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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 one another five 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 1,494 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 (unadjusted p<0.05, same risk allele). The association was not significantly different when genotyping the samples in the second study, was with a SNP in the gene coding for metabolic glutamate receptor 8 (GRM8, R=0.000001, OR=1.62). This unadjusted p value remained significant even after conservative multiple testing correction.

Conclusions: The identification of a CHRNA4 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 G protein-coupled receptor for which in-vitro and in-vivo studies have suggested a potential role in regulating glucose homeostasis. The strong 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 activity towards a more anti-inflammatory one by this A379Y genetic mutation might help explain this paradoxical gene-phenotype association. Further 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 development 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-AH enzyme towards a more anti-inflammatory function.
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-1α gene (IL-1α) is associated with the risk of MI. IL-1α-3 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

P. Marc van der Zee, Hein J. Verberne, Jan P. van Straalen, Johan C. Fischer, Gerard T. B Sanders, Berthe L. F. van Eck, Robbert J. de Winter, Academic Medical Center, Amsterdam, The Netherlands

Background: In patients with overt heart failure, levels of N-terminal pro-BNP (NT-proBNP) are associated with widespread 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-step stress-rest protocol using 99mTc 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 heart rate), 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 log-transformed to a normal distribution.

Results: 15 patients were classified as having myocardial ischemia. Baseline NT-proBNP levels were 75 pg/mL (23-36) (median, IQR 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-Gault), LVEF, and SDS, as assessed from the samples at baseline (adjusted R² of model = 0.537), maximum exercise (adj R² = 0.561), and 4 hours later (adj R² = 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 Feyer, H. F. Nichols, 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 hours, 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 ratio (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. 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=0.84). In the selective invasive group, the median CK-MB ratio for PCI related MI was 2.26 (IQR 1.4-6.8) for spontaneous MI (p=0.74). The incidence of MI (spontaneous and PCI related) with peak CK-MB ratios >6 was 5.3% in the EI group versus 4.9% in the SI group (p=0.8). 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 3.0% 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. Pitchett, 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 (NSTEMI) acute coronary syndromes (ACS).

Objective: To examine the temporal use of invasive strategy in the "real world" management of NSTEMI ACS.

Methods: The Canadian ACS Registries were prospective multicentre observational studies of less selected ACS patients. ACS I enrolled 2778 NSTEMI 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).

Conclusions: The use of in-hospital coronary angiography and revascularization has increased substantially in the management of NSTEMI 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

Manvyn H. Eng, John S. Rumsfeld, Edward P. Havranek, Philip G. Jones, David J. Magid, John C. Messenger, John A. Speros, Saif S. Rathore, Harlan M. Krumholz, Frederik A. Molsdeld, University of Colorado Health Sciences Center, Denver, CO, Mid-America Heart Institute/University of Missouri, Kansas City, Kansas City, MO

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

Raban V. Jeger, Shannon M. Harkness, Krishnan Ramanathan, Christopher E. Buller, Matthias E. Pfisterer, Lynn A. Sleeper, Judith S. Hochman, New York School of Medicine, New York, NY

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; 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 (64±27 vs 71±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=826) 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 IMS and CSA assigned CSA and CSD pts.

Conclusions: CSA pts have 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.

Table

<table>
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<tr>
<th>N=19,753</th>
<th>Non-PCI Hospitals</th>
<th>PCI Hospitals</th>
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<tbody>
<tr>
<td>n (%)</td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Non-PCI</td>
<td>PCI (n=1,959)</td>
<td>Transport to PCI (n=1,045)</td>
</tr>
<tr>
<td>Immediate coronary angiography (n=3,388)</td>
<td></td>
<td></td>
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<tr>
<td>Unstable angina (n=261)</td>
<td>65.8%</td>
<td>62.7%</td>
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<tr>
<td>Death or MI</td>
<td>35.2%</td>
<td>33.1%</td>
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<tr>
<td>STEMI (n=1,690)</td>
<td>79.7%</td>
<td>72.7%</td>
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<tr>
<td>Death or MI</td>
<td>21.0%</td>
<td>21.2%</td>
</tr>
<tr>
<td>STEMI (n=3,728)</td>
<td>44.7%</td>
<td>15.9%</td>
</tr>
<tr>
<td>Death or MI</td>
<td>20.5%</td>
<td>18.9%</td>
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</table>

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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 had better outcome in non-PCI hospitals and transport to PCI only partially improves the outcome.

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, Elliot M. Antman, Anatoly Langer, Neal S. Kleiman, Harvey D. White, Robert J. Chisholm, Robert A. Harrington, James F. 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, 9,978 patients with non-ST elevation ACS were randomly assigned to enoxaparin or unfractionated heparin. Of these, 9,964 patients underwent angiography within 22 (6, 43) hours and 4635 (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 4F, 2.0% 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 randomized 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.

Cardiogenic Shock Complicating Non ST Segment Elevation Myocardial Infarction. Data From Rico Survey

Marianne Zeller, Jack Ravis, Gilles Rouot, Sonia Salmi-Belmihoub, Mohamed Jolak, Jean-Claude Bear, Michel Vincent-Martin, Isabelle L'Huillier, Hamid Makki, Philippe Buffet, Nawal Moreau, Alexandra Oudot, Yoga Cotin, 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 ventricular 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 yrs 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 44 vs 38%, 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.

Myocardial Ischemia and Infarction
Complications During Spasm Provocation Tests Of Acetylcholine - From The Experience Of 927 Consecutive Cases

Shosuo Sueda, Yusuke Isez, Hiroshi Fukuda, Saiseikai Saijo Hospital, Saijo City, Ehime, Japan

Background: There were some reports concerning the severe complications during nonselective spasm provocation test of ergonovine and its complication rate was 0.16-4.7%.

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 nonparepine 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. Intervascular 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.
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 Amtz, Klaus Ellinger, Harald Genzwerker, 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 physicians by obtaining a 12-lead ECG were collected and processed centrally. A total of 64 ambulance systems in Germany were 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, 20% had a previous 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 underwent PCI (65.6%) and 106 (52.6%) patients underwent fibrinolysis. The in-hospital mortality of admitted patients was 33%. In total 96 of 197 patients (48.7%) with STEMI died in the hospital.

Conclusion: Patients with STEMI already diagnosed in the ambulance by emergency physicians treated with early reperfusion therapy and CPR have a high mortality despite an over 90% rate of early reperfusion therapy. The therefore the real world mortality of patients with STEMI is higher than recent clinical trials and in-hospital registries suggest.

Acute Myocardial Infarction: Improving Trends in Patient Care

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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.


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 (58.5 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 76.8%, 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.
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 urban settings. 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, Suhab Al-Kurtass, Yufang Fu, Galen Wagner, Shaun G. Goodman, Robert Welsh, Christopher Granger, Lars Wallentin, Franca Van de Werve, 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 size acuteness (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 lead) adds value to time to treatment in predicting reperfusion, aborted MI and large MI.

**Methods:** ECGs (at baseline, 60 min after lysis) of STEMI pts in ASSENT3 and 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 i.e. CK:5x normal (61.3% vs 71.7%, p<0.001). A multivariate analysis showed both time to treatment >2h (OR=1.68, Cl=1.41-2.00) and AS>2 (OR=1.46, CI=1.20-1.77) are independent predictors of aborted MI. In all pts, complete closure of 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. 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, heart failure, re-infarction and high-graded AV-block. For each hospital day we determined the 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.

**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.

**Conclusion:** Despite its rural location, transport times are similar to those in urban settings. 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.

**1004-236**

**Participation In Thrombolytic Trials Delays Reperfusion Therapy In Acute Myocardial Infarction.**

Wojciech C. Waszek, Sebastian Stec, Tomasz Mazurek, Andrzej Budaj, Beata Klośiewicz-Wasek, Pawel Maciejewski, Bronislaw Bednarsz, 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 reperfusion 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.

**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)**

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<thead>
<tr>
<th>Subgroup of pts with chest pain &lt;1h</th>
<th>Trials</th>
<th>all patients</th>
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<tr>
<td></td>
<td>mean ± SD</td>
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<td>Trials</td>
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**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. Zariris, Demetrios Beldekos, Charalampos Apostolatos, Dionissis Xenos, George Bibis, Olga Ampartzidou, Stamatis Makrygiannis, Paraskevi Psarogianni, George Psarias, Evdokia Adamopoulou, John Hatzisavvas, Stefanos Foussas, Tzario 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 outcomes 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 (NSTEMI). For the purpose of this study 934 consecutive pts with STEMI (458 pts) and NSTEMI (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 NSTEMI 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 NSTEMI (p<0.01). However by multivariate regression analysis, in which all univariate predictors of cardiovascular mortality were included, high plasma tHcy levels were not associated with the 5-year outcome in both STEMI (p=0.9) and NSTEMI (p=0.8).

**Conclusions:** The results of the BIOS study suggest that plasma tHcy levels upon admission cannot be used as an index of early risk stratification in patients with either STEMI or NSTEMI.

**POSTER SESSION**

**1004-235**

Participation In Thrombolytic Trials Delays Reperfusion Therapy In Acute Myocardial Infarction.
Background: Urinary albumin concentration (UAC) has been associated with adverse short-term prognosis. The prognostic significance of HNa in acute coronary syndrome (ACS) is unknown.

Methods: Among ACS patients, we studied urinary albumin quantification (UAC) using a spot urine sample at enrollment and at the end of study. HNa was measured using a commercial diagnostic kit (Dipstick, Roche). The primary endpoint, which was a composite of cardiac death, non-fatal myocardial infarction (MI), revascularization, or hospitalization, was determined using a Cox proportional hazards analysis. Measurement of renal function, such as creatinine and creatinine clearance (creacl), 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: Measurements of renal function, such as creatinine and creatinine clearance (creacl), 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.

Conclusions: Patients with death, MI, stroke or the composite of death, MI or stroke at 2 years each increased mean of 2 years after enrollment, neither statin regime significantly reduced urinary MA. The prognostic significance of HNa in acute coronary syndromes, especially beyond the index hospitalization, is not known.
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 Glu72/Glu72 (β2-AR) polymorphism is directly related to coronary artery disease (CAD).

Methods. Seven hundred and fifty-five consecutive patients were genotyped for Glu72/Glu72 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, Glu72 allele frequency was 39%. In No CAD patients, allele frequency was similar to controls (40%; OR:1.0, 95%CI: 0.61-1.5, NS). In CAD patients, incidence of Glu72 variant was significantly higher (47%; OR:1.4, 95% CI:1.1-1.7; p<0.01 vs controls and NO). The risk for CAD was 1.9 fold higher for Glu72 heterozygotes and 2.4 fold higher for Glu72 homozygotes Glu72 patients (Table).

Conclusion. The incidence of coronary artery disease is higher in patients with Glu72 variant of the β2-adrenergic receptor. The present data suggest that Glu72 polymorphism may play a role in the progression of coronary athervosclerosis and represent a novel risk factor for coronary artery disease.

**TABLE 1**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Placebo</th>
<th>DHEA</th>
</tr>
</thead>
<tbody>
<tr>
<td>DHEA (ng/dl)</td>
<td>103</td>
<td>106</td>
<td>191†</td>
</tr>
<tr>
<td>Estradiol (pmol/l)</td>
<td>69</td>
<td>97</td>
<td>196†</td>
</tr>
<tr>
<td>Testosterone (nmol/l)</td>
<td>11.9</td>
<td>12.6</td>
<td>16.9*</td>
</tr>
<tr>
<td>Nitroglicerine use (tabl/week)</td>
<td>6.1</td>
<td>6.7*</td>
<td>2.9*</td>
</tr>
<tr>
<td>ETT workload (METs)</td>
<td>7.5</td>
<td>7.0</td>
<td>9.5</td>
</tr>
<tr>
<td>ETT duration (min)</td>
<td>6.8</td>
<td>6.4</td>
<td>8.2</td>
</tr>
</tbody>
</table>

* significantly different than placebo
† p<0.001 when comparing to placebo

**Conclusion**

Dietary supplementation with dehydroepiandrosterone (DHEA) has been considered as therapeutic modality in coronary patients. We aimed to determine the effects 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/d 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 improvement in quality of life (physical function, vitality, body 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. (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(40.6%), TT 10(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 susceptibility gene for VAP.

**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**

**T006-215**

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


**Background.** Dietary supplementation with dehydroepiandrosterone (DHEA) has been considered as therapeutic modality in coronary patients. We aimed to determine the effects 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/d 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 improvement in quality of life (physical function, vitality, body 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.

**T006-216**

Endothelin-1 Gene LYS198ASN Polymorphism in Human Variant Angina Pectoris

Ju Young 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 endothelin derived relaxation factor (EDRF) was assumed to be one of the key factors causing VAP. Recently, the polymorphisms of EDRF and other vasoconstrictors 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 ergonovine (ERG) provocation coronary angiography (CAG)(n=58, 43.7%). Absence of the fixed coronary artery disease

**T006-217**

GLU27 Variant of Beta 2 Adrenergic Receptor Polymorphism is a Risk Factor for Coronary Artery Disease

Emmanuel Barbato, Alexandre Berger, Leen Delrue, Ganesh Manoharan, Eddy van Schuerbeeck, William Wijns, Hans De Beenhouwer, Quirino Climp, Jozef Bartunkov, O.L.V. Clinic, Cardiovascular Center, Aalst, Belgium, Fatesbenefratelli 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 Glu72/Glu72 (β2-AR) polymorphism is directly related to coronary artery disease (CAD).

**Methods.** Seven hundred and fifty-five consecutive patients were genotyped for Glu72/Glu72 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: 0.61-1.5, NS). In CAD patients, incidence of Glu27 variant was significantly higher (47%; OR:1.4, 95% CI:1.1-1.7; p<0.01 vs controls and NO). The risk for CAD was 1.9 fold higher for Glu27 heterozygotes and 2.4 fold higher for Glu27 homozygotes Glu27 patients (Table).

**Conclusion.** The incidence of coronary artery disease is higher in patients with Glu27 variant of the β2-adrenergic receptor. The present data suggest that Glu27 polymorphism may play a role in the progression of coronary athervosclerosis and represent a novel risk factor for coronary artery disease.
Background: Sarpogrelate HCl is a novel serotonin blocker, which specifically antagonizes 5-HT2A receptors, and it has potential as an antithrombotic 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, 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 osilometric technique (form PWVABI, 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.

ABSTRACTS - Myocardial Ischemia and Infarction

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

Ryo Matsumoto, Takashi Omura, Minoru Yoshimura, Tetsuya Hayashi, Yasutakus Izumi, Yasuhiro Nakamura, Kaname Aikio, 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 ischemic regions.

Methods: Bone marrow mononuclear cells of Lewis rats were cultured with low glucose DMEM for MSCs outgrowth. The human VEGF<sub>165</sub> gene was transcribed 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 one week after MI, a cardiospecific marker, left ventricular end-diastolic and end-systolic dimensions, ejection fraction, W 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.

Conclusion: 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

Jyhui 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-azacytidine 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( 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, myocardial generation, and improved cardiac function after implantation in infarcted myocardium.

Methods and Results: In vitro study: Human MSCs were treated with BMP-2 + 4FGF (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. Echocardiographic 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 Fluvasatin Enhances the Mobilization of CD34<sup>+</sup>,CD117<sup>+</sup>, CCR4<sup>+</sup>, C-met<sup>+</sup> Stem Cells Into Peripheral Blood in Patients With Acute Myocardial Infarction: LAVA Trial

Wojciech Wisnawski, Anna Michalowska, Marcin Majka, Katarzyna Maslankiewicz, Ratał Wyderka, Marek Krol, Andrzej Ochala, Marusz Z, Ratałajczak, 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. Stains 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 days after admission) treatment with 80 mg of fluvas tin 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...
Dose-Dependent Contribution of CD34-positive Cell Transplantation to Cardiomyogenesis, Vasculogenesis and Arteriogenesis with Functional Recovery Post-Mycardial Infarction

Hiroto Kawai, Atsushi Kawamoto, Masakazu Ishikawa, Akira Oyamada, Shuko Nishimura, Kazuyo Sadamoto, Miki Horii, Satoshi Murasawa, Hiroto Iwasaki, Atsuhiko Kawamoto, Masakazu Ishikawa

Aims: Stem cell transplantation has been well demonstrated to improve cardiac function after myocardial infarction (MI). Recently, we could generate CD34+, CD117+ and CD117+ cells from blood mononuclear cells with pluripotent characteristics that differentiate into various somatic cell types. This study investigated whether these programmable cells of mononuclear 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 mononuclear cells of male origin served as control. 6 weeks after transplantation, all animals underwent transthoracic echocardiographic examination for assessment of LV dimensions and cardiac function. Additionally, PCR for the rat sex determining region of the Y-chromosome was performed on the different areas of infarcted heart muscle using microdissection technique.

Results: Intramyocardial injection of PCMO significantly improved LV function of infarcted hearts (systolic function (EF) 53.0 ± 15.2% in animals injected 24 hours postinfarction and EF 50.8 ± 4.3% in animals injected 6 days after MI versus EF 38.3 ± 8.7% in untreated rats, p<0.05) while transplantation of naive blood mononuclear cells 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 improves 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 approach.

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.

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 Swei, Jianming Fang, Fad Saab, Miree Petria, Kim A. Eagle, Deborah 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 may 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 dysrhythmias and MACCE 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.
When EF is normal. Pts presenting with possible ACS should have EF assessed routinely. The presence of TnI elevations increases mortality 2 fold or more for any given EF, even if EF is a powerful predictor of mortality in pts admitted for exclusion of MI. CONCLUSIONS: EF assessed, MI was diagnosed by TnI elevations in 545 pts (18%). AMI pts were more frequent in patients with HF than those without HF. Fasting glucose > 110 mg/dL was associated with an increased risk of hospitalization with ACS (75 vs 63 y, p<0.001). Mean fasting blood glucose (FG) was determined at the time of admission (85 vs 74 b/min, p<0.01) and higher incidence of altered LVEF (p=0.001). 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 (p=0.001). There was a significant increase in hospital mortality in the HF group (12 vs 3 y, p<0.001). Logistic regression analysis, HF was a strong independent predictor of hospital death (OR, 4.53; 99% CI, 2.01-10.17, p<0.001). FG abnormality was an independent predictor of HF, even after adjustment for covariates (age, gender, race, smoking status, history of hypertension, prior MI, STEMI, LVEF, and creatinine level) (OR, 2.58; 99% CI, 1.58-3.96, p<0.001). 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.

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

Marianne Zeller, Jack Ravisi, Gilles Rioufol, Hamid Makki, Mohamed Jolak, Alexandra Oddot, Luz Jamin-Maréchal, Isabelle Lhuillier, Jean Eric Wolf, Bruno Verges, Luc Rochette, Yves Cotto, 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 (FG), on the outcome of in-hospital cardiacogenic shock development and mortality after acute myocardial infarction (MI). However, very few studies have investigated the influence of abnormal fasting glycaemia 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 cardiacogenic 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 enrolled, 202 (22%) had HF. Median age was significantly higher in the HF group than in patients without HF (75 vs 63 y, p<0.001). Moreover, patients with HF had significantly higher rate of cardiovascular risk factors. Patients with HF were therefore likely to have a FG abnormality (69 vs 45 %, p<0.01), and had higher HbA1c median level (6.1 vs 5.7 %, p<0.01). The incidence of MI with HF (STEMI) or with anterior location was similar for the 2 groups (p=ns). Patients with HF had increased median pulses measured at the time of admission (85 vs 74 b/min, p<0.01) and higher incidence of altered LVEF (p<0.01). There was a significant increase in hospital mortality in the HF group (12 vs 3 y, p<0.001). Logistic regression analysis, HF was a strong independent predictor of hospital death (OR, 4.53; 99% CI, 2.01-10.17, p<0.001). FG abnormality was an independent predictor of HF, even after adjustment for covariates (age, gender, race, smoking status, history of hypertension, prior MI, STEMI, LVEF, and creatinine level) (OR, 2.58; 99% CI, 1.58-3.96, p<0.001). 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.

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 University, 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, Tnl). EF was assessed using gated SPECT, coronary angiography, or echocardiography during hospital admission. An elevated Tnl was defined using the ACC/ESC criteria. One year cardiac mortality was compared in those with and without Tnl elevations.

RESULTS: Among the 3,074 consecutive pts admitted without ST elevation MI who had EF assessed, MI was diagnosed by Tnl elevations in 545 pts (18%). AMI pts were more likely to have an systolic dysfunction (EF<50%) 51% vs 30%, p<0.001) and an EF<35% (25% vs 11%, p<0.001) than those without Tnl elevations. There was a stepwise increase in mortality based on both Tnl status and EF (Figure).

CONCLUSIONS: EF is a powerful predictor of mortality in pts admitted for exclusion of MI. The presence of Tnl 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.

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=62,674), 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 17.0% of lean patients, 33.5% of overweight patients and 47.7% 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<0.0001 across groups). Use of reperfusion therapy was higher in obese (83.6%) and overweight patients (82.4%) 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.
200A  ABSTRACTS - Myocardial Ischemia and Infarction

TOS1-220

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, 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 diabetic. Diabetes was associated with a 90% increase in in-hospital mortality (12.5% vs. 6.4%, p<0.001). More often female (58% vs. 50%, p<0.001), with 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 (2.6% vs. 6.4%, p<0.001), peripheral artery disease (3.0% vs. 0.01%, p<0.001), pre-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 (47.2% vs. 72.9%, p<0.001). Intracoronary balloon pumping 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 (73% 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: Diabetes 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.

TOS1-221

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, Noryuki Naya, Keiichi Imagawa, Kenji Onoue, Yasuhiro Iwashita, Shiro Asai, Satoshi Okajima, Yukiji Takeda, Satoru Hisamichi, Shinji Yamauchi, Katsuhisa Shiozawa, and Minoru Hattori, National Cardiovascular Center Research Institute, Suita, Osaka, Japan

Background: Attenuating myocardial infarction (MI), efficient myocardial cooling could not be obtained by cardiac over-expression of PlGF. Here we investigate the 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 (CA-CS) (just after RC of the occluded CA was significantly higher than the value before RC (14.1±10.6 vs. 0.0±7.1 pg/ml, p<0.001), 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 correlate 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=0.0089). Mouse study: In mouse models of MI, tissue PIGF mRNA expression was increased 26.5 fold (p=0.001) compared with sham operated heart. Immunohistochemical staining showed that PIGF protein was over-expressed mainly in endothelial cells of coronary artery in the infarct region, but scarcely in non-infarct region.

Conclusions: PIGF 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.

1034-126  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 Dalsas, Alain Kaly, Mark Turco, Heinz P. Schultheiss, Barry Rutherford, Mitchell W. Kruskoff, Raymond Gibbons, Alessandra J. Lanksky, 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 with 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 vs. without distal protection with the 0.28” 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.

<table>
<thead>
<tr>
<th></th>
<th>GuardWire (n=252)</th>
<th>Control (n=249)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Final TIMI-3</td>
<td>9.6%</td>
<td>9.3%</td>
<td>0.44</td>
</tr>
<tr>
<td>Final blush grade 3</td>
<td>61.1%</td>
<td>52.9%</td>
<td>0.09</td>
</tr>
<tr>
<td>STR 30 mins</td>
<td>62.2%</td>
<td>60.6%</td>
<td>0.77</td>
</tr>
<tr>
<td>Infarct size (%)</td>
<td>18.3 ± 19.4</td>
<td>16.2 ± 19.1</td>
<td>0.26</td>
</tr>
<tr>
<td>3mo death</td>
<td>1.9%</td>
<td>2.4%</td>
<td>0.31</td>
</tr>
<tr>
<td>6mo reinfarction</td>
<td>2.5%</td>
<td>4.0%</td>
<td>0.37</td>
</tr>
<tr>
<td>6mo disabling stroke</td>
<td>0.9%</td>
<td>1.8%</td>
<td>0.37</td>
</tr>
<tr>
<td>6mo TVR</td>
<td>6.4%</td>
<td>6.0%</td>
<td>0.83</td>
</tr>
<tr>
<td>6mo MACCE</td>
<td>10.1%</td>
<td>11.3%</td>
<td>0.61</td>
</tr>
</tbody>
</table>

Conclusions: The GuardWire distal protection device may be used safely as an adjunct to primary PCI in AMI, and effectively removes 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.

1034-195  Catheter-Based Trans-coronary Myocardial Hypothermia Attenuates Arrhythmia and Myocardial Necrosis in Pigs With Acute Myocardial Infarction

Hirotsugu Oota, Junya Shiki, Yoshito Shrinkie, Naoide Yoshikawa, Oscar Luis Parades, Yuake Imura, Satoshi Watanabe, Takaaki Murata, Tsukasa Sawa, Daisuke Anide, and Koji Osawawa, Kyoto University Graduate School of Medicine, Kobe, Japan

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 (OTWBB) lumen.
Methods: Anesthetized pigs received 60 min of coronary artery occlusion with OTWB and 2 hr 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 animals with cold saline (4°C) was given to ischecmic myocardium through the wire lumen of OTWB with 150 ml (determined with preliminary study). In N pigs, same volume of non-thermal saline (36.5°C) was administered through OTWB. Myocardial and systemic temperature, impedance of ventricular tachycardia (VT), coronary flow reserve (CFR) by Doppler flow wire, serum troponin T variables, and ratio of necrosis to ischemic area using blue dye and triphenyltetrazolium chloride staining were evaluated.

Result: In H group, myocardial temperature significantly decreased from 36.3±1.0°C to 35.6±1.2°C (p<0.001) without significant change in rectal temperature. In N group, myocardial temperatures in N group did not change. Incidence of VT was 38% in H and 73% in N group. At 1 hr reperfusion, CFR in H was significantly higher than that in N (H:24.4±5.6 vs N:17.5±5.0, p=0.01). The values of troponin T was significantly lower in H than in N (H:0.85±0.61 µg/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 myocardial area using OTWB. This method dramatically reduced arrhythmia and MI size in reperfusion.

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 endpoint.

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 (36% 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 (3.9% vs. 6.3%, 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 inhospital 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.

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 endpoint.

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 (36% 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 (3.9% vs. 6.3%, 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.
1034-201
Effects Of Hypothermia On Haemostasis And Inflammation During Myocardial Infarction
Laurent Payot, Jean-Philippe Colet, Gilles Montalescot, Annick Avtk, Farzin Beygui, Remi Chouat, 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 (iCool6) 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), plasminogen activator inhibitor-1 antigen (PAI-1), plasminogen, FVIIIc, vWF 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.

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 Dimer and Protein S. These variations were found to be statistically significant for vWF, IPA antigen, and antithrombin III. We have paired our patients according to the age, the sex, the killop score, Timi flow at the end of PCI with patients who were not treated with endovascular cooling. Of interest, vWF and PAI-1 antigen at release (T3-T1) was found to be lower in patients who received endovascular cooling as compared to controls (1.0 vs 35.3, p=0.001 and -4.2 vs 12.2±0.2, 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 (NSTEMI) 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, 2,440 did not have any open label antithrombin therapy before randomization, and 268 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-pre-treatment subgroup (n=2,440), 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 613 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, Gianbatista Isabella, Renato Razzolini, Sabino Iliceto, University of Padova, Padova, Italy

Background: According to published meta-analysis, primary angioplasty (PCI) compared to thrombolysis therapy (TT) is associated with an absolute mortality reduction of 2%. This result, however, is unlikely to be applied to all patients.

Methods: We tested the benefit of primary PCI as function of mortality risk, we examined the treatment effect of PCI compared to TT across 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 for 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 Ermen, Fatemeh Uzer, Ebru Ortuturk, Mahmut Cakmak, Olaver Oz, Muhammed Gundogar, Aycan Eser, Ali Buturak, Birsen Ersek, Siyiemi Enerek-Thronick and 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 mg/kg, followed by 0.15 mg/kg for 24 hrs). 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±19 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.
In the setting of secondary prevention, IR is a strong and independent predictor of cardiovascular events in diabetic patients. Here, we examine the predictive power of clinical insulin resistance (IR) and preserved left-ventricular function. Despite the progress in coronary artery disease (CAD) risk stratification models, there is no consensus on the best treatment for patients with stable multi-vessel CAD (8.5%) individuals with refractory angina requiring revascularization; 40 (6.5%) individuals died during the follow-up period of two years. 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 of the incidence of vascular events (OR = 1.725 (1.166 - 2.567); 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 [1.026-3.01] (p = 0.01). 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.

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

Neusa Lopes, Aecio Guis, Alexandre Pereira, Antonio Gaghardi, Jorge Borges, Paulo Soares, Luz Cesar, Whady Hube, 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 patients with coronary 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, hypertension, hypertriglyceridemia, low HDL cholesterol, and hyperinsulinemia, 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 in 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. In the multivariate analysis, the presence of the metabolic syndrome (p=0.05) and glucose intolerance (p=0.04) were associated with an increased mortality risk, only the presence of the metabolic syndrome: insulin resistance, obesity, hypertension, diabetes, smoking status and total cholesterol. The main subgroup analysis showing this difference was a significant shift towards a worse outcome in the subgroup of patients with diabetes compared to patients with coronary disease but no angina.

Methods: We identified angina patients enrolled in one of two U.S. managed care organizations based on the combination of an angina diagnosis in a minimum of three 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 costs for the year were $58,806 vs $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).

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.

Myocardial Ischemia and Infarction

ABSTRACTS - Myocardial Ischemia and Infarction 203A

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 history 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 analysis 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.

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


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 in a minimum of three 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 costs for the year were $58,806 vs $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).

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

<table>
<thead>
<tr>
<th></th>
<th>All Charges</th>
<th>Medical</th>
<th>Drug</th>
</tr>
</thead>
<tbody>
<tr>
<td>Relative Difference</td>
<td>25%</td>
<td>18%</td>
<td>107%</td>
</tr>
<tr>
<td>Absolute Difference</td>
<td>$10,101</td>
<td>$8,384</td>
<td>$3,411</td>
</tr>
</tbody>
</table>

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 Dewandika, on behalf of the SAGE steering committee and investigators, UCSF School of Medicine, San Francisco, CA, VACHCS, Fresno, CA

Background: Few trials have specifically investigated the effects of lipid-lowering therapy with statins in elderly patients. The Study Assessing Goals in the Elderly (SAGE) investigated statin therapy as a novel approach to the treatment of myocardial ischemia in this age-group population.

Methods: SAGE was a prospective, 12-month, double-blind study conducted at 192 sites worldwide. Qualifying patients were 65-85 years; LDL-C between 100 and 250 mg/dL who had at least 1 episode of myocardial ischemia during the year prior to randomization. The randomization was 1:1 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 (50% vs. 32% compared to P). 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). The proportion of patients free of ischemia at Month 12 was 54% for A vs. 45% for P. The proportion of patients who were 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.

Conclusion: SPRINT was the first large, multi-center international trial to demonstrate the efficacy of lidopropoxy 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 Artery Disease

Michael Domanjic, 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 8280 patients with stable CAD & left ventricular ejection fraction > 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) >30 kg/m², is an independent risk factor for the composite endpoint of stroke, non-fatal myocardial infarction, revascularization, or cardiovascular death (MACE-1) & 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 & 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] 1.19-1.53; p<0.001), but not in women (HR 0.97; 95% CI 0.73-1.29; 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.

1036-233 Ineffectiveness of Precordial Thump for Mechanical Cardioversion of Malignant Ventricular Tachyarrhythmias

Offer Adj: Jorge E. Schlamsier, Neemer Samanaih, Basil S. Lewis, Arie Millianu, 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 3-4 hours duration. After one year all certified lay volunteers underwent a 1-hour review test and a retraining if needed 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).

Results. 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.

1036-234 Continuous Oxygen Insufflation is Superior to Intermittent Positive Pressure Ventilation During Cardiopulmonary Resuscitation

Melinda M. Hayes, Ronald W. Hlwig, Arthur B. Sanders, Robert A. Berg, Nathan Anany, Kari 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% of time. 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 (20-1 kg) were anesthetized, and solid state micromanometer-tipped catheters were placed to measure aortic, right atrial, and ITF. Following 6 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 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 (p <0.06). Mean neurological deficit score was significantly less in the COI group (1.30±0.3 vs 2.60±1.0; p<0.05). Mean ITF was less with COI than either IPPV group (31±6 vs 33±5 vs 13±4; p<0.02). Arterial pH differed among all three groups (7.48±0.3 vs 7.65±0.2 vs 7.22±0.2; p<0.001), but was not related to outcome.

Conclusion. COI resulted in less increase in ITF 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.
ABSTRACTS - Myocardial Ischemia and Infarction

205A

Cardiac function was measured by echocardiography after surgery. The area at risk (AR) was defined as the region without full recovery of myocardial perfusion after reperfusion.

Methods: We generated acute myocardial infarction in the male wild type mice (wt) and cd39-/- mice underwent left

Results: The results showed that TAM significantly decreased leukocyte infiltration (% area) in CD36-/- group (25%±8 vs 35.1 µg/dL respectively, p=0.001). A long interval before initiation of cardiopulmonary resuscitation was associated with relative arterial insufficiency (5 IQR [3-10] vs 3 IQR [3-5] min, p=0.03). Eighty patients experienced early post-resuscitation shock requiring vasocactive drugs, of whom 13 died of irreversible multigorgan failure. The presence of relative arterial 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 arterial 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.

1059-229

Adverse Event Reports on Automatic External Defibrillators from 1996 - 2003

Oscar H. Tovar, Beverly Albrocht Gallareux, 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 for 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

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths</th>
<th>Malfunctions</th>
<th>Injuries</th>
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</thead>
<tbody>
<tr>
<td>99</td>
<td>2</td>
<td>17</td>
<td>3</td>
</tr>
<tr>
<td>98</td>
<td>2</td>
<td>13</td>
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<td>99</td>
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<td>2002</td>
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<td>2003</td>
<td>104</td>
<td>273</td>
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</tr>
<tr>
<td>Total</td>
<td>291</td>
<td>537</td>
<td>94</td>
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Table 2. Manufacturers' conclusions

<table>
<thead>
<tr>
<th>Year</th>
<th>Deaths</th>
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<tr>
<td>Total</td>
<td>291</td>
<td>537</td>
<td>94</td>
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</table>

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.

1059-205

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

Mika Ogawa, Noriko Ogawa, Masaharu Nakayama, Eva Csizmadia, Keiichi Enjoji, Masahiro Kohzuki, Simon C. Robson, Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA, Tokohu 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-/- mice 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 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 heart 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 area risk 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. 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 may 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

Xiaorang Zhou, Maria Febbraro, 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 (CD36+/KU) rats. LV end-diastolic size and diastolic 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 88%, P=0.001). Vessel density increased in CD36-/- group at 24 days (14.5±3.7 vs 8.2±5.6 vessels/mm², 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 function of CD36 in CD36-/- rats may serve as a novel pathway for optimizing LV function after AMI.

1059-206

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

Pedro Geradot, Hugues Gosselin, Jean-François Tanguay, Robert Clément, Angéline 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 and without coronary artery disease. The partial estrogen receptor agonist Tamoxifen (TAM) may modify MMP activation and cardiac remodeling in acute phase post MI.

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 (CD36+/KU) rats. LV end-diastolic size and diastolic 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 88%, P=0.001). Vessel density increased in CD36-/- group at 24 days (14.5±3.7 vs 8.2±5.6 vessels/mm², 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 function of CD36 in CD36-/- rats may serve as a novel pathway for optimizing LV function after AMI.

1059-207

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

Huy Phan, Elizabeth Junemore, Lisa Castellano, Nicholle Johnson, Steven Goldman, Mohamed Gaballa, Hoang M. Thai, Southern Arizona VA Health Care System, Tucson, AZ, Barer 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 constitutive 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 (t strain) are measured via M-mode echocardiography. CM and eNOS were determined via immunoblot techniques.
**Poster Title:** Abnormal Infarct Resolution One Year After Acute Myocardial Infarction: Serial Measurements by Contrast Hymperenhancement Magnetic Resonance Imaging

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

**Background:** Late myocardial infarct resolution 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 year 1. Twenty-seven patients with unchanged or improved LV function and 20 patients had LV remodeling with a decline in LVEF > 10%. Patients with LV remodeling had significantly larger LV scar 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 resolution 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**

<table>
<thead>
<tr>
<th>Ce-MRI Infarct Size (%)</th>
<th>Without Remodeling (n=27)</th>
<th>With Remodeling (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>12.6 ± 6.1</td>
<td>24.0 ± 13.3</td>
</tr>
<tr>
<td>3 Months</td>
<td>15.3 ± 7.2</td>
<td>25.3 ± 10.6</td>
</tr>
<tr>
<td>12 Months</td>
<td>12.3 ± 8.9</td>
<td>25.9 ± 13.7</td>
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**Poster Title:** Quest for a Sensitive ECG Sign of Myocardial Infarction Scar: Beyond Q wave

**Authors:** 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 postulated that an abnormal fragmented QRS (fQRS) pattern could be better than the baseline Q wave to detect myocardial ischemia as compared to the presence of Q wave alone on EKG.

**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 technical reasons). MPI was consistent with scar in 112 (47%) pts. The LAD scar (n=38) had Q in 26, fQRS in 25 and Q + fQRS in 11 pts. The sensitivity of MPI scar with Q wave decreased 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.
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unstable angina requiring re-hospitalization, revascularization, and stroke at 2-year follow-up. There was no difference in angiographic group coronary arteries and those with mild-CAD matched well with regard to the qualifying normal coronary arteries and 124/178 patients (69%) with mild-CAD. Patients with normal unstable angina requiring re-hospitalization, revascularization, and stroke at 2-year follow-up. Consequently, recurrence of chest pain symptoms in non-obstructive (>50% stenosis) CAD is often disregarded and, more importantly, there is a tendency not to recommend preventive therapy in these patients.

Methods. The TIMI 22 trial enrolled 3850 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 the present study. 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 59/178 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 2 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. Angiography was chosen by revascularization that implies acceleration of the underlying atherosclerotic process. Aggressive treatment for this "hidden" CAD is timely.

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

Luis Gruberg, Haim Hammerman, Michael Kapeliovich, Walter Markiewicz, Rafael Beyer, 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 hypertension. The mean age was 61±12 years, 40% were diabetics, 37% smokers and 44% had hypertension. Mean cTnI was 11.6±14.1 μg/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 18% and was normal in 15%. 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:

| Percent diameter stenosis (%) | 52.3±21.4 |
| Minimal lumen diameter (mm) | 9.9±0.72 |
| Reference vessel diameter (mm) | 2.52±0.84 |
| Lesion length (mm) | 8.05±4.7 |
| Plaque area (mm²) | 7.0±3.3 |
| 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.

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

Takayoshi Sakai, Yasunori Ueda, Yoji Okuyama, Yuzuru Takano, Atsushi Hayama, Kazuhisa Kodama, Osaka Police Hospital, Osaka, Japan

Background: Elevated troponin T (TnT) predicts adverse outcome in non-ST elevation-acute coronary syndrome (NSTEMI) patients. The relation between the culprit lesion morphology and elevated TnT level is poorly understood.

Objectives: In this study, we analyzed the culprit lesion morphology by using coronary angiography and intravascular ultrasound (IVUS) in relation to different TnT levels in patients with NSTEMI-ACS.

Methods: A series of 57 patients with NSTEMI-ACS who underwent angiographic and IVUS examinations were enrolled. Patients were divided into three groups based on TnT levels on admission. (<0.01 μg/L, n=31; 0.01 to 1.0 μg/L, n=15; >1.0 μg/L, n=11). In angiographic analysis, we assessed the number of yellow plaques, the color grade of yellow plaques (Grade 1: 1, Grade 2: 2, Grade 3: 3, Grade 4: 4), and the presence of FVM. With IVUS analysis, we also evaluated 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 with TnT >0.01 μg/L, 6 of 11 patients (54.5%) had >1 yellow plaque. In 3 of 31 patients (9.7%) with TnT ≤ 0.01 μg/L, >1 yellow plaque were detected. In the IVUS analysis, the plaque color grade was 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 thrombosis at culprit lesions increased in proportion to the levels of TnT. The percentage of plaque area evaluated by IVUS was 57.7±9.9%, 60.2±11.5%, 64.2±8.9% (P<0.05), respectively.

Conclusion: In patients with NSTEMI-ACS, the elevated TnT levels did not associate with the plaque burden, but related with the plaque color intensity and the presence of intraluminal thrombus. These results may indicate the plaque vulnerability and likelihood of thrombus in NSTEMI-ACS patients with positive TnT.

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

Takao Kunimasa, Masao Moroi, Tatsuhiko Furushashi, Hiroshi Fukuda, Kaoru Sugiy, Toho University School of Medicine, Ohashi Hospital, Tokyo, Japan

Recent clinical observations have suggested that the disruption in 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 (Aquilion 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 (1.0 mm²) 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 (42%) 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.
Culprit Coronary Levels of Angiotensin II and Impaired Microvascular Reperfusion in Patients With ST-Segment Elevation Myocardial Infarction

Makoto Suzuki, Masamiichi Tanaka, Eiki Hirose, Hideyuki Saeki, Tsuyoshi Matsunaka, Shinichi Hiramatsu, Yuico Kazastani, 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 all 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 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±4 µg/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 ng/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 all with incomplete microvascular reperfusion (<30% MB, 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.
adverse event. Accordingly, we undertook a study of 16,849 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 MI (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.

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 Piancavelli, Jule Thomas, Hans Stiinger, 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), 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 the infarct-related artery and treatment with abciximab (i.e. bolus injection of 0.25mg/kg), we performed gasotromium contrast-enhanced 3D inversion recovery gradient echo MRI sequences with complete coverage of the LV-myocardium in short axis slices. The mass of infarcted tissue based on the volume of hypoenhanced 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 (IU/L), CRP (IU/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).

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 contrast-enhanced MRI. No correlations were found between absolute size of infarctions (g) as well as relative size (LV%) with peak values of CRP.

ST Resolution after Mechanical Reperpufusion Closely Correlates With Myocardial Salvage And Depends On The Severity of Area at Risk By 99mTc Tetrofosmin Imaging

Takuo Shirakako, Hitoshi Matsuo, Takatomo Watanabe, Shun-ichiro Wafter, 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 repertusion, 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=38), or no resolution (<30%, n=13). Results: Patients with no resolution tended to be more prolonged than those with partial and complete resolution (complete: >70%, partial: 40±17, <30%, n=58). For the complete resolution group, peak CK (r=0.72) and peak CRP (r=0.43) were significantly elevated compared to the partial resolution group. Conclusions: Decreased D-dimer Levels Indicate Reduced Risk of New Ischemic Events After a Myocardial Infarction - Beneficial Effects of Ximelagatran

Christina Christersson, Jonas Odgren, 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 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). Conclusions: Early D-dimer levels were related to decreased risk of new ischemic events.

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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 Petrea, 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 assess 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 OM, 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.
Use of Reperfusion Therapy in Elderly Patients with Acute Myocardial Infarction

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

Background: Despite advances in reperfusion therapy for acute myocardial infarction (AMI), survival of elderly patients with AMI remain inferior to that of younger patients. These differences cannot be explained by differences in baseline characteristics or in the use of reperfusion therapy. This study was designed to determine whether gender influenced short-term outcomes in a cohort of AMI patients.

Methods: We conducted a retrospective cohort study of all patients undergoing angiography for acute myocardial infarction (AMI) at a single university-affiliated hospital between 1997 and 1999. No patients were excluded for reasons of age or gender. Patients were divided into those who received angiography within 24 hours of the latest episode of angina.

Results: Overall, 1,284 patients received reperfusion therapy, with 1,561 (20.1%) receiving fibrinolysis and 1,206 (15.5%) undergoing primary PCI. A higher proportion of patients who received reperfusion therapy at PCI capable hospitals compared with patients treated at cath lab only hospitals or hospitals with no cath lab capability (46.2%, 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.
Early Agressive Versus Conservative Management 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 Cardiody 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/NST-STEMI). Aggressive therapy at 4 to 48 hours versus conservative therapy was analyzed to identify the prognostic factors of mortality. Multivariate analysis was performed to evaluate prognostic factors of 1 year survival.

RESULTS: 128 (32%) of our patients underwent AM and 268 (68%) received CM. CM had in-hospital and long-term mortality in patients over 80 years old treated with aggressive management (AM) compared with the conservative management (CM).

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 NSTE-AMI Acute Coronary Syndrome.

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 Emilia, Modena, Italy

Background: The influence of CRP elevation on prognosis in patients with ST elevation acute myocardial infarction (STEMI) in recent reperfusion era remains to be determined. 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: 1.0g to 3.0mg/dl, highest tertile: >3.0mg/dl).

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.

Conclusions: The CRP level is an independent predictor of in-hospital and long-term mortality in patients with STEMI.
Conclusion: Exercise-induced myocardial ischemia is markedly attenuated on the ramp ergocycle compared to the Bruce protocol treadmill, an effect explained by exercise intensity (VO2) or cardiac work (RPP). The more gradually increasing workload of the ramp ergocycle protocol may have favoured a "warm-up" ischaemic effect despite achieving higher RPP than the Bruce protocol treadmill suggesting it may be physiologically preferable for exercise prescription in patients with HD.

1063-235

Prognostic Value Of hsCRP In Patients With Stable Coronary Disease And Angina Of Effort, Unvariately And In The Presence Of NT-proBNP And Other Risk Factors
Ian Ford, Michelle Blackiston, David Gaze, Henry J. Dargie, Lisa Garsin, Paul Collins, 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 myocardial infarction versus placebo in patients with stable coronary disease and angiography. 1505 patients were included in the sub-study of whom 90 had a non-fatal MI or died from non-cardiac causes (cause of death was unknown for 14 patients who died of unknown cause). The associations between prognostic factors and outcomes were investigated using Cox proportional hazards models, first for log(hsCRP) (log mg/L) and then for the logarithm of hsCRP levels (log mg/L) and its interaction with treatment allocation.

Results: hscrP levels were significantly univariately associated with both coronary events and all-cause mortality and became non-significant for coronary events and for all-cause mortality after adjusting for traditional risk factors and for NT proBNP, becoming non-significant for coronary events and for all-cause mortality after adjusting for other cardiovascular risk factors and for the logarithm of NT-proBNP levels (log pg/mL). Models were adjusted for randomised treatment allocation.

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.
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.

<table>
<thead>
<tr>
<th></th>
<th>UA(n=36)</th>
<th>ST(n=252)</th>
<th>CON(n=140)</th>
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<tbody>
<tr>
<td>CRP(mg/dl)</td>
<td>0.21 (0.11, 0.31)</td>
<td>0.09 (0.06, 0.15)</td>
<td>0.08 (0.06, 0.12)</td>
</tr>
<tr>
<td>SAA(µg/ml)</td>
<td>12.4 (6.1, 12.6)</td>
<td>4.2 (2.5, 7.1)</td>
<td>4.4 (2.7, 6.4)</td>
</tr>
<tr>
<td>SAA/LLD(µg/ml)</td>
<td>62.0 (36.8, 81.9)</td>
<td>20.5 (14.0, 30.4)</td>
<td>27.3 (11.8, 27.6)</td>
</tr>
</tbody>
</table>

By logistic regression analysis, SAA/LLD 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 marginally (p=0.047-0.076). ROC analysis showed that SAA/LLD was equivalent with CRP for the diagnosis of CAD (AUC=0.613,0.593, respectively; p>0.20), and that SAA/LLD was superior to CRP in discriminating unstable angina (AUC=0.838,0.733, respectively; p=0.013).

CONCLUSION: The serum level of SAA/LLD can predict the existence of both CAD and unstable angina more accurately than CRP.
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, Attilio Paliotti, Gianluca Perseghin, Giorgio Bassanelli, Giillosa 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 (HF) and high carbohydrate (HC) meals.

Methods: Ten pts (9 males, age 68±7 years) were allocated to placebo (P) and TMZ (40 mg t.i.d.), both administered from 24 hrs before F, HFM and HC, according to a randomized, double-blind design study. All pts underwent stress (treadmill exercise testing-Bruce protocol) echocardiography after F (hrs), HF and HC (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 383±106 to 292±123 sec, p=0.02). Compared to TMZ improved time 1mm after F, HF 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 resulted in a greater impairment of coronary reserve compared to HF. The observed beneficial effects of the partial fatty acid inhibitor TMZ seem to be independent on meal composition.

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

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

Francesco Pelliciog, Paolo Salvini, Domenico Cartoni, Loredana Macali, Fiammetta Albi, Bruno Poletta, Giuseppe Mercuro, Pietro Tarsi, San Filippo Neri Hospital, Rome, Italy, San Camillo Hospital, Rome, Italy

Background: TIMI risk score is commonly estimated at triage in Emergency Department (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 4,393 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%), ≤90 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/CA/AB (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 ED stay may be necessary particularly in these subsets of pts.

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


Background: Uncertainty remains about the dose 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 hours scantaneously. 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-enrolment) by renal function (creatinine clearance [CCr]) and age. Outcomes were assessed by clinically relevant body mass index (BMI) groupings (<25 [27.4% of pts], ≤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% vs 15.4%, p=0.593] and bleeding [4.5% vs 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 vs UFH).

Conclusions: Patients with lower CCr 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 or comparison of serum markers between enoxaparin and UFH in these clinically important subgroups were seen.

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

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Enoxaparin</th>
<th>UFH</th>
</tr>
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<tbody>
<tr>
<td>CCr &gt; 60</td>
<td>6869</td>
<td>76.1</td>
<td>76.0</td>
</tr>
<tr>
<td>CCr &gt; 60</td>
<td>870</td>
<td>70.1</td>
<td>69.9</td>
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<tr>
<td>CCr &gt; 60</td>
<td>1108</td>
<td>61.4</td>
<td>65.1</td>
</tr>
<tr>
<td>CCr &gt; 60</td>
<td>1332</td>
<td>65.7</td>
<td>63.0</td>
</tr>
</tbody>
</table>

812C 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 synthesized 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 we 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).

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 underline the usefulness of NT-proBNP for risk stratification in patients presenting with an ACS. The therapeutic consequences need to be further investigated.
Increased In-Hospital Mortality in Patients Without Traditional Risk Factors Presenting With Non-ST-Segment Elevation Myocardial Infarction: Insights From the CRUSADE Initiative


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) 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.

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

Hung Q. Ly, Aly 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 10,783 STEMI patients pooled from the TIMI trials database.

Results: Median platelet counts on presentation were 240×10^9/L. 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 <200×10^9/L.

Conclusion: In the setting of STEMI, elevated platelet counts on presentation was independently associated with adverse clinical outcomes.
### Table: Association of moderate-severe MR with outcomes

<table>
<thead>
<tr>
<th>Hazard Ratio</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>2.3</td>
<td>1.2-4.5</td>
</tr>
<tr>
<td>CV death</td>
<td>2.2</td>
<td>1.4-3.5</td>
</tr>
<tr>
<td>Combined end point</td>
<td>2.1</td>
<td>1.3-3.5</td>
</tr>
</tbody>
</table>

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

### Abstract: Transfer to Acute PCI Improves Outcome for Patients With ST-elevation Myocardial Infarction

**Background:** The multicenter hospital-based Myocardial Infarction Registry Brandenburg - representing a weakly populated German state - included 2391 patients (pts) with acute myocardial infarction (MI).

**Methods:** Pts were randomized to 14.703 pts with heart failure and/or systolic dysfunction to 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: 123.6 ± 43.3 ml, and severe MR: 135.1 ± 43.3 ml) and end-systolic (no MR: 67.3 ± 19.8 ml, mild MR: 76.8 ± 23.4 ml, and severe MR: 88 ± 33 ml) volumes increased with worsening MR, and ejection fraction decreased (no MR: 40.4 ± 5.1%, mild MR: 38.4 ± 5.8%, and severe MR: 37.7 ± 4.7%) (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.
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.

ABSTRACTS - Myocardial Ischemia and Infarction
21A

TO08-195

Admission α1-Antitrypsin Levels Predicts Myocardial Infarction Size

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

Introduction: α1-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 α1-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 ZE34K2 and S-E364V 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 levels in patients with higher admission levels as compared to patients with lower levels (74% vs. 77%, p<0.05). 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.

<table>
<thead>
<tr>
<th>Marker</th>
<th># Positive (%)</th>
<th>30 Day Death, %</th>
<th>1 Year Death, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>MYO</td>
<td>Marker (-)</td>
<td>Marker (+)</td>
<td>Marker (-)</td>
</tr>
<tr>
<td>CK-MB</td>
<td>697 (20)</td>
<td>1.3</td>
<td>2.0</td>
</tr>
<tr>
<td>Troponin</td>
<td>515 (17)</td>
<td>1.6</td>
<td>7.6</td>
</tr>
<tr>
<td>Troponin</td>
<td>2496 (90)</td>
<td>0.0</td>
<td>6.0</td>
</tr>
<tr>
<td>Troponin</td>
<td>533 (16)</td>
<td>3.2</td>
<td>13.7</td>
</tr>
<tr>
<td>TnI</td>
<td>234 (8.6)</td>
<td>NA</td>
<td>8.8</td>
</tr>
<tr>
<td>TnI</td>
<td>204 (5.9)</td>
<td>12.7</td>
<td>NA</td>
</tr>
</tbody>
</table>

TO08-196

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 Fussoli, 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 nmol/L), 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=0.001 respectively). The rate of death was 9.1% (n=257/275) in diabetic patients compared to 4.3% (n=52/1208) in non diabetic (p=0.001)

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 risk of MI.

TO08-197

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 to our hospital. An initial blood sample was obtained for serum neopterin by immunoassay and compared to admission TIMI risk scores calculated by ACC/AHA guidelines. 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.

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 (+) 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.
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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 983 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.

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Value</th>
<th>OR (95% CI)</th>
<th>p value</th>
<th>Value</th>
<th>OR (95% CI)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>65</td>
<td>2.8</td>
<td>2.2, 3.6</td>
<td>&lt;0.001</td>
<td>1.5</td>
<td>1.0, 2.1</td>
<td>0.03</td>
</tr>
<tr>
<td>Prior MI</td>
<td>1.5</td>
<td>1.1, 2.0</td>
<td>&lt;0.01</td>
<td>1.6</td>
<td>1.3, 1.9</td>
<td>0.02</td>
</tr>
<tr>
<td>Ischemic ECG</td>
<td>1.6</td>
<td>1.1, 2.1</td>
<td>&lt;0.001</td>
<td>2.3</td>
<td>1.6, 3.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>CK-MB (+)</td>
<td>2.8</td>
<td>2.1, 3.7</td>
<td>&lt;0.0001</td>
<td>2.3</td>
<td>1.6, 3.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>TnI (+)</td>
<td>1.4</td>
<td>0.96, 2.0</td>
<td>0.08</td>
<td>1.5</td>
<td>0.95, 2.3</td>
<td>0.08</td>
</tr>
</tbody>
</table>

1089-201 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 mg/dL), whereas HDL-Cholesterol was significantly lower in the UAP group than in the AMI group (43 ± 10 mg/dL). Moreover, C-reactive protein (CRP) progressively increased from control to AMI.

Conclusion: Total cholesterol and CRP in UAP were significantly higher than that of control. COHb in UAP was significantly lower than that of control. COHb might be considered as a useful indicator for the risk of acute coronary syndrome.

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 Silk Yoon, Sang Yub Lim, Kyung Ho Yun, Dong Koo Kang, Sang Hyun Lee, Yeon Sang Lee, Kye Hun Kim, Young Joong Hong, Hyung Wool Park, Ju Han Kim, Woon Kim, Myung Ho Jeong, Jeong Gwan Cho, Jong Chun Park, Jung Chae Kang, The Heart Center of Chonnam National University Hospital, Gwangju, South Korea

Background: Elevated N-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±4.4 years, 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 mg/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 ± 339 vs. 78 ± 91.1 pg/mL, p=0.005). At the standard cut-off 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.

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 Ottavanger, Menko-Jan de Boer, Eric Boersma, Cindy Grines, Cindy Westerhout, Chris Granger, Felix Zijlstra, PCAT collaborators, Isala Klinieken, locatie 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.

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

Michael E. Fartuch, Krishnan Ramananathan, Evey A. 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 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 coronary artery reperfusion (88.9 vs 97.5%, p=0.02) 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-month mortality rates of DM and the NDM were not equivalent (33.7% vs 12.9%, p<0.001). The magnitude of the benefit of an ERV strategy was similar in the DM and NDM groups (hazard ratio (HR) NDM 0.78, p=0.58). Even after adjusting for the interaction 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 current study ratifies the conclusion in NDM that mortality is a function of the 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.

Automated External Defibrillator Analysis Specifically Designed for Pediatric Patients

Dianne Atkin, Ian Law, Andrew Blalou, William Scott, McDonald Dick, Wangcai Liao, Jamil Sobh, 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 annotated by pediatric cardiologists as clinically 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 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).

Conclusion: New pediatric rhythm detection criteria were defined, and analysis based on these criteria demonstrated both high sensitivity (coarse VF, rapid VT) and specificity (nonshockable rhythms, including SVT). A pediatric-based AED can correctly detect shockable rhythms, making it safe and exceptionally effective for children.

Mycocardial Ischemia and Infarction

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Blood pressure > 130/85 mm Hg or waist circumference > 102/Mm88/Fm. Patients were classified according to their age (young (<45) and old (>45)) and to the presence of MS. Results: Of the 663 MI patients included, 63% (407) were young (≤45) (median 27-75 years) and 37% (376) were old (median 50-65 years). Blood pressure was similar for young and old patients (132/80 vs 132/80, p=0.66). With regard to the prevalence of females and tobacco use, the data for young MS patients were similar to those for young non-MS patients (respectively, 41% vs 42% and 26% vs 23%). Among patients with MS, there was a higher percentage of females (40 vs 15%, p<0.001) and lower tobacco use (18 vs 34%, p≤0.01) than patients without MS. Among patients with MS, abnormal fasting glycemia (102% and hypertension (218%)) are predominant in old patients, while low HDL (206%) and elevated triglycerides levels (197%) 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 predominant 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.

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

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

Background: Thrombosis at the culprit lesion in acute myocardial infarction (AMI) will remain as a chronic lesion after primary percutaneous coronary intervention (PCI) and one year mortality is associated with chronic residual thrombus. 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 angiography at 1 month (36±5 days, n=49), 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 were 73.9%, 53.1% 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).

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

<table>
<thead>
<tr>
<th>Interval from onset to observation</th>
<th>Statins (n=71)</th>
<th>No statins (n=117)</th>
<th>Odds Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 month</td>
<td>40.9% (29)</td>
<td>60.4% (66)</td>
<td>0.38 (0.13-1.15)</td>
<td>0.76</td>
</tr>
<tr>
<td>3 months</td>
<td>34.3% (16)</td>
<td>56.1% (33)</td>
<td>0.57 (0.29-1.00)</td>
<td>0.04</td>
</tr>
<tr>
<td>6 months</td>
<td>29.5% (24)</td>
<td>62.9% (50)</td>
<td>0.36 (0.15-0.86)</td>
<td>0.03</td>
</tr>
<tr>
<td>9 months</td>
<td>0.0% (0)</td>
<td>27.3% (3)</td>
<td>0.03 (0.03-0.77)</td>
<td>0.25</td>
</tr>
</tbody>
</table>

The Prognostic Impact ofTransient Hyperglycemia During Acute Myocardial Infarction in Non-Diabetic Patients Who Undergo Primary Percutaneous Coronary Intervention

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

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 who present transient hyperglycemia (TH) is not well understood.

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 patients at one day, and at 1 week. The endpoint of death and target lesion revascularization (TLR) was lower in normoglycemic patients (HR: 0.89, 95% CI: 0.46-0.99, p=0.04 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 not 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 (p=0.22). One year TLR rates were significantly higher in diabetics compared to normoglycemic and transient hyperglycemic patients.
High Continuation Rate of Statin Treatment Among Patients With Acute Myocardial Infarction

Jeppe N. Rasmussen, Gunnar Gislason, Steen Z. Abildstrom, Søren Rasmussen, Perminle Bach, 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, which 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 no pauses longer than 30 days and 70% 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.).

Proportion of statin treated patients who did not have treatment pauses longer than the various lengths indicated

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.


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

Background: The streptokinase (SK) regimen (1.5 MU/30 ml 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 classical SK 1.5 MU/60 min. in patients (pts.) with STEMI.

Methods: A group of 1142 consecutive pts. were thrombolysed within the first 6 hours after the onset of STEMI with one of the following four SK regimens: 1. SK 1.5 MU/30 min. (310 pts.); 2. SK 1.5 MU/30 min. (168 pts.); 3. SK 1.5 MU/20 min (377 pts.); 4. SK 0.75 MU/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) were obtained in the SK1.5/20 and SK0.75/10 group. Hypotension disappeared within 15 min. in all pts. Hypotension was more frequent in the SK1.5/60 group. 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.

Conclusions. 1. The classical SK1.5 MU/60 min. is not the best SK regimen. Higher rates of CR and lower mortalities can be obtained 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.

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


Background: Time dependency is well established for thrombolysis in ST elevation myocardial infarction (STEMI), but not for antplatelet treatment. The aim of the present work is to evaluate the relationship between the pain to abciximab (ABC) bolus time (PTB) and the level of platelet function inhibition (PfFin) 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. PfFin determined with Utegra at admission and after the bolus, and the PfAgIn rate determined, and grouped according to two pre-specified rates (80% and 95%). Sixty six pts completed all protocol determinations. Pts grouped by PTB 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 PTB and PfFin rate (r= -0.31 p= 0.022). (2) A PfFin rate lower than 95% was increasingly frequent with longer PTB: 10%, 40.0% and 47.6%, respectively for < 120 min, < 240 min, and > 240 min. (3) Pts in the lower tercil (< 120 min) were more likely to reach the intermediate efficacy between the SK1.5/60 and SK1.5/20 or SK0.75/10 ones.

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, Hospital 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 platelets, 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 STEMI within 12 hours of pain onset (< 6 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 obtained.
collected and processed immediately before angiography to measure platelet activation markers (P-selectin and PAC-1) and circulating microparticles (MPs) originating from platelet, neutrophils (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.

Methods: 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. 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. If 5% of pts. (3/60 pts.) needed a shock of 100 J. 150 Joule were administered to 2 (4%), 200 Joule to 2 (6%) pts.

Between the different electrode positions there was no significant difference concerning the mean delivered current (anterior posterior 76 ± 31 J vs. 76 ± 47 J). The anterior-lateral position was superior to anterior-posterior electrode configuration concerning the first successful 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. Conclusion: Our data show 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 atrial flutter in an emergency room setting with 75 J using anterior-lateral electrode position.

**POSTER SESSION**

**1091**

**New Observations in Emergency Cardiac Care or Cardiovension**

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-T15**

**Randomized Trial of Biphasic Atrial Flutter Cardioversion**

Kai Mortensen, Tim Riusus, Torkj F. Schwemer, M. Ali Afdin, Simone Henn, Michelle Ortik, 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 necessary 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. Pts. 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.

**ABSTRACTS - Myocardial Ischemia and Infarction 221A**

**Disparities by Sex in Timing of Initial Electrocardiogram for Patients Presenting With Acute Coronary Syndromes**


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 sex and the presence of a delay in initial ECG acquisition. Pts. 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-cardiologist inpatient care, non-white race, insurance status, type of institution, and diabetes (Table). Multivariate Predictors of Delayed (>10 minutes) ECG Acquisition

<table>
<thead>
<tr>
<th>Variables</th>
<th>OR (95% CI)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female vs. male</td>
<td>1.29 (1.25-1.34)</td>
<td>253.0</td>
</tr>
<tr>
<td>Off hours (nights and weekends)</td>
<td>0.86 (0.83-0.90)</td>
<td>50.0</td>
</tr>
<tr>
<td>Prior PCI</td>
<td>0.86 (0.82-0.90)</td>
<td>48.3</td>
</tr>
<tr>
<td>Non-white vs. white</td>
<td>1.16 (1.10-1.22)</td>
<td>33.8</td>
</tr>
<tr>
<td>No insurance vs. HMO/private</td>
<td>0.88 (0.82-0.94)</td>
<td>29.8</td>
</tr>
<tr>
<td>Medicinal insurance vs. HMO/private</td>
<td>1.07 (1.00-1.14)</td>
<td>4.01</td>
</tr>
<tr>
<td>Medicare insurance vs. HMO/private</td>
<td>1.06 (1.02-1.10)</td>
<td>3.08</td>
</tr>
<tr>
<td>Current smoking</td>
<td>0.91 (0.87-0.94)</td>
<td>3.36</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1.03 (1.00-1.10)</td>
<td>1.02</td>
</tr>
</tbody>
</table>

Conclusion: Only 35% of high-risk NSTE ACS patients had an 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.
Myocardial Ischemia and Infarction

2005_5_Myocardial Ischemia and Infarction.indd   222

222A ABSTRACTS - Myocardial Ischemia and Infarction

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<0.001 by t test). Conclusions. The extant 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 L.C. Early ITI-guided therapy may prevent AHF at its preclinical stage in most patients with AMI.

109T126
Endografting For Traumatic Aortic Injury
Taro Shimazaki, Ghin Ishimaru, Satoshi Kawaguchi, Yoshishiko 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 aortic injury.

Methods: Between September 1996 and 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=11). 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 5 mm from descending aortic injury was required before endografting was elected. Endografting was performed under general anesthesia, and an original device, created 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 units/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 cardiorrhaphy bypass with high dose heparin. Therefore, endografting may be preferable to conventional surgery for management of traumatic aortic injury in select populations.

109T127
“Cath Alert” and Transmission of a Prehospital 12-Lead Electrocardiogram Can Shorten Door-to-Balloon Times in Patients With ST-Phase 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). We tested this hypothesis in 153 consecutive patients (age 61±13, 131 male) who were admitted to the ED and triaged with ST-segment elevation 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). We tested this hypothesis in 153 consecutive patients (age 61±13, 131 male) who were admitted to the ED and triaged with ST-segment elevation myocardial infarction (STEMI).

Methods: We tested this hypothesis in 153 consecutive patients (age 61±13, 131 male) who were admitted to the ED and triaged with ST-segment elevation 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). We tested this hypothesis in 153 consecutive patients (age 61±13, 131 male) who were admitted to the ED and triaged with ST-segment elevation myocardial infarction (STEMI).

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 cardiorrhaphy bypass with high dose heparin. Therefore, endografting may be preferable to conventional surgery for management of traumatic aortic injury in select populations.

1092
Off-Pump CABC: Benefits of Avoiding the Machine
Andre Lam, Forough Garshoyar, 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. 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±1 vs. 9.0±1.10, p<0.01).

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

<table>
<thead>
<tr>
<th></th>
<th>Follow-up</th>
<th>One-year</th>
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<tr>
<td></td>
<td>Off-pump</td>
<td>On-pump</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.3/1.21</td>
<td>0.3/1.84</td>
</tr>
<tr>
<td>MI</td>
<td>0.2/0.42</td>
<td>0.1/0.31</td>
</tr>
<tr>
<td>Stroke</td>
<td>0.1/0.30</td>
<td>0.1/0.31</td>
</tr>
<tr>
<td>Revascularization</td>
<td>0.9/2.0</td>
<td>0.1/0.31</td>
</tr>
<tr>
<td>Angioplasty</td>
<td>0.9/2.0</td>
<td>0.1/0.31</td>
</tr>
<tr>
<td>Revascularization</td>
<td>0.9/2.0</td>
<td>0.1/0.31</td>
</tr>
<tr>
<td>p&lt;0.05</td>
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</table>

At one year, the adjusted rates of mortality and MI were similar between off-pump and on-pump CABG surgery 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.
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 mg/dL was compared with the renal failure group (RF) with serum creatinine ≥ 2.5 mg/dL. (p=0.001).

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 (3.2% 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 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 66.2% vs 85.3%, p<0.001). Multivariate analysis identified increasing age, gender, emergent or off-pump surgery, and the combination of RF and increased EF as independent risk factors for early mortality (Table).

Conclusion: CABG patients with renal failure have significantly increased renal and non-renal mortality 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.

Method: Patients in both groups had similar demographics, co-morbidities and number of cardiac procedures. Emerging predictors for mortality in women evaluated for suspected ischemia were analyzed for 56457 patients undergoing CABG without requirement for preoperative dialysis.

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.
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 Vavaranakis, Sophia Vaina, Aris Androutsakis, 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 (Medisepes, 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±0.02°C, p<0.05). Pts with DM had increased DT compared to pts without DM (DT: 0.19±0.03 vs 0.12±0.02°C, 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±0.04°C, 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±0.03°C, p=0.7). (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.

224A ABSTRACTS - Myocardial Ischemia and Infarction

JACC February 1, 2005

2:45 p.m.

814-6

Lipoprotein-Associated Phospholipase A2 Independently Predicts the Angiographic Diagnosis of Coronary Artery Disease

Benjamin D. Horne, Jeffrey L. Anderson, Robert L. Wolfert, Joseph B. Muhlestein, Dale G. Remuld, Jessica L. Clarke, Heidi Thomas, Matthew J. Kolek, Tam L. Bar, 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 A2 (LpPLA2) is an enzyme that may be a cardiovascular-specific inflammatory biomarker. We evaluated the independent association of LpPLA2 to CAD and CV events adjusting for standard factors, lipids, and CRP. Methods: LpPLA2, (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. LpPLA2 weakly correlated with lipids (LDL: r=0.25, p<0.01; HDL: r=-0.13, p<0.001), but not with CRP (r=0.03, p=0.26). LpPLA2 levels differed between patients with CAD (geometric mean: 369.5 [SE: 63] mg/ 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 LpPLA2 predicted increased risk of CAD (vs. Q1) for Q2 (odds ratio [OR]=1.15, 95% CI=0.98-1.37, p=0.048), for Q3 (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). In multivariable logistic regression, increasing quartile (Q) of CRP predicted increased risk of CAD (vs. Q1) for Q2 (odds ratio [OR]=1.15, 95% CI=0.98-1.37, p=0.048), 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). In multivariable Cox regression, LpPLA2 was predictive of new MI (Q1: 2.18, Q2: 1.92, Q3: 4.56, Q4: 19.23, p<0.001). In multivariable Cox regression, LpPLA2 was predictive of ischemic death (Q1: 1.92, Q2: 2.00-6.77, Q3: 11.13, Q4: 19.23, p<0.001). In multivariable Cox regression, LpPLA2 was predictive of CVA (Q1: 2.18, Q2: 1.92, Q3: 4.56, Q4: 19.23, p<0.001). In multivariable Cox regression, LpPLA2 was predictive of all-cause death (Q1: 1.92, Q2: 2.72-11.14, Q3: 19.23, Q4: 11.13, p<0.001). Conclusions: LpPLA2 was confirmed to predict increased CAD risk, and extends this to patients undergoing coronary angiography. LpPLA2 was found to predict longitudinal risk of ischemic death, and did so with a similar effect size. This study suggests that LpPLA2 may be considered as an ischemic-specific inflammatory marker of clinical CV risk along with the non-specific CRP.

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, Takashi 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 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. Thrombus aspiration therapy was carried out in 34 cases with the RESCUE thrombectomy catheter, a PercuSurge GuardWire Plus Temporary Occlusion and Aspiration System. Methods: We performed histological analysis using tissue samples obtained by thrombus aspiration therapy. Results: Five of the 9 polymorphisms (1 in BAT1, 1 in NFKBIL1, and 3 in LTA) were significantly associated with a protective effect against minor myocardial infarction: homoyzgyous carriers of the less frequent alleles were significantly more abundant in the control group than in the group with myocardial infarction (p<0.05). 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 homoyzgyous carriers of the protective haplotype (p=0.008). Conclusions: The BAT1-NFKBIL1-LTA region on chromosome 6 is a susceptibility locus for myocardial infarction in a Japanese population. In contrast to previous findings among Japanese, homozgyous carriers of the less frequent alleles and carriers of a specific haplotype defined by the 9 SNPs present decreased risk of myocardial infarction.
NT Pro-BNP Predicts Clinical Outcomes in Patients With Acute Coronary Syndromes And Preserved Left Ventricular Function

Florenzio 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 (NSTEMI). 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 NSTEMI and preserved LV function.

Methods: From a prospective cohort of 1483 patients with NSTEMI, 590 underwent in-hospital angiography (median 2 days). Among these, 393 patients had LV ejection fraction >40% and confirmed 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<0.001), 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 was the best predictor of MI. (see table)

Conclusions: NT-proBNP is an independent predictor of clinical outcomes in patients with NSTEMI and preserved LV function. It is possible that prognostic information provided by NT-proBNP might be related to other mechanisms than LV dysfunction.

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

<table>
<thead>
<tr>
<th>Inter-hospital delay (min)</th>
<th>&lt; 30</th>
<th>30-59</th>
<th>60-89</th>
<th>&gt; 90</th>
<th>p trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>94</td>
<td>188</td>
<td>194</td>
<td>140</td>
<td></td>
</tr>
<tr>
<td>Ischemic time (min)</td>
<td>185 (136-289)</td>
<td>190 (156-247)</td>
<td>220 (172-286)</td>
<td>232 (201-389)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Door-to-balloon time (min)</td>
<td>41 (29-60)</td>
<td>38 (27-51)</td>
<td>37 (25-51)</td>
<td>37 (25-51)</td>
<td>NS</td>
</tr>
<tr>
<td>Patient delay (min)</td>
<td>117 (72-198)</td>
<td>105 (70-155)</td>
<td>110 (60-180)</td>
<td>90 (60-180)</td>
<td>NS</td>
</tr>
<tr>
<td>Myocardial infarction rate</td>
<td>81.5</td>
<td>79.0</td>
<td>79.7</td>
<td>71.7</td>
<td>0.09</td>
</tr>
<tr>
<td>D/L (UL)</td>
<td>1150 (689-2510)</td>
<td>1944 (1011-3300)</td>
<td>3131 (1261-7386)</td>
<td>1976 (1103-3300)</td>
<td>0.049</td>
</tr>
<tr>
<td>Year mortality (%)</td>
<td>3.2</td>
<td>6.4</td>
<td>6.2</td>
<td>2.1</td>
<td>0.5</td>
</tr>
</tbody>
</table>

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.

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 Haven, CT

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.
Myocardial Ischemia and Infarction

Time To Treatment Of Acute Myocardial Infarction (AMI) Can Be Optimized By An Integrated Infarction Network According To Guidelines.

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

Background: Recent studies have demonstrated a benefit 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 24/7 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 via 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 resuscitation (CPR). Delay from onset of symptoms till arrival in the cathlab was significantly longer for transferred patients (2.4h ± 6.6 h ± 8.1; p<0.01)

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 rates.

Off-hour Primary Angioplasty: Why Is Mortality Higher?


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 incidence 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 was performed during off-hour. It remains unknown whether differences in clinical or angiographic factors are responsible.

Results: The majority occurred during routine hours (443±30), 75% of median time from symptom onset to PCI was shorter during off-hours (4.0±5.1 hours, p=0.05). Clinical and demographic characteristics did not differ, including age, gender, race, diabetes, hypertension, hypercholesterolaemia, smoking, history of coronary disease or heart failure, and presentation with cardiogenic shock (off-hours 18.2% vs. 15.0%, p=0.32).

Conclusion: In-hospital mortality was highest during off-hours, it remains unknown whether differences in clinical or angiographic factors are responsible.

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 Hallock, Faraz Kerendi, Ping-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 Vinter-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 ml, n=7), 3 x 10^6 MSCs/kg (3 ml, n=8), or 10 x 10^6 MSCs/kg (10 ml, n=8). MSCs were pre-labeled with Dil and DAPI fluorescent markers. Myocardial flow reserve (intra-ventricular 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 ml (2.5 ± 0.3), 3 ml (2.9 ± 0.7), and 10 ml (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 IV) in the scar zone was 23% greater in the 1 ml and 3 ml groups, and 30% greater in the 10 ml group vs Control (p=0.005). Preload-recruitable stroke work (mmHg/g) was higher in the 3 ml (39 ± 4.3) and 10 ml (44 ± 2.4) groups, but not in the 1 ml group, compared to Control (26 ± 4.0, p=0.005). Systolic performance (slope of end-systolic pressure-volume relationship, mmHg/ml) was also greater in 3 ml (1.4 ± 0.1) and 10 ml (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.

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

Audrey Rosenberg, Pierre Voisine, Gulu Wu, Evan Applebaum, Susan Yeon, Seung Lee, Joseph Carozza, Frank Sellek, 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 cardiomycocytes 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 only). Animals were assessed 4 weeks later with hemodynamics, LV function and perfusion (MRI), echocardiography, ultrasonic crystals, microspheres, and morphometric analysis using tetracub (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 (10.3±3.5% vs 11.3±1.9% of total septum, p<0.005)

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

Angélique Calderon, Jessica Drapeau, Joceilyn Dupuis, Viviane El-Helou, Frédéric Leteurtre, 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, immunofluorescent- and peripherin-positive fibers were visualized in the scar by immunofluorescence. Co-localisation with nestin, a marker of neural stem cells, was evident. Immunoblotting of scar tissue from infarcted heart revealed a significant increase in nestin levels compared to the control group (n=6). In addition, immunofluorescent staining showed that nestin-expressing neural stem cells were located in the scar of the infarcted heart but not in the non-infarcted left ventricle. Unexpectedly, nestin-expressing neural stem cells in the infarcted region did not co-localize with GFAP-positive cells. Conclusion: These data have demonstrated that nestin-expressing neural stem cells were identified in the infarcted region of the damaged heart, possess a capacity to proliferate, and are not derived from the bone marrow, and may represent the progenitor cell that subsequently differentiates to a neuronal phenotype.

5:00 p.m.

Improvement of Left Ventricular Function by Autologous 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 Dil. Phosphate buffered saline (n=36) or allogeneic MSCs (n=39, 2x10⁶ cells each) were injected directly into the scar of a 1 week old myocardial infarction in female Fischer rats. Four weeks of Dil fluorescence and LV ejection fraction (LVEF) were assessed by angiography, 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±6.10%, n=12) compared to the control group (38.8±1.1%, n=12, p=0.005). At 4 weeks there was a trend toward smaller post-mortem volumes in the MSC group (20.5±29.1 mm³) versus the control group (20.6±30.0 mm³, p=0.16) and scar mass thickness in the MSC group was 0.46±0.02 mm versus the control group at 0.45±0.04 mm, p=0.44. 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 =40.0±2.0 mm³ in MSC group versus 44.4±0.2 mm³ in control group, p=0.2; and scar mass thickness = 0.41±0.02 mm in MSC group versus 0.41±0.02 mm in control group, p=0.85). At 6 months Dil positive cells were observed in the central scar region of rats in the MSC group, and these cells expressed the muscle-specific markers -actin, 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 Willebrand factor. No Dil 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 not improve global LV function at 4 weeks with a trend towards less remodelling 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.

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

Fatma Maskali, Nguyen Tran, Joseph Nigla, Marie Hélène Laurens, Pierre-Yves Marie, Gilles Karofer, 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 Aimed 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 isolated from ACI rats (n=10) were injected within 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 MMBq of Indium-111 oxine resulted in a time-dependent labeling efficiency and cytotoxicity. Using a 10 min incubation-period, labeling efficiency was high (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 infarcted areas.

8:30 a.m.

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

Rafael Valencia, Salvatore Cavaleri, Christopher B. Granger, Kenneth W. Mahaffey, Gudyea Tessa, Pierre Theroux, Paul W. Armstrong, Michael Hudson, Thomas G. Todaro, Chris Mojik, 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 Re duktion of Infarct size after Angioplasty or Lytics (CARDINAL) program that investigated perixeluzumab, a monoclonal antibody against C5 complement, in STEMI patients to evaluate the relationship between SIRS and the development of CS, CHF and death within 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 >12×10⁹/L or <4×10⁹/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 troponin levels (2.0 vs. 1.3), and higher cumulative ST-segment elevation (10.5 vs. 7.8). We have recently shown that SIRS patients tend 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 troponin levels (2.0 vs. 1.3), and higher cumulative ST-segment elevation (10.5 vs. 7.8). We have recently shown that SIRS patients tend 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 troponin levels (2.0 vs. 1.3), and higher cumulative ST-segment elevation (10.5 vs. 7.8).

*8:30 a.m.*
Myocardial Ischemia and Infarction

8:45 a.m.

**228A**

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

**Authors:** Kausik 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

**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 7.8 pg/ml; p<0.002) & in TACTICS: diabetics (n=267) vs non-diabetics (n=662) CRP 6.6 vs 5.2 mg/l (p=0.0055). Stratifying by population median CRP in OPUS (fig 1), diabetics vs CRP> median were at highest risk of death or MI while non-diabetics with CRP > median & 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<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

**Follow up Months**

| DM low CRP vs Non DM high CRP p=0.1 |
| DM high CRP vs other groups p=0.001 |

**Figure 2:** The interaction between glucose and CRP on Death or MI among Diabetics in OPUS-TIMI 16

| P for trend across Range<0.0001 |
| DM low CRP vs Non DM high CRP p=0.1 |
| DM high CRP vs other groups p=0.001 |

**9:00 a.m.**

**832-5**

**Abstract Title:** Elevated Levels of Interleukin-10 are Strongly Associated with Raised Mortality in Non-ST Elevation Acute Coronary Syndrome

**Authors:** Anders Malarping, 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 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.

**Results:** The median level of IL-10 was 1.06 pg/ml [25:th-75:th percentile; 0.63-1.87]. The median level of IL-10 was 1.06 pg/ml [25:th-75:th percentile; 0.63-1.87].

**Conclusion:** Increased plasma levels of IL-10 were strongly associated with higher mortality in the present study, in contrast to previous findings.
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 Nomura, Takashi Nozawa, Akira Matsuji, Teruo Nakadate, Norio Igarashi, Bunio Kato, Kazuo Fujii, Akihiko Iwase, Hideyasu Asano, 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 successively occluded for 30 min and thereafter reperfused. Cardiac intestinal 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-pyrroline-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). Atenolol 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 (0.02 ± 0.01). However, significantly increased with 0.32±0.15 after reperfusion. Conclusions: Cardiac denervation protected myocytes against ischemia-reperfusion injury primarily through decreasing direct NE toxicity via adornogenic signal activation, but not through suppressing NE-derived free radical formation.

ABSTRACTS - Myocardial Ischemia and Infarction 229A

Glutathione Monoester 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. Abdoco, 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 monoester (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 subjected to 4 weeks and underwent echocardiographic and hemodynamic assessment. Hearts were sectioned for histological analysis.

Results: End-diastolic pressure (EDP) was higher (24.0±8.8 mm Hg) in Group 4 than in Groups 1 and 2 (20.7±11.3 and 19.7±3.3 mm Hg, respectively; p<0.05), but lower than Group in Group 4 (13.4±2.7 mm Hg; p<0.05). Myocardial (inotropic) performance was increased in Group 2 (111.7-205) vs. Group 1 (111.7-204) (p=0.02), equivalent to Group 1 (110.5±6.6; p=0.06), and decreased compared to Group 3 (133.6±19.2, p=0.01). Left ventricular free-wall/sample collagen content was lower in Group 4 than in Group 3 (61% vs. 71%, p=0.05), but not different to Group 1 (56% vs. 61%, p=0.87). 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 myocardial size, decreased collagen scar formation, and higher FS. Future studies may determine a clinical role for this compound in common IR syndromes.

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

Tadayoshi Ohya, Sadas Yoshi Funata, Toshimitsu Horii, Haruyoshi Ueno, Noriko Shinashi, Masahiro Amakawa, Takahiko Murata, Kaken pharmaceutical Co., Ltd., Kyoto, Japan

Background: KP-102 (GHRP-2: prerolactine) 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.

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.

1117-205
Human Hibernating Myocardium: Altered Calcium Regulatory System Contributes to Contractile Dysfunction

Holger M. Neff, Heike Möllmann, Thorsten Dill, Roland Brandt, Woltei Skwarra, Birgit Bölck, Robert H.G. Schwingert, 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 the intracellular 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), calcium-calmodulin-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 revascularization. The protein amount of phosphorylated PLN represented 6% (0.6±0.1 vs. 0.6±0.1, p<0.05), and RyR2 (0.9±0.2 vs. 0.9±0.2, p<0.05). Furthermore in HHM maximal SERCA2a activity (Vmax) was significantly reduced (419.9±19.9 vs. 526.8±25.4 mmol/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 binding-sites Ser16 and Thr17 was significantly reduced (Ser16: 1.0±0.1 vs. 0.6±0.1, 1.3±0.1, 1.3±0.1, p>0.05). Furthermore in HHM maximal SERCA2a activity (Vmax) was significantly reduced (419.9±19.9 vs. 526.8±25.4 mmol/mg protein/min, p<0.05).

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

Tadashi Ohya, Sadas Yoshi Funata, Toshimitsu Horii, Haruyoshi Ueno, Noriko Shinashi, Masahiro Amakawa, Takahiko Murata, Kaken pharmaceutical Co., Ltd., Kyoto, Japan
Infarct size was determined by TTC staining and was expressed as a percent of the area at risk on the basis of collateral blood flow of <0.03 mL/min/g. Treatment with KP-102 significantly reduced infarct size (49 ± 4% in CON+SPT vs. 47 ± 5% in CON); however, RPC+SPT reversed the protective benefit of RPC (50 ± 3% in RPC+SPT vs. 49 ± 4% in RPC). Conclusion: Remote renal postconditioning applied immediately before the onset of coronary reperfusion provides potent cardioprotection likely exerted during the first minutes of reperfusion. This finding is likely mediated by adenosine receptor activation as the protective benefit is inhibited by the simultaneous administration of a non-selective adenosine receptor inhibitor.

Mixed L-amino Acids Provide Cardioprotection Mediated By Translational And Transcriptional Regulation Of De Novo Protein Synthesis
Carol Chen-Scarbabelli, Zuhair Aliebban, Ruggero Ama’, Howard Rosman, Louis Saravolatz, Giulio 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/reperfusion (IR) 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 (IR) 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 min; IR control: exposed to 35 min and 120 min R; treated group: given a single oral dose (1g/kg) of 11, mainly essential, mixed AA, and exposed, after 6 hours, to IR; actinomycin D (AcdD) and cycloheximide (Chx) groups: pretreated with AcdD (1.5 mg/g, ip), inhibiting transcription (DNA →mRNA), or Chx (1 mg/g, ip), inhibiting translation (mRNA →protein), 1 hour prior to AA supplementation, and exposed to IR; AA reduced infarct size and release of creatine kinase, promoting posts ischemic recovery of cardiac function; lesserened 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 Qo consumption rate in myocardial skinned bundles, and elevated ratio of Bcl-2 to Bax (p<0.05). These effects were reduced by pretreatment with both Chx (-80%), and AcdD (-60%). Although differences in dry/wet weight ratios between hearts from different groups were not significant, AA induced an increase in myocardial protein content (530±67 ug/mg vs 473±375 ug/mg), which was abetted by pretreatment with both Chx and AcdD (all p<0.05).

Conclusion: AA reduced posts ischemic 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.

230A ABSTRACTS - Myocardial Ischemia and 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. Giannetti, Emory University School of Medicine, Atlanta, GA
Objective: A series of brief coronary artery reperfusion and reocclusions applied during the early minutes of coronary reflow (myocardial “postconditioning”) attenuates reperfusion injury. Using as 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 h h of reperfusion were randomized to: 1) CON SPT = no RA occlusion; 2) RPC = RA occlusion was performed for 5 min before ischemia and 2 h 30 min of ischemia, no RA occlusion; 3) CON RP = RA occlusion was performed for 5 min before ischemia and 2 h 30 min of ischemia, no RA occlusion; 4) Remote 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 immediately prior to the onset of coronary reperfusion provides potent cardioprotection likely exerted during the first minutes of reperfusion. This finding is likely mediated by adenosine receptor activation as the protective benefit is inhibited by the simultaneous administration of 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-Scarbabelli, Zuhair Aliebban, Ruggero Ama’, Howard Rosman, Louis Saravolatz, Giulio 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/reperfusion (IR) 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 (IR) 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 min; IR control: exposed to 35 min and 120 min R; treated group: given a single oral dose (1g/kg) of 11, mainly essential, mixed AA, and exposed, after 6 hours, to IR; actinomycin D (AcdD) and cycloheximide (Chx) groups: pretreated with AcdD (1.5 mg/g, ip), inhibiting transcription (DNA →mRNA), or Chx (1 mg/g, ip), inhibiting translation (mRNA →protein), 1 hour prior to AA supplementation, and exposed to IR; AA reduced infarct size and release of creatine kinase, promoting posts ischemic recovery of cardiac function; lesserened 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 O2 consumption rate in myocardial skinned bundles, and elevated ratio of Bcl-2 to Bax (p<0.05). These effects were reduced by pretreatment with both Chx (-80%), and AcdD (-60%). Although differences in dry/wet weight ratios between hearts from different groups were not significant, AA induced an increase in myocardial protein content (530±67 ug/mg vs 473±375 ug/mg), which was abetted by pretreatment with both Chx and AcdD (all p<0.05).

Conclusion: AA reduced posts ischemic 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.
Effect Of Dual Antiplatelet Therapy On Platelet Activation In Patients With Acute Coronary Syndromes
In The Presence Of Eluted Crp And Soluble Cd 40 Ligand.

Manolis Vavuranakis, Dimitris Aggelis, Sophia Vaina, Maria Drakopoulou, Konstantinos Louati, James J. Ferguson, for the SYNERGY Trial Investigators, Duke Clinical Research Institute, Durham, NC

Background: In patients (pts) with unstable angina and acute myocardial infarction without ST elevation (ACS), an increase in risk for adverse outcome has been observed if high sensitivity C-reactive protein (hs-CRP) and serum soluble CD 40 Ligand (sCD-40 L) are elevated. Platelet activation, as reflected by soluble p-selectin (sP-selectin) 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, sP-selectin is superior to UFH in acute coronary syndromes.

Aims: To evaluate in pts with ACS without ST-elevation the use of sP-selectin to assess platelet activity.

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 Beck Depression Inventory (BDI). Patients were randomly assigned to a double-blind treatment with 140 mg of aspirin, placebo or 140 mg of aspirin + 50 mg b.i.d. of sertraline (n=10) or placebo (n=10). All pts had clinical and biochemical evaluation before the intervention. A 12 lead ECG was continuously monitored for 24 hours. The primary outcome measure was the area under the curve of sP-selectin during the first 24 hours after admission. Other measures evaluated were the rate of re-infarction and the rate of in-hospital mortality.

Results: In the sertraline group, sP-selectin was lower as compared with placebo (700 vs 1000 ng/ml, p=0.008). The incidence of re-infarction and in-hospital mortality was not different between the two groups.

Conclusions: The use of selective serotonin re-uptake inhibitors (SSRIs) can improve outcome of pts with ACS without ST-elevation, and the use of sP-selectin is associated with better outcome in pts with ACS and depressive symptoms.
Myocardial Ischemia and Infarction

Blood Transusions in Patients Admitted With Non-ST-Segment Elevation Acute Coronary Syndromes: Results From CRUSADE

Eric D. Peterson, Arika Y. Chen, Xing Yang, Matthew T. Roe, Sunil V. Rao, Raj 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 2.36 [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 2.92 [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 65. There was no difference in transfusion rate among patients admitted on days of the week.

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.

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

Jacek Kowalczyk, Radoslaw Lenarczyk, Zbigniew Kalanus, Janusz Prokopczuk, Grzegorz Hornisz, Teresa Zielinska, Joanna Szabryla-Deska, Patrycja Pruszkowska-Skrzypek, Oskar Kowski, Agata Musialik-Lydkwa, Maciej Gasior, Lech Poloniski, 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 occurrence and recurrence in 1027 consecutive AMI pts who underwent PCI was performed. 89.8% of them had diabetes mellitus (DM), 70% hypertension, 64% dyslipidemia, 53% prior MI. A total of 532 pts (52%) had PCI for non-ST-segment elevation acute coronary syndrome. Results: Remote survival in CIN pts was lower than in controls (68.4% vs 90.3%, 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 an independent predictor for any-cause death only among CIN DM pts. Adjusted hazard ratio (HR) for death in CIN vs controls was 2.35 (CI: 1.95–2.75, p<0.001). In CIN and CIN DM vs controls HR was not significant.

Conclusion: In diabetic pts significantly and independently influences survival in AMI pts treated with PCI and is associated with increase of death hazard.
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 (5.1±2.1 months) clinical follow-up data were collected from 1,099 consecutive patients with AMI who underwent primary PCI.

Overall, an optimal primary PCI result was achieved in 958 patients (95%). Cardiogenic shock (OR 2.92, 95% CI 1.46-5.83; p=0.002) and age (OR 1.029, 95% CI 1.002-1.056) 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 (27% vs 19%; p=0.0001) 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=0.69; 4% vs 5%, p=0.92; 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.

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

Beth A. Bartholomew, Cindy L. Grines, Gregg W. Stone, Eugina Nikolovsky, Judith A. Boura, David A. Cox, Bruce R. Brodie, William O. D’Onell, William Beaumont Hospital, Royal Oak, MI

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 48 h after PCI and in-hospital 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 diabetes (odds ratio (OR) = 4.4, p=0.0001), final thrombus present (OR=0.3, p<0.0001), ejection fraction <50% (OR=2.2, p=0.0006), left ventricular ejection fraction <20% (OR=0.7, p<0.0001), female gender (OR=0.5, 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=0.0001), and composite major cardiac events (OR=4.1, p=0.0001).

Conclusion: 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

<table>
<thead>
<tr>
<th>Event</th>
<th>10% HCT Drop</th>
<th>11-15% HCT Drop</th>
<th>&gt;15% HCT Drop</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3.2%</td>
<td>5.3%</td>
<td>8.1%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>0.9%</td>
<td>1.7%</td>
<td>6.4%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Revascularization</td>
<td>1.7%</td>
<td>4.8%</td>
<td>5.9%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Severe Stroke</td>
<td>0.08%</td>
<td>3.2%</td>
<td>1.0%</td>
<td>0.011</td>
</tr>
<tr>
<td>MACE (combined)</td>
<td>3.2%</td>
<td>8.1%</td>
<td>16.2%</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

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


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 unstable cardiac disease 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.

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

Oliver D’Silva, Sandeep Nathan, Akshay Gupta, Amit Amin, Shaun Center, Arun Kumar, Lloyd W. Klein, Rush University Medical Center, Chicago, IL, Cook County Hospital, Chicago, IL

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 SSBp<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. 64.0% pts underwent angiography, 37.6% pts received IABP support, and 69.1% pts were revascularized (63.6% PCI, 15.6% CABG). Deferral of angiography, first SBP<100, any SBP>20 or DBP>30 mm Hg and LVEF<40% 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.

ABSTRACTS - Myocardial Ischemia and Infarction 233A

<table>
<thead>
<tr>
<th>Event</th>
<th>LMWH Only (n=14,817)</th>
<th>UFH Only (n=20,987)</th>
<th>LMWH and UFH (n=1,979)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>13.8%</td>
<td>15.2%</td>
<td>7.0%</td>
<td>0.81 (0.76-0.87)</td>
</tr>
<tr>
<td>Non-CABG pts</td>
<td>7.1%</td>
<td>9.5%</td>
<td>8.7%</td>
<td>0.77 (0.70-0.84)</td>
</tr>
</tbody>
</table>

GP IIb/IIIa inhibitors | 31.7% | 35.1% | 69.0% | ns |

Clotting/diag: 48 h | 41.7% | 37.0% | 62.7% | ns |

Cardiac cath | 71.0% | 81.0% | 82.7% | ns |

PCI | 78.8% | 88.5% | 71.2% | ns |

CABG | 13.0% | 13.7% | 6.5% | ns |

For LMWH alone versus UFH alone, CABG + coronary artery bypass grafting. GP = glycoprotein; cath = catheterization; PCI = percutaneous coronary intervention.
Approach to Post-Myocardial Infarction Ventricular Septal Defect: Conservative, Percutaneous Device Closure or Surgical Repair

Pankaj Gupta, Atul Mathur, S. Radhakrishnan, S. Srivastava, A. Seth, R. Kapoor, N. Chandra, Z. S. Mehrotra, A. Omar, R. R. Kaslawal, N. Trehan, Escorts Heart Institute and Research Centre, New Delhi, India

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 (43-69 years).

Result: Of these 33 patients, 16 were managed conservatively (group A), 12 by percutaneous device closure (group B) and 6 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. Cross 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 ± 5.6 mmeters (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 53.5 ± 9.9% in group A, 35.8% ± 8.5% in group B and 39 ± 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.

T119-233

Predictors of Death in Patients Treated by Facilitated Percutaneous Coronary Intervention for Acute Myocardial Infarction

Philippe Garot, Thierry Lefèvre, Yves Louvard, Jean-Yves Le Tarnec, Alain Margenet, Claude Pouget, Pierre Dumas, Dominique Thebert, Ivan Laurent, Marie-Claude Morice, Institut Cardiovasculaire Paris Sud, Quincy, France

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 > 2000 consecutive patients 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 IIb/IIIa inhibitors.

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 IIb/IIIa inhibitors.

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 9354 patients 3100 were treated with primary PCI, 3646 with fibrinolysis and 2577 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 LVEF at discharge. These results support the open heart hypothesis which suggests a clinical benefit of reperfusion therapy for STEMI beyond preservation of LVEF.

1-Year mortality related to LVEF at discharge
Background: 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.

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 (NST), 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 one with a combination of TIMI≥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.

Table 1: Mean systemic blood pressure before and after PCI

<table>
<thead>
<tr>
<th>Patients post-PCI</th>
<th>SBP</th>
<th>DBP</th>
</tr>
</thead>
<tbody>
<tr>
<td>SBP</td>
<td>DBP</td>
<td></td>
</tr>
<tr>
<td>Pre-PCI (at hospital dock)</td>
<td>200</td>
<td>140</td>
</tr>
<tr>
<td>Post-PCI</td>
<td>180</td>
<td>120</td>
</tr>
</tbody>
</table>

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

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

Matthew T. Bonding, Joseph B. Muhlstein, Benjamin Horne, Tame Bair, Jeffrey L. Anderson, University of Utah, Salt Lake City, UT, LDS Hospital, Salt Lake City, UT

Background: Previous case series and small series reports have described situations in which patients have presented with acute myocardial infarction (AMI) but having 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 [Tnl] ≥21 ng/ml) but with normal coronary arteries by angiography and compared their clinical presentation and long-term mortality to 3,736 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±15 years [p = 0.001]) and more likely to be female (40% versus 70% [p = 0.001]) than those with advanced CAD and had lower peak levels of Tnl (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: 10.8% vs. 15.3% [p = 0.06] for normal vs. CAD patients, respectively). When non-fatal AMI events are 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.

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


Background: Despite the benefit of early mechanical revascularization in cardiogenic shock (CS), a high 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 intraaerous pressures. Revascularization success was achieved in 61/10 (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 the following:

- younger age (OR 3.4, CI 2.7-4.5, p = 0.001),
- diabetes (OR 2.4, CI 1.8-3.2, p = 0.001),
- use of IIb/IIIa inhibitors (OR 1.6, CI 1.3-2.0, p = 0.001),
- creatinine clearance (CrCl) < 30 (OR 1.5, CI 1.2-1.9, p = 0.001),
- multi-vessel disease (OR 1.6, CI 1.2-2.0, p = 0.001),
- hypertension (OR 1.3, CI 1.1-1.6, p = 0.001),
- use of an IABP (OR 1.4, CI 1.1-1.7, p = 0.001),
- SBP < 90 (OR 1.6, CI 1.2-2.1, p = 0.001),
- SBP < 80 (OR 2.1, CI 1.6-2.7, p = 0.001),
- SBP < 70 (OR 2.5, CI 1.9-3.3, p = 0.001),
- SBP < 60 (OR 2.7, CI 2.1-3.5, p = 0.001),
- SBP < 50 (OR 3.1, CI 2.4-4.0, p = 0.001),
- SBP < 40 (OR 3.5, CI 2.6-4.7, p = 0.001),
- SBP < 30 (OR 4.0, CI 2.9-5.3, p = 0.001),
- SBP < 20 (OR 4.5, CI 3.2-6.3, p = 0.001),
- SBP < 10 (OR 5.0, CI 3.4-7.3, p = 0.001),
- SBP < 0 (OR 6.0, CI 3.8-9.0, p = 0.001).

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.
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.

1121-224 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, Stony Brook, 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 class Angina III (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 (53.8 vs 52.8 %), CAD duration (9.9 vs 11.5 years), multivessel CAD (72.4 vs 80.4 %), EF (48.8 vs 46.9 %). 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 77% of Mild and 71% of Severe pts with similar decreases in angina [2.9 ± 8.6 times/week] and Ntg use. Post EECP 31.5% of Mild and 14.3% of Severe pts were free of angina. Angina reduction was preserved in both Mild and Severe groups at 1 year [44.7 ± 24.1 % with no angina; 21.8 ± 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 ± 6.9 %], MI [2.7 ± 7.2 %], overall MACE [11.9 ± 21.4 %]. CABG [4.1 ± 3.2 %] and PCI [4.9 ± 8.4 %] rates were similar.

Conclusions: End stage-revascularizable CAD pts with severe angina have "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.

1121-226 Low-Dose Pioglitazone Safely Provides Clinical Antithrombotic Effect For Patients With Coronary Artery Disease and Metabolic Syndrome

Tatsuki 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 1 year, or to group-C where they continued therapy without thiazolidinedione. We evaluated serum lipid and glycemic variables. We noninvasively 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=19) 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, HDL: from 42±11 to 60±4, 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±1.5, p=ns). PWV also improved after medication in group-L (172±76±9/cm/sec, to 166±24±3/cm/sec, p=0.03) but not in group-C (171±12±8±4/cm/sec, to 174±12±4±4/cm/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

Sandep 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 was defined by ≥ 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 pts 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, and older pts all evidenced increased PCAD risk (p<0.05). Total mortality at 3.47 yrs mean follow-up was 5.8% and was higher with severe CAD (9.2% vs CAD vs 4.2% if no CAD, p=0.044). Diabetes mellitus (DM) (OR 3.71 [1.13-12.2], p<0.001) 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.

1121-227 The Prevalence of Impaired Functional Status in Unrecognized Myocardial Infarction: A Population Based Study

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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/UOMI/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 abnormal functional status.
N-Terminal pro-BNP Predicts Coronary Stenosis

Thomas Wolber, Mica Maeder, Ramim Atefi, Walter Riesen, Peter Ammann, Hans Rickli, Kantonsspital St. Gallen, St. Gallen, Switzerland

Background: Type B Natriuretic Peptide (BNP) and its precursor, N-terminal pro-BNP (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 ventilricular 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 (NT-proBNP 24 ± 19 ng/ml vs. 12 ± 6 ng/ml, p = 0.03). Receiver operating curve analysis showed an area under the curve of 0.68. NT-proBNP levels above 300 ng/ml had a specificity of 93% for CAD. Systolic left ventricular function was similar in both groups (ejection fraction 0.65 ± 0.06 vs. 0.72 ± 0.06, p = 0.10). Patients requiring percutaneous coronary interventions (PCI) (n=13) or bypass surgery (CABG) (n=11) had significantly higher NT-proBNP levels than patients (n=35) who were managed with medical treatment only (plasma NT-proBNP 167 ± 149 ng/ml vs. 276 ± 230 ng/ml, 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.

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

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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, thoracographic 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 51.5±79% depending on the chosen parameter. With 3 parameters positive, the specificity of the test was a 97% and the accuracy was 85%-88%.

Conclusion: Resting magnetocardiographic imaging is an accurate and rapid test for the diagnosis of obstructive coronary artery disease in patients with chronic ischemic heart disease.
Granulocyte-Colony Stimulating Factor in the Acute Myocardial Infarction (The Rigenera Study)
Antonio Maria Leone, Leonardo Galullo, Giovanna Lizzio, Alessandro Giordano, Maria Lucia Cardagni, Barbara Garramone, Maria Benedetta Giannico, Fiannetta Cirillo, Luigi M. Biasucci, Antonio G. Rebuffi, Filippo Crea, Universita Cattolica del Sacro Cuore Institute of Cardiology, Rome, Italy, Universita 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 PTCA. Nine patients (8 males, 54±11 yrs) were treated with G-CSF (250 mcg s.c./bd + exenaparin 80U/kg s.c./bd) and compared to 3 patients (3 males; 57±3s) 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 complete 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±3.01 cell/µl. After 5 days from the end of the G-CSF therapy CD34+ cells’ concentration came back to 4.32±2.7 cell/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), LVEF (from 150±46 to 115±45 ml, 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, 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 FJ.

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.

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 Tarea, Giacomo Temponi, Tullio Usmini, Maurizio D'Amico, Giorgio Milesiello, Marco Sicuro, Mauro Giorgi, Luca Checco, Pierluigi Sbarra, Massimo Baccega, Mario Campana, Irene Ricca, Paola Omeddi, Fiorella Sanavio, Marco Boccardo, Michele Casaccia, Azienda Ospedaliera San Giovanni Battista, Torino, Italy

Background: Myocardial regeneration and neovascularisation of the ischemic myocardium may be obtained either in animal models or in human by intracoronary or intramyocardial 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 stem cell populations characterized using flow cytometry. ii) to monitor and mobilized stem cell populations characterized using flow cytometry. iii) to verify feasibility and safety of PBSC mobilization. Method: 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 with 24 hours from PTCA). All pt underwent coronary angiography, intracoronary doppler flow study, echoangiography, and nuclear Thallium scan before and after 1 to day 5 (starting within 24 hours from PTCA). All pt underwent coronary angiography, intracoronary doppler flow study, echoangiography, and nuclear Thallium scan before and after 1 to day 5 (starting within 24 hours from PTCA). All pt underwent coronary angiography, intracoronary doppler flow study, echoangiography, and nuclear Thallium scan before and after 1 to day 5 (starting within 24 hours from PTCA).

Results: WBC and PBSC peaked during the 3rd day of mobilization. Mean WBC and PBSC peaks were 34960±10794 leukocytes/µl and 29.7±30.8 CD34+/µl. Five in hospital adverse events were recorded: severe hypotension in 3 pt, atrial fibrillation in 1 pt, recurrent ischemia in 1 pt. No death was observed. At present 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 to 57.1±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 statistically significant we observed a global myocardial function improvement; d) the 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.
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 vs. 4.9±3.0 vs 19.4±4.9 ng/mL, respectively, p<0.01) and just after the reperfusion (1.5±0.9 vs. 2.3±1.8 vs 8.4±3.6 ng/mL, respectively, p<0.01). MBG uptake in ischemic region was greater in group I (n=7) than in group II (n=7) or group III (n=7) (0.02±0.03 vs 0.03±0.01 vs 0.04±0.03, respectively, 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 vs 24.6±1.3, p<0.05).

Conclusion: A brief episode of ischemia before sustained ischemia attenuated suppression of MBG uptake in the remote portion of ischemic tissue after the ischemic insult, i.e., the phenomenon of neuro 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 neuro preconditioning.

1145-207
Exogenous Nitric Oxide Inhibits AMP-activated Protein Kinase (AMPK) Phosphorylation and GLUT4 Translocation to Sarcolemma in Ischemic Myocardium

Biao Lei, Ken Matsuo, Volodymyr Labinsky, Anna Ahn, Margaret P. Chandler, Martin Altajeros, William C. Stanley, Fabio A. Recchia, New York Medical College, Valhalla, NY, Case Western Reserve University, Cleveland, OH

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 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 5 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. GLUT4 translocation was stimulated by phosphorylated AMPK and in fact we found that AMPK phosphorylation was inhibited in ISC-NG compared to 76±7.1% vs 167±17.0%.

Results: NG did not cause any change in LAD myocardial flow distribution and systemic hemodynamics. Although transient ischemia induced by 66% reduction in LAD flow were reduced by PQQ. Additional rats received PQQ (5, 15, 50 mg/kg, 4 rats each dose) LGLUT4 (73±7 %) did not change. In control group, PQQ (10 mg/kg) did not change.

Conclusion: Either Pretreatment or Treatment at Reperfusion with Pyyroloquinoline Quinone Reduces Lipid Peroxidation and Is Cardioprotective in a Rat Model of Ischemia/Reperfusion

Bozhu Zhu; Hui-zhong Zhou, John R. Teerlink, Joel S. Kalliner, University of California San Francisco, VA Medical Center, San Francisco, CA

Background: The essential nutrient pyroloquinoline quinone (PQQ) has been newly identified as a redox co-factor for vitamins. 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 or immediately after ischemia. Controls were 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 in lower episodes of ventricular fibrillation (VF). In separate experiments, PQQ 5-20 mg/kg given as Pretreatment was inversely related to infarct size (n=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, 15, 50 mg/kg, 4 rats each dose). LGLUT4 (73±7 %) did not change. 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 time 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 (IR)

Table: 

<table>
<thead>
<tr>
<th>Groups</th>
<th>Infarct size (%)</th>
<th>LV dP/dt (mmHg)</th>
<th>LV dP/dt (mmHg)</th>
<th>LV dP/dt (mmHg)</th>
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<td>422±12</td>
<td>490±12</td>
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1145-208
Gp91-Phox Expression Increases in the Remote Noninfarcted Myocardium After Myocardial Infarction in Rabbis: Association With Myocyte Apoptosis

Fucheng Qin, Megan Simeone, Chang-seng Liang, University of Rochester, Rochester, NY

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: Rabbis 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 rats rabbits exhibited an increase of left ventricular (LV) end-diasstolic dimension (EDD) and a decrease of LV dP/dt. The infarct size was 29±0.25 %. Gp91-phox protein and mRNA expression was increased in RM after MI. Immunoblotting revealed that gp91-phox was present in myocytes. We also found a decrease in GSH/GSSG ratio and increased p38 MAPK activity and myocyte apoptosis.

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.

Table: 

<table>
<thead>
<tr>
<th>Group</th>
<th>gp91-phox protein (arbitrary unit)</th>
<th>GSH/GSSG</th>
<th>MalDI (arbitrary unit)</th>
<th>p38 MAPK</th>
<th>Apoptotic cells (3000 cells)</th>
<th>TUNEL</th>
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<td>Sham</td>
<td>1±0.1</td>
<td>6±1.2</td>
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<td>6±1.2</td>
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<tr>
<td>MI</td>
<td>1±0.1</td>
<td>6±1.2</td>
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n=8-12. Values are means±SE. *P<0.05 vs Sham. W: week.
**Background:** The association between estimated 10-year risk for coronary heart disease (CHD) is unknown, 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±66 (95% confidence interval [CI], 712 to 1,116±66), 10,222±66 (95% CI, 2,283 to 17,607±66), 21.9±66 (95% CI, 12.5 to 29.4±66) and 1.5±66 (95% CI 0.8 to 2.3±66), respectively, higher, respectively, than 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**

<table>
<thead>
<tr>
<th>Intermediate risk</th>
<th>High risk</th>
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<tbody>
<tr>
<td>CRP ≥0.21 mg/dL</td>
<td>1.12 (1.00, 1.26)</td>
</tr>
<tr>
<td>CRP ≥0.10 mg/dL</td>
<td>1.07 (0.89, 1.30)</td>
</tr>
<tr>
<td>Fibrinogen ≥3.77 mg/dL</td>
<td>0.97 (0.83, 1.14)</td>
</tr>
<tr>
<td>Homocysteine ≥13.5 µmol/L</td>
<td>1.11 (0.98, 1.29)</td>
</tr>
</tbody>
</table>

Values of Inflammatory Markers at the Site of Plaque

**Elevated Wbc Count Not Associated With Obstructing Coronary Lesions in Patients Presenting With Non-st Segment Elevation Acute Coronary Syndromes.**

Malta Zahid, Ali F. Soret, Lauren Wall, Chester Bernie Good, Center for Health Equity Research and Promotion, VA Pittsburgh Healthcare System, 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 >10,000/mm³. Significant CAD was defined as any stenosis of >70% and/or left main stenosis >50%. Univariate logistic regression modeling categorized by the sites but not confirmed by the core lab.

**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=0.18-0.89, 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.

**Infiltration of Neutrophils Directly Relates to the Clinical Severity in Patients with Unstable Angina Pectoris.**

Taichi Adachi, Takahiko Naruko, Akira Itoh, Kazuo Haze, Michikido Hirayama, Takehisa Suekane, Hiroko Fukushima, Yoshimi Sugama, Nobuyuki Shirai, Shichiro Ebara, Yoshitomo Ikura, Masahiko Okawa, Makito Ueda, Osaka City General Hospital, Osaka, Japan, Osaka City University Graduate School of Medicine, Osaka, Japan

**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, 2000). 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 IIb-IIIb and Braunwald's IIb. 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 IIb group than in the Braunwald's IIb-IIIb group.

**Conclusions:** These findings strongly suggest a correlation between the magnitude of neutrophil infiltration and the clinical severity of UAP.

**Levels of Inflammatory Markers at the Site of Plaque Rupture in Acute Myocardial Infarction Depend on Preceding Symptoms.**

Lukas A. Altwegg, Arnold von Eckardstein, Roberto Corti, Marco Roffi, Franz Robert Eberli, Thomas Felix Luescher, Willibald Maier, Cardiology, University Hospital, Zurich, Switzerland, Institute of Clinical Chemistry, Zurich, Switzerland

**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 with respect to the onset characteristics (more versus less acute).

**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 (PericorSurge 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 adjusted, 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[3.0-14.4] mg/L, SAA was 28.6 [22.8-324.3] versus 23.3 [14.6-93.4] mg/L, and CRP was 5.5 [1.8-15.5] versus 1.7 [0.8-3.0] 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.
Hypertensive Patients Have Increased Sensitivity To Meteorological Parameters For Myocardial Infarction Occurrence. Analysis From Rico Database

Clothilde Royer, Jean-Claude Be, Marianne Zeller, Jean-Pierre Besancenot, Jean Raviney, Isabelle Lhullier, Micheline Vincent-Marion, Yves Laurent, Alexandra Ourdet, Jean-Eric Wolf, Hamb Makki, Yves Cotelle, 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, data from 748 patients 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 (-4.9 to -4°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 (+42%) of MI when the difference in temperature between the day before and the day of MI onset was >5°C (0.81 vs 0.51 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 (+64%, 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 normotensive patients.

Conclusion: Our results show for the first time the increased sensitivity of hypertensive patients with CAD to cold temperatures.

Hypertensive Population is Associated with Increased Risk for Myocardial Infarction: A Comprehensive Analysis of the RICO Cohort

ABSTRACTS - Myocardial Ischemia and Infarction 241A

A 70% stenosis of a major epicardial coronary artery; of these, 14 patients were HIV positive. On unadjusted analysis, HIV status was 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.

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.

1147-107 Protection of LV Remodeling by Intravenous Infusion of Human Atrial Natriuretic Polypeptide in the Patients with Acute Anteroseptal Myocardial Infarction. - Prospective Randomized Trial Assessed by Quantitative Gated SPECT Imaging-

Hitoshi Matsuo, Tomonori Segawa, Takanobu Watanabe, Shunichiro Wataris, Shunichiro Waris, Tai Kojina, Taketa Shiroki, Takeshi Hirose, Makoto Iwama, Kouji Ono, Masahiko Kouda, Haruki Takashiki, 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 were assessed by biplane cineangiography and MRI imaging.

Results: No differences in patients backgrounds were observed. HANP suppressed LVDDVI increase in comparison with placebo (HANP:3.2±1.6 control:16.0±2.3 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 LVDDVI 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 suppressive 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 infarction size (r=0.28, p<0.05) as well as wall motion severity score (r=0.32, p<0.01).

Conclusion: This study clearly demonstrates that HANP can suppress LV volume expansion despite no difference of infarct size.

LV remodeling vs infarct size (Randomized trial of HANP)

<table>
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<tr>
<th>Infarct size</th>
<th>HANP(-)</th>
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<td>-50</td>
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<td>-10</td>
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1147-198 Effects Of Early Acet inhibition In Patients With Non-STEMI Acute Myocardial Infarction.
Claudio Borghi, Stefano Bacchelli, Daniela Degi Esposito, 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 a 0.43 fold (p=0.001) increase in risk for non-ACE-inhibition treatment, and none of them underwent coronary 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%; p=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 effect 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 it improves the clinical outcome.

1147-220 Aqueous Oxygen Therapy for ST Segment Elevation Myocardial Infarction: Final Results and One Year Follow Up of the AMIHOIT Trial.
Jack L. Martin, Pranobe V. Oemrawsingh, Antonio B. Bartorelli, Simon D. Dixon, Mitchell W. Krucoff, Barbara S. Lindsay, Douwe A. Atsma, William W. O’Neill, Main Line Health System, Bryn Mawr, PA, William Beaumont Hospital, Royal Oak, MI.

Background: Despite rapid reperfusion in ST segment elevation myocardial infarction (STEMI) reduces mortality, epicardial vessel patency does not ensure full restoration of regional flow at the tissue level. Animal and clinical 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 ± 23.3 %, p< 0.05). Anterior MI patients randomized to AO therapy (n=70) after PCI demonstrated more complete resolution and less marked areas of infarction (area >6000) persistence (4% vs 16% and 9 vs 21%, p< 0.023). Core laboratory data demonstrates more improvement in regional wall motion scores, ST segment resolution and day 14 SPECT defects. 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.

1147-221 Caldaret (MCC-135) Lowers the Frequency of Severe Systolic Left Ventricular Dysfunction in STEMI patients undergoing PCI.
Mark Hibberd, Dan Tzivoni, Fritz Bar, 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 lowered infarct size and increased early LVEF in anterior MI. We investigated whether the frequency of severe LV dysfunction (LVEF <20%) will be reduced in caldaret-treated STEMI patients.

Methods: CASTEMI enrolled 387 patients with STEMI and myocardial infarction size sum of 75% LV area (75.7 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. Patients 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: Percentages of patients in each treatment group with severe LVEF≤30%, by location of index MI and pre-PCI TIMI flow.

<table>
<thead>
<tr>
<th>Location</th>
<th>Day of SPECT</th>
<th>Timi Flow</th>
<th>Timi Flow</th>
<th>Timi Flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>MI</td>
<td>All</td>
<td>Placebo</td>
<td>Caldaret</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>D 7</td>
<td>D 30</td>
<td>D 70</td>
<td>D 70</td>
</tr>
<tr>
<td>All</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MI</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>D 70</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All</td>
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<tr>
<td>MI</td>
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<td></td>
<td>D 7</td>
<td>D 30</td>
<td>D 70</td>
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<tr>
<td>All</td>
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<td>MI</td>
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<td>D 70</td>
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</table>

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 Intraoperative Hyperbaric Oxygen Administered During Primary Percutaneous Coronary Intervention Prevents One Month Left Ventricular Remodeling.
Hazem M. Warsi, Johan G. Bosch, Jeroen J. Bax, Douwe E. Atsma, Wouter J. Jukema, Ernst E. Van der Wall, Martin J. Schall, Pranobe V. Oemrawsingh, Leiden University Medical Center, Leiden, The Netherlands.

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. Anatomic angiographic 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, 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 LVEF volume at 1 month follow up. Also, patients with Ao therapy showed improved ejection fraction at 1 month follow up.
ABSTRACTS - Myocardial Ischemia and Infarction 243A

BENEFICIAL EFFECT OF FOLIC ACID ON ENDOTHELIAL DYSFUNCTION IN PATIENTS WITH NORMO- AND HYPERHOMOCYTESTENIA AFTER AN ACUTE MYOCARDIAL INFARCTION.

An L. Morey, Marc J. Claesys, 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 and methods: A randomized, double-blind crossover study was performed in 35 patients with AMI. In group A, FA (10 mg/day) 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).

Conclusions: Folic acid has a beneficial effect on endothelial dysfunction in patients with normo- and hyperhomocysteinemia after an AMI.

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, LBS 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;40:1383), but the relationship is incompletely defined. Thus, we performed a post-hoc analysis of the EPHESUS 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 (CMV), CV hospitalization (CHV), CV mortality +CHV, 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), CMV by 20% (P=0.002), CMV +CHV 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.

Does Facilitated Percutaneous Coronary Intervention Improve Angieographic and Clinical Outcomes in ST Elevation Myocardial Infarction? A Quantitative Review

Thomas T. Tsai, Brahmajee K. Nallamothu, P. Michael Grossman, Debabrata Mukherjee, Stanley Chetouti, Mauro Mosucci, Eric R. Bates, University of Michigan, Ann Arbor, MI

Background: Facilitated percutaneous coronary intervention (PCI) combines the rapidity and availability of fibrinolysis with the inter-artery stenting of PCIs 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. RCTs were identified as relevant RCTs. A RCT was included if it: 1) included 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). 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.

FACILE PCI RESULTS HIGHER RATES OF EARLY TIMI-3 FLOW THAN PRIMARY PCI

1147-205 Single High-Dose Bolus TiRofibAn and Sirolimus Eluting STEnt Versus Abciximab and Bare Metal Stent in Acute Myocardial Infarction (STRATEGY) Study

Marco Valgimigli, Gianfranco Percoco, Giordano Ccocchetti, Patrizia Malagutti, Gianluca Campo, Fabrizio Ferrarì, Dario Barbieri, Lucia Ansani, Roberto Ferrarì, 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 benefit is used 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/min for 1.5 hours) versus placebo plus standard therapy. Significant differences in terms of the primary outcome were shown at 6 months. Kaplan-Meier curve analysis showed a more significant improvement in the primary endpoint, which included the sumation 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 versus placebo. In the tirofiban group, there were 1 major and 7 minor bleeds, while 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.

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 Infarct Study (HIS)

Hendrik-Jan van Mieghem, Elvira V. van Horssen, Ferry M.K.J. Herrebau, Marc A. Brouwer, Arnoud W. van 't Hof, Ad J. van Boven, Wil 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 hours 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.
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.

Risk of First Coronary Ischemic Events Following First Atrial Fibrillation: Data from 2 Decades (1980-2000)

Yoko Miyagaki, 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 time-varying effects.

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 2867 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, and 1580 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:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hazard Ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Year</td>
<td>1.03</td>
<td>1.027</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>1.014</td>
<td>0.998</td>
</tr>
<tr>
<td>History of ASO</td>
<td>1.522</td>
<td>2.101 (P=0.010)</td>
</tr>
<tr>
<td>History of diabetes mellitus</td>
<td>1.451</td>
<td>1.955 (P=0.014)</td>
</tr>
<tr>
<td>History of dyslipidemia</td>
<td>1.139</td>
<td>1.411 (P=0.216)</td>
</tr>
<tr>
<td>History of hypertension</td>
<td>1.982</td>
<td>2.544 (P&lt;0.001)</td>
</tr>
<tr>
<td>Current and past smoker</td>
<td>3.947</td>
<td>1.511 (P=0.583)</td>
</tr>
<tr>
<td>T / Creatinine (d/L)</td>
<td>2.086</td>
<td>1.215 (P=0.408)</td>
</tr>
<tr>
<td>Log glucose</td>
<td>0.991</td>
<td>0.942 (P=0.50699)</td>
</tr>
</tbody>
</table>

1148-223 - Should Erectile Dysfunction Be Considered as a Sign of Occult Coronary Artery Disease?

Charalambos Vlachopoulos, Nikolaos Iakovidis, Konstantinos Rokkas, Konstantina Aggel, Andreas Michaelides, Konstantinos Aznouarids, Athanassios Asklis, Christodoulos Stefanidis, Athens Medical School, Athens, Greece

Background: Erectile dysfunction (ED) shares many risk factors with coronary disease (CAD) and is underdiagnosed and undertreated. ED may have a high prevalence 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 comprehensively evaluated using medical history, exercise treadmill 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 cardiac evaluation 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 (6 pts/20%) and family history (3 pts/11%). Moreover, 19 (73%) men had two or more risk factors. One patient presented with myocardial infarction caused by 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 demonstrated that 5 patients had single- vessel disease (1 pt LAD, 3 pts L CX, 1 RCA) and 1 patient had coronary artery ectasia.
Prognostic Value of N-Terminal Pro-Brain Natriuretic Peptide in Patients with Chronic Stable Angina

Gin N. Deppe, Siegmund Braun, Kathrin Niemöller, Julinda Mehilli, Nicolas von Beckerath, Olga Gorochkova, Wolfgang Vogt, Albert Schömig, Adnan Kastrati, Deutsches Herz Zentrum, 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 was equal than 1048 pg/ml (the high NT-proBNP group, 208 patients) and the group with NT-proBNP less than 1048 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 0.92, 95% CI 0.91 - 0.93, 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.

Long-term Prognosis Of Dobutamine-atropine Stress Echocardiography: The Impact Of Heart Rate Response

Boudewijn J. Krenning, Jeroen J. Bax, Elena Bigioni, Vittonia Rizzello, Arend FL. 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 atroplone 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, 56% vs 48%, 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 atroplone. 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.
Myocardial Ischemia and Infarction

246A ABSTRACTS - Myocardial Ischemia and Infarction

1149-197 Sustained Regional Improvement in Myocardial Perfusion One Year After Transplantation of Autologous Bone Marrow Cells in Patients With Diffuse Coronary Artery Disease

Luiz Henrique W. Quevedo, Isolmar T. Schettetti, Carlos Eduardo Rochitte, Luiz Antonio M. Casar, Protesilaos 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 angiographic effect 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-veesel CAD, not amenable to complete CABG due to the diffuseness of the disease were enrolled. BMC were obtained immediately prior to surgery, and the lymphomonoeytic fraction separated by density gradient centrifugation. During surgery, 4ml containing 13±3x10^6 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<0.0002) 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, 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 angiographic 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 Martins, 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 Cornell criteria were also predictive of mortality, but less so.

Methods: Excluded were 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 increased mortality (log rank: χ²=259, P<0.0001).

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, Ilili William P. Gunnar, Edward Hines Jr, Veterans 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 monitoring 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 (83%) where as only 6 of these patients (22%) had an EKG diagnosis of perioperative MI. Of the 666 survivors 23% had a post operative TROP =>15ng/mL and 8.6% had perioperative MI by EKG.

Conclusions: Thirty day mortality was directly related to the maximum postoperative value of TROP.

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 monkey C5. We demonstrated the ability of this aptamer to inhibit primate plasma C5.

Methods: To determine if Rottman et al. C5 aptamer would inhibit C5 cleavage and C'-mediated lysis of sheep erythrocytes. We studied the ability of this aptamer to inhibit human C5-mediated damage isolated, perfused mouse hearts and to inhibit primate C5 activity in vivo.

Results: Mouse hearts were perfused with Krebs-Heinselait 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.

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.

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 Kd = 600 +/- -100 µM) 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-Heinselait 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 5-fold or 10-fold molar excess over plasma C5 (25 µM or 10 µM), myocardial dysfunction and C5b deposition were observed in 0% 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 S/5 mice, respectively. The heart perfusate 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.
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, Aliar M. Rahnman, 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 PGE2 and PGI2 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 Orbifiban in Patients with Unstable coronary Syndromes (OPUS-TIMI-16) trial that compared orbifiban (ORBO) and placebo in 10,288 patients with ACS. All patients received ASA 162 mg/d.

Results: GI bleeding occurred in 1.89% and 2.3% of the patients +/− statins (p<0.001). Statins were associated with less overall bleeding in both the ORBO (p<0.001) and placebo (p<0.001) groups (Fig 1b). Logistic regression analysis showed that the use of statins (OR 0.57; 95% CI 0.38-0.85; p=0.005), age >65 y (5.27; 3.53-7.87; p<0.001), ORBO treatment (4.07; 2.45-6.77; p<0.001), Killip ≥2 (1.81; 1.05-2.51; p=0.030), history of cardiovascular disease (1.99; 1.04-3.79; p=0.036), and the use of calcium channel blocker (1.47; 1.02-2.07; p=0.027) were independently associated with the risk of GI bleeding.

Use of Statins Is Associated With Decreased Risk of Bleeding in Patients With Unstable Coronary Syndromes Treated With Antiplatelet Therapy

Kausik K. Ray, Christopher P. Cannon, Richard Cairns, Ayaj 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 80 mg vs standard (pravastatin 40 mg) statin therapy on CRP (n=3627) 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 >150 mg/dl (p<0.0005), HDL<50 mg/dl (p=0.001), glucose (p=0.009), on treatment LDL (p=0.001), % 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)

<table>
<thead>
<tr>
<th>Sub-Groups</th>
<th>Standard Therapy (atorvastatin 40mg)</th>
<th>Intensive therapy atorvastatin 80mg</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;65</td>
<td>2.12 (1.46)</td>
<td>1.41 (0.73)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Female</td>
<td>3.44 (1.4,7.2)</td>
<td>2.22 (1.5, 5.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (Baseline)</td>
<td>2.2 (1.4,8)</td>
<td>1.42 (0.7,3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current Smokers</td>
<td>2.4 (1.5,6.7)</td>
<td>1.77 (0.8,3.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabetes (Baseline)</td>
<td>2.74 (1.3,5.5)</td>
<td>1.51 (0.7,3.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Glucose &gt;110 mg/dl</td>
<td>2.89 (1.2,6)</td>
<td>1.44 (0.7,3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HDL &lt;50 mg/dl</td>
<td>2.15 (1.4,5)</td>
<td>1.34 (0.7,3.1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>High creatinine</td>
<td>0.38 (1.2,5.1)</td>
<td>1.68 (0.8,3.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BP &gt;130/85</td>
<td>0.5 (1.0,8)</td>
<td>0.39 (0.2,7)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

2:15 p.m.

2:00 p.m.

2:30 p.m.
Enfocus Software - Customer Support  
12/23/04   10:07:33 AM  
2005_5_MyocaIschInfarction.indd   248

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, Srihari Nair, Manish Panik, 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 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 multi vessel 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.

<table>
<thead>
<tr>
<th></th>
<th>Single vessel PCI (n=2441 patients)</th>
<th>Multi vessel PCI (n=1805 patients)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>66.1 +/- 12.0</td>
<td>64.8 +/- 12.3</td>
<td>0.002</td>
</tr>
<tr>
<td>Male sex (%)</td>
<td>63.7</td>
<td>64.3</td>
<td>NS</td>
</tr>
<tr>
<td>History of stroke (%)</td>
<td>5.4</td>
<td>4.2</td>
<td>NS</td>
</tr>
<tr>
<td>Peripheral vascular disease (%)</td>
<td>13.4</td>
<td>11.1</td>
<td>0.024</td>
</tr>
<tr>
<td>Diabetes mellitus (%)</td>
<td>29.0</td>
<td>25.4</td>
<td>0.010</td>
</tr>
<tr>
<td>Renal insufficiency (%)</td>
<td>2.0</td>
<td>1.2</td>
<td>0.028</td>
</tr>
<tr>
<td>Congestive failure on admission (%)</td>
<td>3.2</td>
<td>3.5</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Angiographic and procedural characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>54.5 +/- 10.8</td>
<td>55.4 +/- 10.4</td>
<td>0.008</td>
</tr>
<tr>
<td>Lesions &gt;70% (per lesion)</td>
<td>3.2</td>
<td>3.2</td>
<td>NS</td>
</tr>
<tr>
<td>GPIIb/IIIa inhibitor use (%)</td>
<td>38.5</td>
<td>33.5</td>
<td>0.001</td>
</tr>
<tr>
<td>CTO present (%)</td>
<td>37.9</td>
<td>17.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCI for CTO (%)</td>
<td>8.2</td>
<td>10.4</td>
<td>0.019</td>
</tr>
<tr>
<td><strong>Outcomes</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal failure with dialysis (%)</td>
<td>3.1</td>
<td>3.2</td>
<td>NS</td>
</tr>
<tr>
<td>Stroke (%)</td>
<td>0.2</td>
<td>0.1</td>
<td>NS</td>
</tr>
<tr>
<td>Emergency CABG (%)</td>
<td>0.6</td>
<td>0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Stent thrombosis (%)</td>
<td>0.6</td>
<td>0.2</td>
<td>NS</td>
</tr>
<tr>
<td>Death (%)</td>
<td>0.4</td>
<td>0.7</td>
<td>NS</td>
</tr>
<tr>
<td>MACE (%)</td>
<td>1.2</td>
<td>0.8</td>
<td>NS</td>
</tr>
</tbody>
</table>

It is important to note that the safety of multi vessel PCI is comparable to that of single vessel PCI, thus supporting a more aggressive approach in UA with significant lesions in multiple coronary arteries.

248A  
ABSTRACTS - Myocardial Ischemia and Infarction

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=0.000), 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 NSTEMI ACS.

3:00 p.m.

858-5  
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, Upal Patel, Nilo Ayuyao, Mutahir Khan, James Wilentz, Sui-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 ch² increased from 5.8 to 24.2; p <0.001 for cardiac death and from 7.1 to 23.1, p <0.001 for total mortality).

Conclusion: 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.

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  
Integrity of Lipid Lowering With Statins and Brachial Artery Vascular Endothelium Reactivity After Acute Coronary Syndromes: The BRAVER Trial
Jocelyn Dupuis, Jean-Claude Tartif, Jean-Lucien Rouleau, Joseph Ricci, Malcolm Arnold, Eva Loom, René Roux, Lawrence Title, Jean Dioittad, Nicole Bonafeade, 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 dilation (FMD) was measured after reactive hyperemia while endothelium-independent dilation 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% whereas 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.

3:15 p.m.

850-8  
Novel Risk Stratification Methods

3:15 p.m.

Oral Contributions

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 Jacor, Alex Calizzano, Yannick Neuder, Maik Zine, Patrice Faure, Daniel Fagret, Jacques Macheouer, 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) T2020 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=22). 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-EST 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 a second line diagnostic or prognostic tool.

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th>Group 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>107 (52-172)</td>
<td>103 (100-274)*</td>
</tr>
<tr>
<td>Peak-EST</td>
<td>119 (56-182)</td>
<td>201 (110-311)*</td>
</tr>
<tr>
<td>Post-EST</td>
<td>122 (59-195)</td>
<td>131 (128-326)*</td>
</tr>
<tr>
<td>Baseline - Post EST</td>
<td>75 (6-86)</td>
<td>73 (7-205)*</td>
</tr>
</tbody>
</table>

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

Shrikirth P, Upadhye, Srijal Bangalore, Taripiah Syed, Aseh Malik, Deborah Cantales, Amandeep Kaur, Lubna Rashid, Veerana Merla, Ranju Soni, Joseph Schappert, Faronq 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: A single pre-stress BNP test provide incremental value in predicting 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 stratification and prognostication.

Table

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Ischemics</th>
<th>Non ischemics</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>66 ± 12</td>
<td>59 ± 14</td>
<td>0.016</td>
</tr>
<tr>
<td>History of heart failure (%)</td>
<td>19 ± 9.4</td>
<td>19 ± 9.5</td>
<td>0.095</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>87</td>
<td>81</td>
<td>NS</td>
</tr>
<tr>
<td>Prior myocardial infarction (%)</td>
<td>19</td>
<td>19</td>
<td>NS</td>
</tr>
<tr>
<td>LVET (%)</td>
<td>49 ± 15</td>
<td>58 ± 4</td>
<td>0.002</td>
</tr>
<tr>
<td>Resting Wall Motion Index</td>
<td>1.5 ± 0.7</td>
<td>1.0 ± 0.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Stress Wall Motion Index</td>
<td>1.5 ± 0.3</td>
<td>1.1 ± 0.3</td>
<td>0.006</td>
</tr>
<tr>
<td>Pre Stress BNP</td>
<td>254.4 ± 451.4</td>
<td>57 ± 62.2</td>
<td>0.006</td>
</tr>
</tbody>
</table>

4:30 p.m.
Clinical Outcomes of Patients with Multivessel Disease Treated With Three or More Sirolimus-eluting Stents


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=0.003) 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 TVR-MACE; TVR 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 of 30 Days and 6 Months

<table>
<thead>
<tr>
<th>Variables, %</th>
<th>Multiple SES (n=31 pts)</th>
<th>Single SES (n=1013 pts)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>At 30 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>3.6</td>
<td>0.6</td>
<td>0.07</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>7.1</td>
<td>0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Q-wave MI</td>
<td>21.4</td>
<td>9.1</td>
<td>0.04</td>
</tr>
<tr>
<td>TVR-MACE</td>
<td>0.9</td>
<td>1.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Subacute stent thrombosis</td>
<td>0.3</td>
<td>0.0</td>
<td>0.03</td>
</tr>
<tr>
<td>At 6 months</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death</td>
<td>6.7</td>
<td>1.9</td>
<td>0.18</td>
</tr>
<tr>
<td>Q-wave MI</td>
<td>23.5</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Q-wave MI</td>
<td>31.6</td>
<td>10.8</td>
<td>0.004</td>
</tr>
<tr>
<td>TVR-MACE</td>
<td>23.5</td>
<td>3.6</td>
<td>0.002</td>
</tr>
<tr>
<td>TLR</td>
<td>8.7</td>
<td>1.1</td>
<td>0.03</td>
</tr>
<tr>
<td>TVR</td>
<td>6.7</td>
<td>2.8</td>
<td>0.37</td>
</tr>
</tbody>
</table>

The Medicine Angioplasty Or Surgery Study (MASS Registry): Impact Of Diabetes On Long-term Prognosis In Patients With Single Or Multivessel Coronary Artery Disease. Five Years Of Follow-up.

Whady Huse, Fernando Costa, Bernard J. Gerh, Nezupa Lopes, Aecio Gois, Paulo Dutra, Desiderio Fereoso, 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 benefits 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 comparison 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.
Methods: We analyzed data from 4370 pts with STEMI or NSTEMI enrolled in the international VALIANT Registry from 1999-2001. Patterns of use on admission and indefinitely after discharge; thienopyridines (Thieno) to pts with ASA intolerance, coronary stents, or NSTEMI; anticoagulation with either UFH or LMWH to patients with STEMI 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 (8.4% vs 3.1%, p<0.001) 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 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 readmission, 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 (8.4% vs 3.1%, p<0.001), but not with primary angioplasty (4.9% vs 4.2%, p=NS).

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 readmission, 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 (8.4% vs 3.1%, p<0.001), but not with primary angioplasty (4.9% vs 4.2%, p=NS).

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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 fluoroscopic 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) Electromechanical: 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.

782-7

Adjunctive Abciximab To Reperfusion Therapy In Patients With Acute St-Segment Elevation Myocardial Infarction: A Meta-analysis Of Randomized Trials


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 readmission, 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 (8.4% vs 3.1%, p<0.001), 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 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 readmission, 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 (8.4% vs 3.1%, p<0.001), but not with primary angioplasty (4.9% vs 4.2%, p=NS).

9:45 a.m.

782-8

In-Hospital Adherence to Current Guidelines is not Optimal for Antiplatelet and Antithrombotic Therapies in Patients With Acute Myocardial Infarction: Insights From the International Valisartan 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; thienopyridine (Thieno) to pts with ASA intolerance, coronary stents, or NSTEMI; anticoagulation with either UFH or LMWH to patients with STEMI, 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 (8.4% vs 3.1%, p<0.001), 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 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 readmission, 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 (8.4% vs 3.1%, p<0.001), but not with primary angioplasty (4.9% vs 4.2%, p=NS).

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 fluoroscopic 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) Electromechanical: 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.
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 NSTE MI pts and 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

877F0 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.

877F Intrinsic Inhibitors of Complement Activation
Dramatically Limit Infarct Following Coronary Occlusion
Nikolay Vasilev, Arman Askari, Feng Lin, Lisa Kutterner-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 groups. 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+/mice, IS%AAR was markedly greater than in WT mice (62.3 ± 7.2, n=8, p<0.001). The absence of DAF had a significantly greater effect (DAF−: 61.7 ± 6.0, n=9; DAF+/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.

877G Angiotensin II Receptor Blockade With Losartan Reduces Apoptosis and Infarct Size Following Ischemia/reperfusion in the Rabbit Heart
Shinji Okubo, Patrick W. Fisher, Fadi Salameh, Ramaz Ockail, Vijay Manwaha, 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 losartan (25 mg/kg) 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.

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

<table>
<thead>
<tr>
<th>Group</th>
<th>IS % RA</th>
<th>RA % LV</th>
<th>MAP</th>
<th>Apoptotic Index</th>
</tr>
</thead>
<tbody>
<tr>
<td>Saline</td>
<td>42.0±2</td>
<td>57.5±7</td>
<td>75±5</td>
<td>2.68±0.64</td>
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<tr>
<td>Losartan (5 mg/kg)</td>
<td>31.5±4</td>
<td>48.0±7</td>
<td>52±3</td>
<td>0.01±0.01*</td>
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<tr>
<td>Losartan (25 mg/kg)</td>
<td>13.7±1</td>
<td>64.8±3</td>
<td>48±6</td>
<td>0.4±0.03</td>
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</table>

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.

877H Effects Of Ramipril, An Angiotensin Converting Enzyme Inhibitor, On Apoptotic Associated Molecular Expression In Ischemic Reperfusion 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 (IR). Attenuation of myocardial apoptotic 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 identify the changes of myocardial apoptosis associated transcripts under the effects of ramipril, an ACEI, in the early IR 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 5-fold or more in ramipril treated sample. Among these probe sets, four apoptotic transcripts which were shown upregulation and eight apoptotic regulated probe set which transcript to caspase-3, caspase-1, Bax, Gadd45, and Bcl-2 were shown downregulation. The up- and down-regulation of these pro-apoptotic genes were further confirmed and characteristic by semi-quantitative reverse-transcription-polymerase chain reaction (RT-PCR), immunoblotting and immunohistochemistry in a time course. The caspase-3 activity was furthermore verified by caspase-3 activity assay (fluorescent AFC-DEVDF method).

The findings have provided a new insight into the mechanism of ACEI in the prevention of myocardial apoptosis following IR injury.

11:30 a.m.

877I Nitroxyl Requires Calcitonin Gene-Related Peptide (CGRP) Signaling but not Protein Kinase C to Afford Early-Preconditioning Effect in Rat Heart
Piercarlo Perlini, Daniele Mancardi, Claudia Penna, Sandra Cappello, Carlo G. Toschetti, David A. Wink, Gianni A. Losano, Nazario Pacorrotti, Dipartimento di Scienze Cliniche e Biologiche dell’Università 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 somewhat 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 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 cardioprotective action appears to be linked to calcitonin gene-related peptide (CGRP) signaling pathway; CGRP blockade has been already shown to prevent NO-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%, n=9, p<0.01). In lieu of isometric PC, the nitroxyl donor Angel's salt (AS, 1µM for 19') similarly reduced IS (38±3%, p<0.01 vs. control, n=8, p<0.05 vs IPC3). The PKC inhibitor iC3BP9023X (0.5 µM for 29') co-infused with AS did not reverse the protection achieved with nitroxyl (IS=31±5%, n=5). In stark contrast, blockade of CGRP receptors by means of the selective antagonist CGRP-83 infusion (0.1µM for 29') completely abrogated nitroxyl-induced cardiac protection (IS=63±5%, n=5, p<0.05 vs. controls).

Conclusions: Herein, we demonstrate for the first time that in isolated rat hearts the preconditioning effects of exogenous nitroxyl, similarly to NO/nitrates donors, involve a CGRP receptor-mediated pathway. However, differently from NO donors HNO does not require the activation of a PKC-dependent pathway to afford protection against reperfusion injury.
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).

Conclusions: The IABP succeeded in reducing the infarct size and the no-reflow phenomenon, probably due to increased CBF during the reperfusion period.