReperfusIon TherapY (CLARITY) - Thrombolysis In Myocardial Infarction (TIMI) 28 is a multicenter, international, randomized, double-blind, placebo-controlled trial enrolling 3500 patients between the ages of 18 and 75 with STEMI, presenting within 12 hours of symptom onset and in whom fibrinolysis is planned. Subjects are randomized in a 1:1 ratio to receive clopidogrel (300 mg loading dose, then 75 mg daily) or placebo. The choice of fibrinolytic and anticoagulant is at the discretion of the treating physician, and all patients are to receive aspirin. Patients are scheduled to undergo angiography during the index hospitalization 48-192 hours after the start of study medication.
Results: The primary results will be ready for presentation at the ACC 2005. The primary endpoint is the composite of death or recurrent MI by the start of coronary angiography or an occluded infarct-related artery (TIMI Flow Grade 0 or 1) on the pre-discharge angiogram. Secondary endpoints are (1) Clinical: death, recurrent MI, or recurrent myocardial ischemia by the time of the start of coronary angiography; (2) Angiographic: TFG 0 or 1 in the infarct-related artery on the pre-discharge angiogram; and (3) Electrocardiographic: degree of ST segment resolution at 180 minutes. The primary safety endpoint is the rate of TIMI major bleeding.
Conclusions: CLARITY-TIMI 28 will help define the role of clopidogrel as a part of the pharmacologic reperfusion regimen in acute STEMI.

9:30 a.m.

872-7 Adjunctive Abciximab To Reperfusion Therapy In Patients With Acute St-segment Elevation Myocardial Infarction: A Meta-analysis Of Randomized Trials

Giuseppe De Luca, Harry Suryapranata, Gregg W. Stone, David Antoniucci, James E. Tcheng, Franz-Josef Neumann, Frans Van de Werf, Elliott M. Antman, Eric J. Topol, De Weezenlanden Hospital, Zwolle, The Netherlands

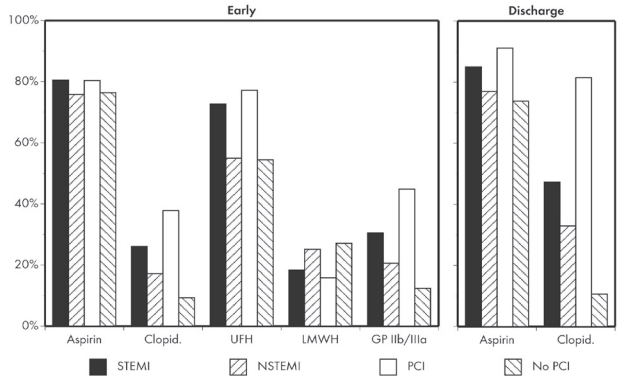
Background. The benefits of abciximab in patients with ST-segment elevation myocardial infarction (STEMI) is still a matter of debate. The aim of this meta-analysis was to combine data from all randomized trials conducted with abciximab in STEMI.
Methods. We obtained results from all completed randomized trials with abciximab in STEMI, by formal searches of electronic databases (MEDLINE, Pubmed). Odds ratio (OR) and 95% confidence intervals (95% CI) were reported. A first analysis was performed according to the treatment strategy (primary angioplasty or thrombolysis). The final analysis was conducted including all trials. The pooled odds ratio was calculated by the Mantel-Haenszel method, whereas the Breslow-Day test was used to examine heterogeneity across the studies.
Results. Fifteen studies were analyzed, involving 13,140 patients randomized to abciximab, and 14,910 to control. When compared to control group, abciximab was associated with a significant reduction in long-term mortality in patients undergoing primary angioplasty (4.4% vs 6.1%, p=0.015), but not in those treated with thrombolysis (8.6% vs 8.3%, p=NS). Furthermore, abciximab was associated with a significant reduction in 30-day reinfarction, both in primary angioplasty (1.0% vs 1.9%, p=0.026) and in thrombolysis trials (2.3% vs 3.5%, p<0.0001), and in all trials combined (2.1% vs 3.3%, p<0.0001). Abciximab did not result in an increased risk of intracranial bleeding (0.65% vs 0.64%, p=NS), but was associated with an increased risk of major bleeding complications when combined with thrombolysis (5.4% vs 3.1%, p<0.0001), but not with primary angioplasty (4.9% vs 4.2%, p=NS).
Conclusions. This meta-analysis shows that, when compared to control group, adjunctive abciximab for STEMI is associated with a significant reduction in long-term mortality in patients treated with primary angioplasty, but not in those receiving thrombolytic therapy. The 30-day reinfarction rate is significantly reduced in patients treated with either thrombolysis or primary angioplasty. A higher risk of major bleeding complications is observed with abciximab in association with thrombolytic therapy.

9:45 a.m.

872-8 In-Hospital Adherence to Current Guidelines is not Optimal for Antiplatelet and Antithrombotic Therapies in Patients With Acute Myocardial Infarction: Insights From the International Valsartan in Acute Myocardial Infarction (VALIANT) Registry

Gustavo B.F. Oliveira, Rakhi Kilaru, Michael P. Hudson, Eric J. Velazquez, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, Henry Ford Hospital, Detroit, MI

Background. Current guidelines recommend aspirin (ASA) to all AMI patients (pts) on admission and indefinitely after discharge; thienopyridines (Thieno) to pts with ASA intolerance, coronary stents, or NSTEMI; anticoagulation with either UFH or LMWH to NSTEMI pts; and GP IIb/IIIa inhibitors to NSTEMI pts and managed with percutaneous coronary intervention (PCI). **Methods.** We analyzed data from 4370 pts with STEMI or NSTEMI enrolled in the international VALIANT Registry from 1999-2001. Patterns of use of antiplatelets (AP) and antithrombins (AT) were assessed to determine actual adherence to guidelines. Early (<24h) and discharge use is displayed by type of AMI and by PCI/no-PCI (Figure). **Results.** Among pts not treated with early or discharge ASA, 86% and 83%, respectively, did not receive any Thieno. In STEMI pts, 16% and 14% did not receive early AP and AT, respectively, and 14% were not discharged on AP. In NSTEMI pts, 21% and 24% did not receive early AP and AT, respectively, and 20% were not discharged on AP. No-PCI patients less frequently received AP upon discharge as compared to PCI-managed pts (75% vs 95%, respectively, $p<0.001$).



Conclusions. STEMI pts and those managed with PCI more frequently received early GP IIb/IIIa inhibitors and UFH, and ASA and Thieno both early and at discharge, than NSTEMI pts and no-PCI pts. Only LMWH was preferentially used in NSTEMI pts and in no-PCI pts. Despite guidelines, many eligible AMI pts do not receive AP and AT appropriately, and no-PCI pts are particularly undertreated.

ORAL CONTRIBUTIONS

877FO Featured Oral Session...Recent Advances in Cardioprotection

Wednesday, March 09, 2005, 10:30 a.m.-Noon
Orange County Convention Center, Room 304E

10:45 a.m.

877-4 Intrinsic Inhibitors of Complement Activation Dramatically Limit Infarct Following Coronary Occlusion

Nikolay Vasilyev, Arman Askari, Feng Lin, Lisa Kuttner-Kondo, Maryann Fitzmaurice, Edward Medof, Marc S. Penn, Cleveland Clinic Foundation, Cleveland, OH, Case Western Reserve University, Cleveland, OH

Background: The extent of myocardial damage following coronary occlusion is determined not only by the area deprived of perfusion but also by hypoxic reperfusion injury extending from this site. Although complement has been implicated in this process, the role of the cell surface *intrinsic* complement regulators (which protect self cells from complement mediated damage) in limiting the extension is unstudied. Important among these regulators are decay accelerating factor (DAF) and CD59.
Methods: To address this issue we compared infarct size and mortality in wild type (WT) and mice targeted in the DAF, CD59 or both genes. After 30 min of ischemia and 60 min of reperfusion following LAD occlusion, infarct size was assessed as percent area at risk (IS%AAR) using tetrazolium/Evan's blue staining. To verify the involvement of complement, we assessed C3b and C9 deposition by immunohistochemistry.
Results: In *Daf*$^{-/-}$*CD59*$^{-/-}$ mice, IS%AAR was markedly greater than in WT mice (62.3 ± 4.0% (n=4) vs. 47.4 ± 2.3% (n=5), p<0.001). C3b and C9 deposition in microvasculature was greatly enhanced. To determine the relative importance of DAF and CD59, we compared IS%AAR in *Daf*$^{-/-}$ and *CD59*$^{-/-}$ mice. The absence of DAF had a significantly greater effect (*Daf*$^{-/-}$*: 61.7* ± 6.0, n=9; *CD59*$^{-/-}$: 53.2 ± 1.9, n=8, p<0.001).
Conclusion: These data establish that *intrinsic* complement regulators play a key role in protecting microvascular patency, and consequently attenuate infarct size in the course of infarction. They show that DAF plays a greater role than CD59 and open the possibility of developing new agents for therapeutic intervention in myocardial infarction patients.

11:00 a.m.

877-5 Angiotensin II Receptor Blockade With Losartan Reduces Apoptosis and Infarct Size Following Ischemia/reperfusion in the Rabbit Heart

Shinji Okubo, Patrick W. Fisher, Fadi Salloum, Ramzi Ockaili, Vijay Marwaha, Giuseppe Ambrosio, Michael L. Hess, Rakesh C. Kukreja, Virginia Commonwealth University Medical Center, Richmond, VA, University of Perugia School of Medicine, Perugia, Italy

Background: Recent studies suggest that cardiac renin angiotensin system is activated during acute myocardial ischemia. Formation of angiotensin II (A-II) may contribute to neutrophil activation, resulting in tissue injury during reflow. We hypothesized that blockade of A-II receptors with losartan may attenuate ischemia/reperfusion (IR) injury in vivo.
Methods: Three groups of rabbits (n=6/group) were treated with either saline, losartan 5 mg/kg or 25 mg/kg iv 30 min prior to ischemia. All animals were subjected to regional ischemia by 30 min LAD occlusion with 3 hrs of reperfusion. Risk area (RA) was determined by injection of Evan's blue. Infarct size (IS) was determined by morphometry of tetrazolium stained sections. Apoptotic Index ([TUNEL positive myocyte nuclei/total myocyte nuclei] x 100) was determined using TUNEL technique in cryosections from infarct border zone.
Results: RA was not significantly different between groups (P>0.05). Losartan-treated rabbits exhibited a dose-dependent reduction in IS following IR. In contrast, mean arterial blood pressure (MAP) during reperfusion was significantly lower in losartan group (5 mg/kg) compared to saline. Apoptosis was increased in saline group compared to all groups, the most marked reduction being in losartan (5 mg/kg) vs. losartan (25 mg/kg). These results indicate that A-II receptor blockade exerts a potent anti-infarct and anti-apoptotic effect in rabbit heart, by a mechanism that is independent of MAP-lowering.

Effect of Losartan on Infarct Size, Mean Arterial Blood Pressure, and Apoptosis

Group	IS	RA	MAP	Apoptotic Index
	(% RA)	(% LV)	(mmHg)	(%)
Saline	42.0±2	57±7	75±5	2.86±0.6
Losartan (5 mg/kg)	31.5±4*	48.0±7	52±3*	0.01±0.01$^{*,\#}$
Losartan (25 mg/kg)	13.7±1*,‡	54.8±3	48±5*	0.43±0.3*

P<0.05 vs. saline, ‡P<0.05 vs. losartan (5 mg/kg), #P<0.001 vs. losartan (25 mg/kg).

11:15 a.m.

877-6 Effects Of Ramipril, An Angiotensin Converting Enzyme Inhibitor, On Apoptotic Associated Molecular Expression In Ischemic Reperfused Myocardium

Zhong Jing Wang, How Sung Lee, Yi Zhun Zhu, National University of Singapore, Singapore, Singapore

Apoptosis has been emerged as a predominant mode contributed to cardiomyocyte loss with the pathophysiological consequences and may associate to the ventricular remodeling and left ventricular dysfunction after myocardial ischemia/reperfusion (I/R). Attenuation of cardiomyocyte apoptosis may be one of the cardioprotective mechanisms by Angiotensin Converting Enzyme inhibitors (ACEI) in preventing adverse cardiac hypertrophy/remodeling and preservation of global left ventricular function. The purpose of this study was to globe identify the changes of myocardial apoptosis associated transcripts under the effects of ramipril, an ACEI, in the early I/R phase and specifically to further define these genes in myocardium. Using Affymetrix oligonucleotide microarray technology, we identified and analyzed several ACE mediated transcripts in reperfused myocardium. 103 probe sets showed increase whereas 101 probe sets demonstrated decrease in 2-fold or more in ramipril treated sample. Among these probe set, four apoptotic transcripts which encoding Bcl-2, NF-κB, SOD-1 and CCAAT/enhancer binding protein-β (Cebp-β) were shown upregulation and eight apoptotic associated probe set which transcript to caspase-3, caspase-1, Bax, Bad, Bcl-xS, TNFR-1, p53 and Gsk3-β were shown downregulation. The up- and down-regulation of these pro-apoptotic genes were further confirmed and characteristic by semi-quantitative reverse-transcription-polymerase china reaction (RT-PCR), immunobloting and immunohistochemistry in a time course. The caspase-3 activity was furthermore verified by caspase-3 activity assay (fluorogenic AFC-DEVD method). The findings have provided a new insight into the mechanism of ACEI in the prevention of myocardial apoptosis following I/R injury.

11:30 a.m.

877-7 Nitroxyl Requires Calcitonin Gene-Related Peptide (CGRP) Signaling but not Protein Kinase C to Afford Early-Preconditioning Effect in Rat Heart.

Pasquale Pagliaro, Daniele Mancardi, Claudia Penna, Sandra Cappello, Carlo G. Tocchetti, David A. Wink, Gianni A. Losano, Nazareno Paolocci, Dipartimento di Scienze Cliniche e Biologiche dell'Universita di Torino, Orbassano, Italy, Johns Hopkins Medical Institutions, Baltimore, MD

Background: Donors of nitroxyl (HNO/NO^{-}), the reduced form of nitric oxide (NO), induce early preconditioning (PC)-like effects in isolated rat hearts. Nitroxyl-induced protection is somehow larger than that afforded by equimolar doses of NO donors. Then, it is plausible to hypothesize that HNO and NO donors can use, at least in part, discrete signaling pathways to protect myocardium against reperfusion injury. Protein kinase C (PKC) activation is one of the tenets of NO-induced protection. On the other hand, *in vivo* HNO cardiotropic action appears to be linked to *calcitonin gene-related peptide* (CGRP) signaling pathway. CGRP blockade has been already shown to prevent NO/nitrate-induced early-PC effect in rats. Here we tested whether nitroxyl early PC-like action is dependent upon PKC activation and assessed the involvement of CGRP receptors in HNO-induced myocardial protection.
Methods: Isolated rat hearts were subjected to 30' global ischemia followed by 120' reperfusion. Infarct size (IS) was measured by staining myocardium with nitro-blue tetrazolium.
Results: In controls, IS was 67±6% (n=9). Three cycles of PC (3' global ischemia + 5' reperfusion each = IPC3) substantially reduced IS (32±5.5%, n=9, p<.01). In lieu of ischemic PC, the nitroxyl donor Angeli's salt (AS, 1μM for 19') similarly reduced IS (38±3.5%, p<.01 vs. control, n=8, p=NS vs IPC3). The PKC inhibitor GF109203X (0.5 μM for 29') co-infused with AS did not reverse the protection achieved with nitroxyl (IS=31±5.5%, n=5). In stark contrast, blockade of CGRP receptors by means of the selective antagonist $CGRP_{8-37}$ infusion (0.1μM for 29') completely abrogated nitroxyl-induced cardiac protection (IS=63±9%, n=5, p=NS vs. controls).
Conclusions: Herein, we demonstrate for the first time that in isolated rat hearts the preconditioning effects of exogenous nitroxyl, similarly to NO/nitrate donors, involve a CGRP receptor-coupled pathway. However, differently from NO donors HNO does not require the activation of a PKC-dependent pathway to afford protection against reperfusion injury.

11:45 a.m.

877-8 **Intra-Aortic Balloon Counterpulsation During Myocardial Reperfusion Increases Coronary Blood Flow and Myocardial Salvage: Experimental Study**

Michalis Bonios, Argirios Ntalianis, Stavros Stavrakis, Stavros Drakos, Paraskevi Savvari, Dimitrios Koudoumas, Paraskevi Dolou, Charalampos Pierrakos, Apostolos Papalois, John Nanas, University of Athens, Athens, Greece

Background: The beneficial effects of the IABP on the outcome of patients undergoing primary angioplasty in the setting of acute myocardial infarction have been controversial. We sought to investigate the effects of the IABP on the extent of infarct size, the no-reflow phenomenon and coronary blood flow (CBF) during reperfusion in an ischemia-reperfusion experimental model.
Methods: A 30-ml IABP was placed in the descending aorta of 11 open-chest pigs. Each pig underwent occlusion of the mid left anterior descending (LAD) coronary artery for 1 h, followed by reperfusion for 2 h. The mean CBF, distal to the LAD occlusion site was measured with a transit-time ultrasound flowmeter. In 6 experiments, IABP support was used during reperfusion. At the end of each experiment the infarcted (IA) and the no-reflow (NRA) area were also measured with the use of coloring matters (tetrazolium and thioflavine).
Results: The results are shown in the table. CBF at reperfusion was normalized with respect to baseline values (% of baseline CBF).

		Reperfusion (min)						
		1	15	30	45	60	90	120
CBF (ml/min)	IABP yes	241+/-88%	240+/-63%	189+/-57%	155+/-43%	90+/-71%	87+/-43%	55+/-61%
	IABP no	121+/-112%	73+/-105%	50+/-83%	51+/-75%	17+/-63%	-0.07+/-45%	-18+/-45%
	p	0.06	0.01	0.01	0.03	0.05	0.05	0.01
NRA	IABP yes							36.4%
	IABP no							69.4%
	p							0.01
IA	IABP yes							36.7%
	IABP no							72.0%
	p							0.02

Conclusions: The IABP succeeded in reducing the infarct size and the no-reflow phenomenon, probably due to increased CBF during the reperfusion period.