The goal of this study was to examine the relationship between contrast agent type (ionic vs. non-ionic) and angiographic, electrocardiographic, and clinical outcomes following thrombolytic administration in acute MI.

The choice of contrast agents during angiography and PCI is a subject of controversy. Non-ionic contrast was used more frequently than ionic contrast (69%, n=51 vs 31%, n=26). There was no relationship between contrast agent type and overall patency, rate of TIMI grade 3 flow, or corrected TIMI frame counts (CTFCs) in open culprit arteries at 90 min or post-PCI. Patients receiving ionic contrast had greater rates of Q-wave MI, less frequent complete ST segment resolution (>70%), longer chest pain duration, and slightly but significantly lower ejection fractions at 90 minutes. Conclusion: No significant relationship was identified between contrast type & epicardial flow at 90 min, or post-PCI in acute MI. However, ionic dye use was associated with poorer ST segment resolution, greater rate of Q-wave MI, longer chest pain duration, and slightly lower ejection fractions, perhaps as a result of increased microvascular dysfunction or the trend toward increased thrombus burden. It should be confirmed that dye type is balanced across arms of trial & further studies of dye type impact on outcomes are warranted.

Non-ionic dye & ionic dye

<table>
<thead>
<tr>
<th>Dye Type</th>
<th>TIMI 3 at 90 min (%)</th>
<th>OTTO at 60 min</th>
<th>TIMI 3 post-PCI (%)</th>
<th>CTFc post-PCI</th>
<th>EF at 90 min</th>
<th>EGc Res-% (%)</th>
<th>Q-wave MI (%)</th>
<th>Chent pain duration (ms)</th>
<th>Thrombus (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ionic</td>
<td>63.3%</td>
<td>0.04±2.0</td>
<td>85.7%</td>
<td>27.7±20.1</td>
<td>56.2±16.5</td>
<td>61.7%</td>
<td>50.6%</td>
<td>2.8±1.6, n=256</td>
<td>77.3%</td>
<td>0.0003</td>
</tr>
<tr>
<td>Non-ionic</td>
<td>82.2%</td>
<td>0.06±2.4</td>
<td>89.6%</td>
<td>26.5±23.1</td>
<td>59.8±14.4</td>
<td>55.3%</td>
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Background: Several randomized trials have compared primary stenting with primary balloon angioplasty (PTCA) for acute myocardial infarction (AMI), although many studies have shown to be better. In reducing the need for target vessel revascularization (TVR), uncertainty exists in regard to the relative merits of stenting in post-infarction mortality and the risk of MI. Methods: We performed a meta-analysis of all randomized trials published up to August 2000 which compared these two revascularization strategies in acute MI. Results: Six randomized trials (FRASCO, GRAMI, ESCOBAR, PASTA, STENTH2) were identified through searching the Medline database. They studied a total of 1,728 patients (pts), with 869 pts randomized to stent implantation and 869 pts to PTCA. Of the 6 trials, FRASCO and GRAMI included pts with cardiogenic shock at admission (22 pts). The death due to refractory cardiogenic shock was not included in the meta-analysis. The summary data are shown below. Conclusions: Based on the meta-analysis of these 6 trials, primary stenting is found to be superior to univariate PTCA (p<0.05) in reducing the need for TVR due to reinfarction. There was also a tendency for lower incidence of re-MI in the stent group during the 1-year follow-up period. A nonsignificantly higher mortality was observed in the stent group. However, this finding was dependent on a very small number of actual events and the small number of patients contributed the need for further trials.

Pooled odds ratio (95% confidence interval) for stenting versus PTCA

<table>
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<th>Death</th>
<th>MI</th>
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</tr>
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<tbody>
<tr>
<td>1 month</td>
<td>1.42 (0.79-2.56)</td>
<td>0.43 (0.19-0.95)</td>
<td>0.33 (0.19-0.57)</td>
</tr>
<tr>
<td>0 - 12 months</td>
<td>1.48 (0.82-2.63)</td>
<td>0.37 (0.18-0.77)</td>
<td>0.30 (0.17-0.52)</td>
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</table>

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Pooled odds ratio (95% confidence interval) for stenting versus PTCA.
Primary Angioplasty in Patients With Acute Myocardial Infarction and Multi Vessel Disease. One-Year Outcome 

1001-206

Background: During acute myocardial infarction (AMI), >50% ST-segment elevation resolution (STER) after epicardial recanalization both with thrombolysis or balloon angioplasty is a reliable ECG marker of myocardial reperfusion and predicts LV recovery.

Methods: We recorded IC ECG and 12-lead surface ECG in 42 pts with first AMI undergoing primary stenting <12 hours from symptoms onset, and correlated the ECG results with the degree of late lumen compression at the target lesion. All pts had TIMI flow grade 0-1 of the myocardial infarction (MI) vessel, successful stenting (TIMI 3, residual stenosis <20%), and TIMI 3 flow at 6-month angiography. IC ECG was recorded proximal to the stented lesion, distal (bailout situation), and 30 seconds after reperfusion; surface ECG was recorded before reperfusion and 3 hours later.

Results: IC ST elevation was measured 20 msec after the J point and STER was defined as >50% decrease of ST elevation from baseline. All pts (pts<11 yrs; 71% anterior AMI; ischemic time 19-627 min) underwent coagulation prophylaxis before procedure and 6 months later. Infarct zone Wall Motion Score Index (WMSI) was derived. Results: IC ST elevation was absent proximal in all and ~4 mm distal in 19/47 pts. After stenting, IC STER was present in 30 pts (78% group A; from 9.3 +/- 8.6 mm to 1.5 +/- 2.5 mm) and absent in 9 (group B; from 9.1 +/- 4.8 mm to 6.7 +/- 1.9 mm). On surface ECG, TIMI flow was present in 29/32 (87%) group A and in 1 (11%) group B. Mean ischemic time was 201 +/- 103 vs 271 +/- 108 min (p<0.05), peak CK 2706 +/- 2266 vs 4886 +/- 4811 U/l (p<0.08). At 6 months UVEF was 46 +/- 7 vs 37 +/- 9 (p=0.003), WMSI decreased from 2.2 +/- 0.7 to 1.7 +/- 0.4 in group A, but not in group B (from 2.2 +/- 0.4 to 2.2 +/- 0.5; p<0.01). Conclusions: Intracoronary ST elevation monitoring during primary stenting is a readily accessible and inexpensive tool to assess myocardial reperfusion after MI vessel recanilization and predicts late WMSI recovery. Thus, it allows prompt identification of pts without reperfusion need who will benefit from additional therapeutic interventions (i.e. GP IIb/IIIa inhibitors, aspirin, verapamil).
**Relationship Between White Blood Cell Count and the Occurrence of Silent Ischemia After Myocardial Infarction**

Malgorzata Kuperska, Ewa Toczo, Maria Krzeminska-Pakula, Zbigniew M. Bednarkiewicz. Medical Academy, Lodz, Poland

**Background:** White blood cell count (WBC) is a sensitive marker of inflammation which may accelerate the progression of coronary artery disease (CAD). Silent ischemia (SI) is known to be at least as prognostically unfavorable as symptomatic one. The aim of the study was to assess the relation between WBC and the occurrence of SI in asymptomatic patients after MI. **Methods:** The study group consisted of 114 pts who had Q-wave MI 3-6 months before. All were clinically asymptomatic. WBC was measured two times in a week interval and the average WBC was calculated for each patient. The pts were divided into two groups: Group I-48 pts with WBC ≥ 7000/μl and Group II-66 pts with WBC < 7000/μl. Differences in demographics, risk factors, localisation of MI, left ventricular function, medical treatment, 24-hour Holter monitoring were analyzed by Student’s t-test, Mann-Whitney U test and Chi-square test. A significant association was observed between the genotypes and CAD status. The presence of SI in totally asymptomatic postinfarction pts appeared to be strongly correlated with increasing leucocytosis. 2 Postinfarction patients with increased leucocytosis are likely to have more severe CAD even if they are asymptomatic.

**Conclusion:** The p-ranking polymorphism in the HO-1 gene is associated with CAD susceptibility in Japanese hypercholesterolemic patients. HO-1 may play an important anti-atherogenic role in hypercholesterolemic patients.
308A ABSTRACTS - Myocardial Ischemia and Infarction

POSTER SESSION

1016 Ultrastructural Observations and Regulation of Apoptosis

Sunday, March 18, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Time: 1:00 p.m.-2:00 p.m.

1016-77 Hypoxia Regulates Connexin 43 Content in Synchronously Contracting Cardiac Myocytes

Mark S. Turner, Guy A. Hayward, W. H. Evans, Keith A. Webster, Nanette H. Shib朝鲜. University of Miami, Miami, FL, Weisbad Heart Research Institute, Gerfaut, United Kingdom

Background: Hypoxia causes uncoupling of cardiac myocytes and has been suggested to reduce the Connexin (Cx)43/Cx43gap and the number of gap junctions. Hypoxia, however, is a combination of hypoxia, reduction in glucose, acidosis and buildup of toxic metabolites. We used an established hypoxia model in beating cultured neonatal rat cardiac myocytes to examine the effect of hypoxia on Cx43 levels. Functional gap junctional properties are responsible for synchronizing of beating in this model. Methods: Primary cultures of neonatal rat cardiac myocytes were prepared from 1-3 day old Sprague-Dawley rats. Cells were obtained with 5% fetal calf serum for 4 days and then for 3 days without serum prior to experimentation. All cultures were beating synchronously at 200-300 beats per minute. Cells were exposed to hypoxia (0.5% oxygen) within a sealed chamber for 8-20 hours. The medium was supplemented with additional glucose and was changed after 8 hours of hypoxia. Apoptotic and necrotic cells were assessed within the chamber without reoxygenation. Results: Cells were stained in a similar chamber for 8-20 hours. Upon reoxygenation Cx43/43 levels decimated by 26.4% after 4 hours (n=5, p=0.038). Conclusions: Hypoxia decreases the Cx43 content of cardiac myocytes in culture within 6 hours; this increase is sustained for a minimum of 20 hours and is at least partially reversed by reoxygenation. Functional coupling is maintained during hypoxia in the absence of glucose deprivation. Thus, hypoxia alone does not mediate a reduction in gap junction protein content or coupling.

1016-78 Ischemic Preconditioning Prevents Mitochondrial Bcl-2 Depletion and Limits Infarct Size in the Ischemic Rabbit Heart

Tai-Hung M. Fang, Zhe Jiao, Olana M. Gorodnya, Xi-Ming Yang, University of South Alabama, Mobile, AL

Background: We have previously shown that ischemic preconditioning (PC) could suppress cardiomyocyte apoptosis induced by ischemia/reperfusion. The present study was undertaken to address the question whether Bcl-2, a mitochondrial protein well known for its anti-apoptosis property, plays a role in the cardioprotection of PC. Methods: The control group consisted of 6 isolated, perfused rabbit hearts subjected to 30 min of global ischemia followed by 2 h of reperfusion. The PC hearts (n=6) received 6 min of global ischemia followed by 10 min of reperfusion prior to the 30-min ischemia/2-h reperfusion period. Intact size was determined by computer morphometry of TTC stained sections. Mitochondrial Bcl-2 was determined by Western blot analysis in a separate series of hearts, in which serial biopsies were taken at baseline and at 5, 10, 20, 30 min of ischemia. Results: In this global ischemia/reperfusion model, PC effectively reduced the infarct size by 50% (p<0.01 vs control). Mitochondrial Bcl-2 levels were well maintained in ischemia (p<0.02 vs baseline). In contrast, PC hearts exhibited a 38.41% increase in Bcl-2 levels (p<0.05 vs baseline) during the entire 30 min of ischemia. Interestingly, 20 min of global ischemia followed by 2 h of reperfusion resulted in significant contractile dysfunction but produced little evidence of infarction (infarct size 3.31±2.3%, n=6). Conclusion: In this global ischemia/reperfusion model, PC effectively reduced the infarct size and apoptosis in a rat model of myocardial ischemia and reperfusion. Its anti-digoxigenin detection and expressed as the number of apoptotic cells/total number of nuclei. Western blot analysis of Cx43 and Cx40 content was used for the study. The study revealed that CsA substantially reduced the rate of apoptosis in hearts after long ischemic periods which might indicate potential cardioprotective effects of CsA as well as its metabolic BM 92.0282 reduced infarct size in a 30 min coronary occlusion model, whereas prolonged ischemia eliminates infarct-limiting effects. We hypothesize that the cardioprotective effects of CsA are independent on its s-blocking properties, but might be meditated by potential antioxidant and direct anti-apoptotic effects.

1016-80 Induction of Pro-Apoptotic Bcl-Xs Protein Expression During Myocardial Infarction but Not After Stunning

Byasi Chandrasekar, Gregory L. Freeman, University of Texas Health Science Center, San Antonio, TX

Background: Inhibition of NF-kB activation induces apoptosis in a highly cell and stimulus-specific manner. The goals of this study were (1) to determine whether stunning induces apoptosis, (2) whether inhibition of NF-kB activation during stunning promotes apoptosis, and (3) to analyze whether various genes involved in the regulation of apoptosis are differentially expressed during stunning and infarction. Methods: 32 male WKY rats weighing 450 g (8 each). The study protocol was approved by the Laboratory Animal Care Committee. Results: Apoptosis was highly expressed by both TUNEL and by nuclear morphology in infarcted myocardium. Sham operated animals expressed Fas, bax, bcl-Xs, bax and lower anti-apoptotic (bcl-2 11.53-fold, p<0.001, Fas-L [1.31-fold, p<0.05]), bax [1.26-fold, p<0.05]) and lower anti-apoptotic (bcl-2 [1.5-fold, p<0.05]) gene expression was detected in infarcted myocardium. Conclusions: Inhibition of NF-kB activation does not induce apoptosis during stunning. The balance between pro- and anti-apoptotic genes is critical in inducing apoptosis, and longer durations of ischemia might be required to trigger the balance towards pro-apoptotic gene expression resulting in cell death.

1016-07 Calcineurin Inhibition With Cyclosporin A Preserves Heart Function by Decreasing Apoptosis

Lieven Pool, Thomas M. Mestas, Alexander Fein, Mitrae Ramzan, Tibor Zsigmond, Francesco Pollicino, W. H. Evans, Keith A. Webster, Otrotte H. Bishopric. University of Texas Health Science Center, San Antonio, TX

Background: Here, we show that the addition of cyclosporine A (CsA) to the University of Wisconsin ( UW) solution increased functional recovery from 55% to 100% after 16 hours of hypothermic global ischemia in the working heterotopic heart transplant model. In addition, CsA increased mitochondrial permeability transition pore (MPTP) opening, a known mechanism of inducing apoptosis and to inhibit calcineurin, we determined the rate of apoptosis, the total amount of calcineurin and its degree of activation in this ischemia model.

Methods: Twenty dog hearts were perfused for 16 hours (4°C) under low potassium with UW solution (1 min/m). Six hearts were treated with cyclosporine A (10 mg/ml, CsA) and six served as control (Ctrl). Four biopsies of each heart were taken: before transplantation (A); at the end of reperfusion (B), after (C), and 6 hours (D) of reperfusion. Western blot analysis for total calcineurin was performed and the activity of calcineurin was calculated using indirect method using anti-digoxigenin labeled tyrosine antibodies and 500 pg substrate (both % of control). Lamin B1 staining and TUNEL method were used to detect apoptosis by immunohistochemistry and confocal microscopy in control and infarcted myocardium. Results: Electrophysiological was used to understand the degree of ischemic injury. Results: Evidence for necrosis was absent, myocytes showed moderate ischemic injury that rapidly recovered after operation. ATP was moderately decreased in CsA- but well preserved in Ctrl hearts. During stunning. The balance between pro- and anti-apoptotic genes is critical in inducing apoptosis, and longer durations of ischemia might be required to trigger the balance towards pro-apoptotic gene expression resulting in cell death.

1016-08 Apoptosis and Mitochondrial Dysfunction in Hearts After Long Oxygen Deprivation

Byasi Chandrasekar, Gregory L. Freeman. University of Texas Health Science Center, San Antonio, TX

Background: Recently, we showed that the addition of cyclosporine A (CsA) to the University of Wisconsin ( UW) solution increased functional recovery from 55% to 100% after 16 hours of hypothermic global ischemia in the working heterotopic heart transplant model. In addition, CsA increased mitochondrial permeability transition pore (MPTP) opening, a known mechanism of inducing apoptosis and to inhibit calcineurin, we determined the rate of apoptosis, the total amount of calcineurin and its degree of activation in this ischemia model.

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Background: Global cardiac remodeling after infarction implies reorganization of tissue microstructural components that are integrally linked. We sought to elucidate the effects of ACE inhibitors on the specific organization of the interstitial collagen matrix and viable myocytes in intact, normal, and border zone tissues. Methods: Myocardial infarction was induced by left coronary artery ligation in 12 Sprague-Dawley rats. Rapiplri (1 mg/kg) was administered in drinking water 3 days after infarction for 12 weeks in 7 rats, and placebo was administered to 5 rats. Picrosiris stained microdissected cross-sections were imaged with computer-aided light and digitalized for collagen analysis; thiosemicarbazones were stained with light microscopy and utilized for analysis of viable myocytes in border and remote zones. Automated software developed at UCSF was employed for objective quantification of filter orientation, which was expressed as an Angular standard Deviation (AU: in degrees) with respect to the mean collagen or myocyte orientation in an AOI, to index an microscopic fiber disarray. Five to 10 ROIs each (200×200) were digitized from contiguous midmyocardial locations in remote, border, and infarct zones, and the AU's averaged for each zone over all animals. Results: Rapiplri decreased relative heart mass by 17% at 12 weeks (p<0.05). Rapiplri reduced AD for collagen fibers in the border zone from 20.5±2.9 to 14.6±2.4 degrees; and reduced AD for viable border zone myocytes from 13.8±1.2 to 11.4±1.1 degrees (DUKIY BY ANKUK). The AU's in treated border zones approximated those for remote normal tissues for both collagen and myocytes. The ROIs also showed less effect AD in others remaining normal or remote compared to border zones. Discussion: ACE inhibitors limit both collagen and myocyte disarray in viable border zones after infarction. These salutary changes in border zone microarchitecture may promote more physiological fiber orientations and strains, potentially improving local contractile function and reducing the stimulus to global ventricular remodeling.

1016-83 Distinct Signaling Pathways Account for Endothelial and Myocardial Apoptosis During Ischemia-Reperfusion Injury

Teriano N, Bonekemier, Anastasia Stathopoulos, Carol A. Chen, Terrence J. Cooper, Richard A. Knight, David J. Liptser. University of Miami Miller School of Medicine, Miami, FL.

The present study was aimed to evaluate the relative contribution of the receptor-dependent and mitochondrial signaling pathways in inducing cardiac apoptosis in different cell types during ischemia (I)-reperfusion (R) injury. Materials and Methods, Isolated Langendorf perfused rat hearts were randomized into 5 groups: control group (60' of perfusion), I group (30' of zero flow) and 3 I-R groups (35' of I followed by 5, 60' and 120' of R, respectively). A few animals were treated with specific and irreversible inhibitors of caspase 8 (C8) and 9 (C9) infused during I-R. Immunocytochemical findings were validated by EM. Conclusions: ACE inhibitors limit both collagen and myocyte disarray in viable border zones after infarction. These salutary changes in border zone microarchitecture may promote more physiological fiber orientations and strains, potentially improving local contractile function and reducing the stimulus to global ventricular remodeling.

1017-05 Coronary Dyspnea Syndrome in Women: A 25 Year Comparative Study of the Impact of the Internal Mammary Artery on Short and Long Term Results in Men and Women

Paul Kurlansky, Ernest A. Tread, David L. Gablit, Melinda Zucker, George Ebrani. Miami Heart Research Institute, Miami Beach, FL.

Background: Coronary artery bypass grafting (CABG) carries a higher operative mortality and long-term rates. It is a life-saving procedure for patients with symptomatic coronary artery disease. Methods: We compared 261 consecutive women patients undergoing coronary artery bypass surgery between January 1972 and October 1994 with a computer-generated matched cohort of 261 men undergoing CABG surgery during the same time period. Results: There was no significant difference in operative mortality or morbidity. The women seemed to have improved long-term results. Conclusions: Women patients undergoing CABG surgery have an improved long-term outcome over men.

1017-06 Pressure-Flow Relationship in Coronary Bypass Grafts

Dost A. Walchsh, Dinne Gopaul, Peraa Ilo, Peter Nolden, Otto M. Hoes, Thierry Carrel, Swiss Cardiovascular Center, Bern, Switzerland

Background: Coronary bypass flow is dependant on the quality of the anastomosis, perfusion pressure and distal coronary vascular resistance. The aim of the present study was to assess pressure-flow relations in arterial and venous bypass grafts. Methods: 30

1017-07-86 Cardiac Myofiber Disarray Associated With Postinfarct Remodeling in Viable Border Zones Is Prevented by Treatment With Angiotensin Converting Enzyme (ACE) Inhibitors

Samuel Widdison, Heather Lewis, Jeffrey Omosu, Andrew D. McCulloch, John Allen, Michael Mount, Christopher Hall. Washington University, St Louis, UCSD, San Diego.

Background: Global cardiac remodeling after infarction implies reorganization of tissue microstructural components that are integrally linked. We sought to elucidate the effects of ACE inhibitors on the specific organization of the interstitial collagen matrix and viable myocytes in intact, normal, and border zone tissues. Methods: Myocardial infarction was induced by left coronary artery ligation in 12 Sprague-Dawley rats. Rapiplri (1 mg/kg) was administered in drinking water 3 days after infarction for 12 weeks in 7 rats, and placebo was administered to 5 rats. Picrosiris stained microdissected cross-sections were imaged with computer-aided light and digitalized for collagen analysis; thiosemicarbazones were stained with light microscopy and utilized for analysis of viable myocytes in border and remote zones. Automated software developed at UCSF was employed for objective quantification of filter orientation, which was expressed as an Angular standard Deviation (AU: in degrees) with respect to the mean collagen or myocyte orientation in an AOI, to index an microscopic fiber disarray. Five to 10 ROIs each (200×200) were digitized from contiguous midmyocardial locations in remote, border, and infarct zones, and the AU's averaged for each zone over all animals. Results: Rapiplri decreased relative heart mass by 17% at 12 weeks (p<0.05). Rapiplri reduced AD for collagen fibers in the border zone from 20.5±2.9 to 14.6±2.4 degrees; and reduced AD for viable border zone myocytes from 13.8±1.2 to 11.4±1.1 degrees (DUKIY BY ANKUK). The AU's in treated border zones approximated those for remote normal tissues for both collagen and myocytes, indicating that rapiplri prevented the post infarct disarray of both collagen and myocytes. Rapiplri also had a significant effect AD in other areas remaining normal or remote compared to border zones. Discussion: ACE inhibitors limit both collagen and myocyte disarray in viable border zones after infarction. These salutary changes in border zone microarchitecture may promote more physiological fiber orientations and strains, potentially improving local contractile function and reducing the stimulus to global ventricular remodeling.

1017-14 Distinct Signaling Pathways Account for Endothelial and Myocardial Apoptosis During Ischemia-Reperfusion Injury

Tat W. Koh, Simon Davidson, Gerald S. Carr-White, Anthony DeSouza, John R. Pepper. Royal Brompton Hospital, London, United Kingdom.

Background: Coronary bypass flow is dependant on the quality of the anastomosis, perfusion pressure and distal coronary vascular resistance. The aim of the present study was to assess pressure-flow relations in arterial and venous bypass grafts. Methods: 30
that OPCAB does not decrease the incidence of postoperative AFIB. However, the additional non-steroidal anti-inflammatory drug (NSAID) indomethacin to the medical regimen of patients undergoing CABG with ECC to 18% in those with OPCAB (p=0.013). There was no difference between the groups in the incidence of AFIB on postoperative AFIB in our institution. From 7/1/96 through 6/30/99, 340 patients underwent CABG only, 197 operations were performed with extracorporeal circulation (ECC) and 371 were without (OPCAB). There was no significant difference between the groups in the mean age of the patient (64.4±10 vs. 65.6±10 years), sex (30% vs. 24% men), patient with or without diabetes (4/30 vs. 17/30 patients), number of grafts (2.7±0.2 days vs. 2.5±0.3 days), coronary artery bypass grafts against AFIB with beta-blockers or calcium-channel blockers or length of stay (p<0.05). Indomethacin in response to changes in shear stress (SS), little is known about remodeling in bypass graft and clinical outcome. (Methods) LITA showed enlargement of D to regulate its SS late postoperatively with better graft patency.

With the maximum norepinephrine or nitroglycerin dose respectively, MAP increased by 25% and by 21%, IM graft flow increased by 10% and decreased by 2% (p=0.001) and SVR flow increased by 16% and decreased by 15% (p=0.01) respectively. Resistance changes were not significant for both IM and SVG grafts. There was a significant pressure-flow relationship with a correlation coefficient of r = 0.6 for IMA and r = 0.5 for SVG grafts. Therefore, conclusions: There is a linear pressure-flow relationship for arterial and venous bypass grafts early after revascularization. Coronary vascular resistance remains, however, unchanged suggesting that pressure-flow relationship is maintained even after pharmacologic manipulation. Thus, adequate perfusion pressure is mandatory after myocardial revascularization, especially for IM grafts.

Indomethacin in OPCAB Reduces Postoperative AFIB

Arlene J. McLarty, Edward Woodford, Frank Sellert, Thomas V. Biffinger, Adam E. Saltman, Irvin B. Krahn. University State of New York at Stony Brook, Stony Brook, NY

Background: Post-operative atrial fibrillation (AFIB) is a common complication following CABG. Previous reports have not shown an impact of off pump CABG (OPCAB) on the incidence of AFIB. Methods: We reviewed our experience with CABG over a 12 month period to assess the impact of OPCAB on postoperative AFIB in our institution. From 7/1/96 through 6/30/99, 340 patients underwent CABG only, 197 operations were performed with extracorporeal circulation (ECC) and 371 were without (OPCAB). There was no significant difference between the groups in the mean age of the patient (64.4±9 vs. 65.6±9 years), sex (30% vs. 24% men), patient with or without diabetes (4/30 vs. 17/30 patients), number of grafts (2.7±0.2 days vs. 2.5±0.3 days), coronary artery bypass grafts against AFIB with beta-blockers or calcium-channel blockers or length of stay (p<0.05). Indomethacin in response to changes in shear stress (SS), little is known about remodeling in bypass graft and clinical outcome. (Methods) LITA showed enlargement of D to regulate its SS late postoperatively with better graft patency.

With the maximum norepinephrine or nitroglycerin dose respectively, MAP increased by 25% and by 21%, IM graft flow increased by 10% and decreased by 2% (p=0.001) and SVR flow increased by 16% and decreased by 15% (p=0.01) respectively. Resistance changes were not significant for both IM and SVG grafts. There was a significant pressure-flow relationship with a correlation coefficient of r = 0.6 for IMA and r = 0.5 for SVG grafts. Therefore, conclusions: There is a linear pressure-flow relationship for arterial and venous bypass grafts early after revascularization. Coronary vascular resistance remains, however, unchanged suggesting that pressure-flow relationship is maintained even after pharmacologic manipulation. Thus, adequate perfusion pressure is mandatory after myocardial revascularization, especially for IM grafts.

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Determinants of Persistent Negative T Waves and Early Versus Late T Wave Normalization: After Acute Myocardial Infarction

University Hospital of Liege, Liege, Belgium

Background: The clinical significance of T wave normalization after reperfusion in patients with myocardial infarction is well established. Nevertheless, the effects of the time of normalization on the long-term clinical outcome remain controversial. The aim of the present study was to analyze the relationship between the occurrence of early and late normalization of T waves and long-term clinical outcome.

Methods: The study included 121 consecutive patients with verified anterior ST elevation myocardial infarction who were treated with primary percutaneous coronary intervention (PCI). The patients were divided into two groups based on the time of T wave normalization: Group A (early normalization, ≤12 hours after infarction) and Group B (late normalization, >12 hours after infarction). The primary endpoints were all-cause mortality, cardiovascular death, and non-fatal myocardial infarction at 1 year.

Results: The time of T wave normalization was achieved in 77.2% of patients within 12 hours after infarction. The primary endpoints occurred in 23% of patients in Group A and 33% of patients in Group B (p=0.01). Multivariable analysis revealed that the time of T wave normalization was an independent predictor of the primary endpoints, with a hazard ratio of 0.36 (95% CI 0.18-0.73, p=0.006).

Conclusion: Early T wave normalization after reperfusion is associated with improved long-term clinical outcome compared to late normalization. These findings highlight the importance of prompt and effective reperfusion strategies to achieve early T wave normalization.

ABSTRACTS - Myocardial Ischemia and Infarction 311A

1019-01

Increased QT Dispersion in Patients With Prinzmetal's Variant Angina and Cardiac Arrest

Nikhil Parchure, Juan C. Kaski. Cardiological Sciences, St George's Hospital Medical School, London, United Kingdom

Background: Despite the usually benign course of treated Prinzmetal's variant angina, a proportion of vasospastic angina patients develop ventricular arrhythmias and sudden death associated with coronary spasm. Increased QT dispersion has been suggested to increase susceptibility to ventricular arrhythmias in patients with coronary artery spasm.

Methods: We studied 24 consecutive patients (mean age 68 years; 14 men) with classical Prinzmetal's variant angina and documented coronary artery spasm. The QT dispersion was measured before and after the infusion of nitroglycerin (NGT).

Results: The QT dispersion was significantly higher in patients with cardiac arrest (69.3 ± 16.9 ms) compared to patients with no cardiac arrest (57.3 ± 16.9 ms, p = 0.01). The QT dispersion was significantly higher in patients with cardiac arrest or syncpe (73.4 ± 17.3 ms) compared to patients with no such events (63.3 ± 16.9 ms, p = 0.01).

Conclusion: QT dispersion is increased in patients with Prinzmetal's variant angina complicated by cardiac arrest or syncpe compared to patients without such events.

1019-02

Acute Myocardial Infarction in Patients With High Lip(a) Levels Is Highly Characterized by Absence of Prodomal Angina and Early Culprit Artery Patency and Presence of Cardiac Dysfunction

Tatsuki Inukama, Kiyohiro Moroi, Sumio Mizuno. Fukuoka Cardiovascular Center, Fukuoka, Japan

Background: Although Lp(a) has been recognized as a related factor to coronary artery disease, clinical impacts of high Lp(a) levels on acute myocardial infarction (AMI) remained uncertain in the era of aggressive revascularization strategy. This study investigated clinical characteristics of AMI in patients with high Lp(a) levels. Methods: We investigated clinical and angiographic variables in the consecutive AMI patients who underwent emergent CAG, and compared the variables in patients with high Lp(a) levels (Lp(a)>30 mg/dl) to those in patients with normal Lp(a) levels (Lp(a)<15 mg/dl). Results: There were no significant differences in the coronary risk factors, location of myocardial infarction, culprit artery, number of stented vessels, or collateral supply. Patients of Group-L (n=60) manifested less frequent prodromal angina (PAP), and more frequent cardiac dysfunction defined by abnormal Killip or Forrester class. Patients of Group-L had larger improvement of coronary physiokinesis (CK). Incidence of early patent (TIMI flow grade 3) was low. Left ventricular enddiastolic pressure (LVEDP) was higher. Left ventricular ejection fraction (LVEF) was lower. The differences about cardiac dysfunction remained significant in subgroup analysis from PAP or TIMI flow grade 3. Conclusions: These results indicate that AMI patients with high Lp(a) levels are highly characterized by absence of prodromal angina and early culprit artery patency and presence of cardiac dysfunction, which may be of great clinical implication on management of myocardial infarction.

Clinical and Angiographic Variables in 2 Groups

<table>
<thead>
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<th>Group</th>
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1019-03

Increased QT Dispersion in Patients With Prinzmetal's Variant Angina and Cardiac Arrest

Nikhil Parchure, Juan C. Kaski. Cardiological Sciences, St George's Hospital Medical School, London, United Kingdom

Background: We sought to compare QT dispersion in patients presenting with Prinzmetal's variant angina complicated by cardiac arrest or syncpe and patients with uncomplicated variant angina, to investigate the significance of QT dispersion in patients with coronary artery spasm.

Methods: We studied 30 consecutive patients (mean age 58 years; 14 men) with classical Prinzmetal's variant angina and coronary artery spasm. The QT dispersion was measured before and after the infusion of nitroglycerin (NGT).

Results: The QT dispersion was significantly higher in patients with cardiac arrest (69.3 ± 16.9 ms) compared to patients with no cardiac arrest (57.3 ± 16.9 ms, p = 0.01). The QT dispersion was significantly higher in patients with cardiac arrest or syncpe (73.4 ± 17.3 ms) compared to patients with no such events (63.3 ± 16.9 ms, p = 0.01).

Conclusion: QT dispersion is increased in patients with Prinzmetal's variant angina complicated by cardiac arrest or syncpe compared to patients without such events.

1019-04

Acute Myocardial Infarction in Patients With High Lip(a) Levels Is Highly Characterized by Absence of Prodomal Angina and Early Culprit Artery Patency and Presence of Cardiac Dysfunction

Tatsuki Inukama, Kiyohiro Moroi, Sumio Mizuno. Fukuoka Cardiovascular Center, Fukuoka, Japan

Background: Although Lp(a) has been recognized as a related factor to coronary artery disease, clinical impacts of high Lp(a) levels on acute myocardial infarction (AMI) remained uncertain in the era of aggressive revascularization strategy. This study investigated clinical characteristics of AMI in patients with high Lp(a) levels. Methods: We investigated clinical and angiographic variables in the consecutive AMI patients who underwent emergent CAG, and compared the variables in patients with high Lp(a) levels (Lp(a)>30 mg/dl) to those in patients with normal Lp(a) levels (Lp(a)<15 mg/dl). Results: There were no significant differences in the coronary risk factors, location of myocardial infarction, culprit artery, number of stented vessels, or collateral supply. Patients of Group-L (n=60) manifested less frequent prodromal angina (PAP), and more frequent cardiac dysfunction defined by abnormal Killip or Forrester class. Patients of Group-L had larger improvement of coronary physiokinesis (CK). Incidence of early patent (TIMI flow grade 3) was low. Left ventricular enddiastolic pressure (LVEDP) was higher. Left ventricular ejection fraction (LVEF) was lower. The differences about cardiac dysfunction remained significant in subgroup analysis from PAP or TIMI flow grade 3. Conclusions: These results indicate that AMI patients with high Lp(a) levels are highly characterized by absence of prodromal angina and early culprit artery patency and presence of cardiac dysfunction, which may be of great clinical implication on management of myocardial infarction.

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Elevated C-Reactive Protein Levels on Admission Are Related to Segment Elevation Resolution in Patients With Acute Myocardial Infarction

Michaël Zoiris, Stavros Manousakis, Alexander Stefanidis, Denis Vitalis, George Andritsopoulos, Stelios Kandanos, Kostas Kalogerou, John Hadjicostis, Spyros Anagnostis, Panayiotis Adamopoulos, Stelios Fousias. Cardiology Department, Tzanio Hospital, Piraeus, Greece

Background: Failure of ST segment resolution after thrombolysis for acute myocardial infarction defines a high-risk group of patients. Additionally, high levels of plasma C-reactive protein reactive protein has been postulated in the first few days after acute myocardial infarction have been associated with an unfavorable outcome. However, the real association of C-reactive protein levels with the outcome of thrombolytic therapy has not been clarified yet. The aim of this study was to evaluate the possible association of plasma levels of C-reactive protein to ST-segment resolution and myocardial necrosis for acute myocardial infarction.

Methods and Results: A total of 214 patients presenting <6 hours from onset of acute myocardial infarction were studied. ST segment elevation was measured upon admission and 2 hours after the commencement of thrombolytic therapy. High plasma levels of C-reactive protein on admission was found to be an independent adverse predictor of, the probability of complete ST segment resolution (>70% resolution of the initial sum of ST segment elevations) achieved after 2 hours of administration of thrombolysis. Conclusions: Plasma levels of C-reactive protein levels within 6 hours of acute myocardial infarction can predict the extent of myocardial infarction. Plasma C-reactive protein levels within 6 hours of hospital admission may serve as an affordable and widely available marker for the detection of patients with myocardial reperfusion failure. These patients could benefit from more aggressive pharmacological intervention treatment.

Effects of Angiotensin II Receptor Blockade on Fibrinolysis and Coagulation in Patients With Acute Myocardial Infarction

I Shofuji Doi, M. Ito, Osamu Ogasawara, H. Yamasaki, Daisuke Miyamoto, Ichiro Kajiwara, Hideki Yamamoto. Department of Cardiovaseuc Medicine, Kumamoto University School of Medicine, Kumamoto City, Japan

Background: It has been reported that angiotensin II type 1 (AT1) receptor antagonism is associated with an improvement in mortality in patients with symptomatic heart failure. We have previously reported that AT1 receptor antagonism significantly augmented plasma tissue plasminogen activator (t-PA) levels in patients with acute myocardial infarction. We performed the present study to investigate the effects of AT1 receptor antagonist on fibrinolysis and coagulation in patients with acute myocardial infarction.

Methods and Results: In a randomized, double-blind, placebo-controlled study beginning one week after acute myocardial infarction, 14 patients received enalapril 5 mg daily therapy (enalapril group) and the other 14 received losartan 50 mg daily therapy (losartan group), and treated the patients with acute myocardial infarction. Methods and Results. In a randomized, double-blind, placebo-controlled study beginning one week after acute myocardial infarction, 14 patients received enalapril 5 mg daily therapy (enalapril group) and the other 14 received losartan 50 mg daily therapy (losartan group). Losartan and enalapril groups were significantly lower than that in the placebo group. Hepatocyte growth factor exhibited an initial high level of 7.5 f 2.9 (*t), reaching a maximum level of 5.2 f 1.8 (*+) at 3 days. This second peak was followed by a sustained increase up to a final nadir of 0.3 f 0.04 at 36 hours, that was reversed by a rebound up to a maximum level of 0.29 f 0.05 ng/mL at 3 days. These changes were accompanied by a sustained decline up to a final nadir of 0.3 f 0.04 at 36 hours. Furthermore, patients with extensive myocardial infarction and adverse events exhibited a higher, more sustained increase, whereas patients with limited infarct size (15,7,13,9 versus 2.3,3,2,1.3, p < 0.05).

Conclusion: The initially 27-fold increased hepatocyte growth factor possibly acts as a survival factor against endothelial cell death caused by acute hypoxia due to reduced myocardial perfusion, while the later sustained increased hepatocyte growth factor up to a maximum level possibly functions as a pro-angiogenic and anti-apoptotic activity in severely injured cells. The aim of our study was to elucidate any possible role of this factor in acute myocardial infarction.

Methods: We measured 17 serum-free hepatocyte growth factor levels in 17 patients with first attack of myocardial infarction, admitted and thrombolysed during the acute phase, and no previous History of any other diseases, and compared them to those of 17 sex and age-matched healthy control with mean values. Equal size of all patients in the three phases were well defined by the statistical analysis. The SEM is equal and considered to be statistically significant with p<0.05 when compared to mean values of healthy controls (*). The last serum sample (+).

Results. Hepatocyte growth factor exhibited an initial high level of 7.2 f 2.9 (*), reaching a peak of 5.3 f 2.9 (*), 3 hours after admission, followed by a gradual decrease, reaching a nadir value of 1.5 f 0.8 (*), 96 hours after admission. The second peak was followed by sustained decrease up to a final nadir of 0.1 f 0.04, at 3 days. Furthermore, patients with extensive myocardial infarction and adverse events exhibited a higher, more sustained increase, whereas patients with limited infarct size (15,7,13,9 versus 2.3,3,2,1.3, p < 0.05).

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Several studies showed that triglyceride (TG)-rich lipoproteins contribute to atheroembolic complications in type 2 diabetes mellitus (DM). However, it remains unclear which TG-rich lipoproteins contribute to the risk. We have shown that measurement of remnant-like lipoprotein particles (RLP), assessed by an immunoseparation method that is specific for apoA-1 and apoB-100, is a potential predictor of recurrent cardiovascular events in patients with DM.

The patients with CAD were followed up for 34 months until occurrence of one of the following clinical cardiovascular events: readmission or coronary revascularization due to recurrent or refractory angina pectoris, nonfatal myocardial infarction, and cardiac death. Patients with CAD had higher RLP levels than those without CAD (7.2 ± 1.0 mg cholesterol/dL vs. 4.2 ± 0.5 mg cholesterol/dL, P = 0.001). Multivariate logistic regression analysis showed that high RLP levels (>4.7 mg cholesterol/dL; 75th percentile of the distribution of RLP levels in controls) were a significant risk factor for the presence of CAD independent of age (70 ± 10 years), sex (male), smoking, hypertension, hypercholesterolemia, low LDL levels, low HDL levels, and hypertriglyceridemia (Odds ratio 1:5, 95% CI:1:5-2:2, P < 0.01). Kaplan-Meier analysis demonstrated that high RLP levels had higher probability of developing coronary events in patients with CAD (P = 0.01). In multivariate Cox hazard analysis, high RLP levels were a significant predictor of developing coronary events independent of other risk factors (Odds ratio 1:5, 95% CI:1:5-2:1, P < 0.01). Thus, the increase in remnant lipoprotein levels is a significant risk factor of CAD and predicts future coronary events in type 2 DM patients with CAD independent of other risk factors. Measurement of RLP levels may be useful in assessment of CAD risk in type 2 DM.

**Conclusion:** These findings indicate that prealbumin is a potential predictor of adverse outcome within 1 year in patients on chronic hemodialysis. cTnT could be related to AA and W of both genders in our cohort with higher RFS among those with CHD. Alcohol consumption was defined as alcohol intake on 4 days per week. The patients were divided into two groups based on whether they consumed alcohol (Group I) or not (Group II), and flow-mediated dilation (FMD), an indicator of the brachial artery diameter, was measured. FMD was higher in Group I than in Group II (p = 0.0001). Multivariate analysis showed that alcohol consumption (P = 0.0001) as well as brachial artery diameter after the administration of nitrergic (p = 0.0005) and the number of diseased vessels (p = 0.0043) influenced the FMD. Conclusions: These findings suggest that alcohol consumption may modify the FMD in men with CAD although it may affect other metabolic factors.

**Poster Session**

**1050-102 Effect of Alcohol Consumption on Endothelial Function in Men With Coronary Artery Disease**

Hiroki Terawaga, Yukihito Fukuda, Keiji Matsuda, Kenji Sakai, Sou Takenaka, Fumiharu Miura, Hidekazu Hiroto, Togo Yamagata, Hideo Matsuura, Kazuaki Chayama, Hiroshi University, Aichi, Japan

Background: An inverse association between moderate alcohol consumption and coronary artery disease (CAD) has been observed in several epidemiological studies. Although some possible mechanisms have been proposed, it remains unknown whether alcohol consumption affects the endothelial function which is beneficially associated with alcohol consumption. Therefore, we investigated the effects of alcohol consumption on endothelial function of the brachial artery in men with CAD.

Methods: Forty-five men (mean age 65 years) with CAD, who had 50% stenosis of the major coronary arteries on coronary angiogram were evaluated. Alcohol consumption was defined as alcohol intake on 4 days per week. The patients were divided into two groups based on whether they consumed alcohol (Group I) or not (Group II), and flow-mediated dilation (FMD), an indicator of the brachial artery diameter, was measured. FMD was higher in Group I than in Group II (p = 0.0001). Multivariate analysis showed that alcohol consumption (p = 0.0001) as well as brachial artery diameter after the administration of nitrergic (p = 0.0005) and the number of diseased vessels (p = 0.0043) influenced the FMD. Conclusions: These findings suggest that alcohol consumption may modify endothelial function in men with CAD although it may affect other metabolic factors.

**1050-105 COagulation and Inflammation in Acute Coronary Syndromes: Basic Observations**

Sunday, March 18, 2001, 3:00 p.m.—5:00 p.m.

Orange County Convention Center, Hall A4

Presentation Hour: 4:00 p.m.—5:00 p.m.

Richard C. Becker, Yue Fu Li, Frederick A. Spercek, University of Massachusetts Medical School, Worcester, MA

Background: The pathobiology of acute coronary syndromes (ACS) is characterized by plaque disruption, injured site thrombosis and microcirculatory embolization. Although tissue factor (TF) is a prominent protein in atherothrombosis, the contribution of contact activating factors and the physiologic integration of coagulation pathways must also be...
Background: There is increasing evidence that inflammation, infection and immune reactions play an important role in the acuity/progression of atherosclerosis. Therefore, several cytokines, chemokines and other pro-inflammatory factors like C-reactive protein (CRP) are known to be involved in plaque rupture.

Methods: We studied 103 patients consecutively admitted to our coronary care unit with acute coronary syndromes (51 with unstable angina, 35 with non-ST-elevation myocardial infarction (NSTEMI) and 17 with ST-elevation myocardial infarction (STEMI)). CRP was measured in serum samples obtained at admission and at 48 h. The G-174C polymorphism was genotyped in 23 patients with unstable angina (UA) and in 30 patients with stable angina (SA) using direct sequencing of PCR-amplified DNA. The expression of CRP and hHSP 60 was assessed in 65 of these patients.

Results: Crude plasma CRP concentrations were higher in patients with unstable angina (1.1 ± 1.0 mg/L) than in those with stable angina (0.6 ± 0.6 mg/L; P < 0.001) or in patients with non-ST-segment elevation ACS (0.5 ± 0.5 mg/L). The expression of CRP in peripheral blood mononuclear cells (PBMC) at day 1 was significantly higher in patients with unstable angina (UA) than in patients with non-ST-segment elevation ACS (1.7 ± 1.0 vs. 0.5 ± 0.4, P < 0.001) or in patients with stable angina (0.4 ± 0.2, P < 0.001). The expression of CRP at day 1 was also higher in patients with unstable angina (UA) than in patients with non-ST-segment elevation ACS (1.7 ± 1.0 vs. 0.5 ± 0.4, P < 0.001) or in patients with stable angina (0.4 ± 0.2, P < 0.001).

Conclusion: The G allele of the CRP polymorphism is associated with unstable angina, and not with stable angina or non-ST-segment elevation ACS.

314A ABSTRACTS - Myocardial Ischemia and Infarction

Conclusion: Specific markers of inflammation and infarction are useful in coronary artery disease, the more in other lesions associated with UA. Intracoronary persistence of C. pneumoniae may be an important chronic stimulus for inflammatory and/or stress events involved in plaque rupture.

1051-80 Endogenous Fibrinolytic Activity and Response to Thrombolytic Therapy in Acute Myocardial Infarction

David E. Newby, Nicholas L. M. Cruden, Laura L. Flint, Nicholas A. Boon, Keith A. F. Fox. University of Edinburgh, Edinburgh, United Kingdom

Background: Improved endogenous fibrinolysis may contribute to the pathogenesis of acute myocardial infarction. We postulated that the efficacy and capacity of repurification of the tissue-type plasminogen activator with exogenous thrombomodulin therapy would be enhanced in those patients with low endogenous plasma tissue plasminogen activator (t-PA) activity.

Methods: Admission fibrinolytic parameters were determined in 60 patients, aged 65 ± 11 years (52 men), with acute myocardial infarction. We investigated the role of the tissue factor pathway inhibitor-1 (TFPI-I) in the regulation of monocyte procoagulant activity in AMI.

Results: Forty-eight hours after AMI, TFPI-I transcription and binding to the TF receptor were increased and may contribute to the risk of recurrence and other thrombotic events. This study sought to investigate the role of tissue factor (TF) and its counterpart tissue factor pathway inhibitor-l (TFPI-1) in the regulation of monocyte procoagulant activity in AMI.

Methods: In 40 patients with AMI undergoing revascularization by stent placement, we measured TF proteolytic activity with spectrozyme method. TF-Vlla augmented intrinsic Xa (factors IXa, Villa)-mediated thrombin generation, but only partially inhibited by surface-bound TFPI-1. Anticoagulant therapy by direct inhibition of TF activity may, thus, be particularly effective in AMI.

1051-81 Absence of Interaction Between Clopidogrel and Warfarin in Patients on Long-Term Anticoagulation

C. Lidell, L-E Svedberg, P. Lindell, B. Sandhi, L. Wallentin. Department of Cardiology. Uppsala University Hospital, Uppsala, Sweden

Background: Clopidogrel (C), an ADP receptor antagonist, is indicated for secondary prevention in patients with recent ischaemic stroke, recent myocardial infarction or peripheral arterial disease. Warfarin may be used in patients with antithrombotic, in circumstances which are associated with a history of myocardial infarction or ischaemic stroke. A randomized, double-blind, placebo-controlled, parallel group trial to test for a possible interaction between C and warfarin is warranted.

Methods: Main inclusion criteria were: age 35–75 years; receiving long-term (>2 months) warfarin treatment for chronic or recurrent non-valvular atria fibrillation (AF), with an INR value between 2.5 and 3.5 under constant warfarin regimen, as confirmed by 3 weekly controls performed during a run-in period. Patients were randomly assigned to C 75 mg OD (n = 20) or matching placebo (n = 23) administered for 8 days (weeks 1–4) on top of the constant warfarin regimen. Blood was collected by try 22. The primary endpoint was percent change in INR from baseline through the overall evaluation period including Days 3, 6, 9, 13 and 22. The secondary endpoint was percent change in plasma levels of warfarin enantiomers from baseline at each time point.

Results: Mean INR remained extremely stable under C, the maximum percent change from baseline being 0.9% at Day 6. There was no statistically significant difference between the two treatment groups in the percent change from baseline at any time point. All the 95% confidence intervals remained between 2.9 and 2.7, and a greater than 5% increase in INR under C could be ruled out. Plasma levels of C- and warfarin remained also very stable under C. No serious adverse events were reported during the study, and there were no premature discontinuations of study drug. No bleeding occurred under C.

Conclusion: The stable anticoagulation status of patients on long-term warfarin therapy is not modified by concomitant administration of clopidogrel 75 mg OD. Safety and tolerability of such combination were good in this study.

1051-82 Interleukin-6 G-174C Polymorphism is Associated With Occurrence of Unstable Angina and With In Vitro Increased Monocyte Production of Interleukin-6 in Unstable Patients

Luigi M. Biasucci, Dominick J. Angiolillo, Pier France Pignatti, Chiara Stranieri, Vittoria Rizzello, Cristiana Colicci, Giovanna Luzzo, Attilio Mosleri. Catholic University Rome, Rome, Italy; University of Verona, Verona, Italy.

Background: Interleukin-6 (IL-6), the main inducer of C-reactive protein (CRP) production, is raised in acute coronary syndromes. A common polymorphism G-174C of the human IL-6 gene in the 5' region has been described. In normal subjects the G allele has been associated with higher IL-6 plasma levels. Aim of this study was to assess the role of the G-174C polymorphism in unstable angina (UA). Methods: We studied 62 patients with UA, Braunwald's class IIIb, (29) with CRP=3mg/L and 23 with CRP>3mg/L, and 17 patients with stable angina. All patients were genotyped for the G-174C polymorphism. Results: The frequency of the G allele was higher in UA (81%) versus stable angina (65%, p=0.02), but no significant difference was observed between UA with high or low CRP levels. After LPS stimulation of whole blood in vitro, G homozygote patients (n=15) had higher IL-6 plasma levels than patients with the C/C genotype (n=15) and patients with the C/C genotype (n=15).

Conclusion: The G allele of the IL-6 G-174C polymorphism is associated with unstable angina.
A Polymorphism in the Promoter of the CD14 Receptor Gene Is Associated With Circulating Soluble CD14 Levels and With an Enhanced Pro-Inflammatory Response in Patients With Unstable Angina

Giulio Luzzi, Donatella J. Angelillo, Pier G. Fratantoni, Chiara Orlandi, Matteo Santinari, Rosanna Girgenti, Antonino Buffon, Luigi M. Balsassori, Attilio Masair. Catholic University, Rome, Italy

Background: Activation of circulating monocytes (MO) has been shown in unstable angina (UA). The CD14 membrane receptor is an important mediator for MO activation by bacterial lipopolysaccharide (LPS). CD14 is also present in a soluble form (sCD14), and sCD14 levels are strongly associated with prognosis in gram-negative infections. A C(-260)T polymorphism in the promoter of the CD14 receptor gene was recently associated with increased risk of myocardial infarction. In this study, we examined whether the C(-260)T polymorphism in the CD14 gene influenced sCD14 levels, the activation of circulating MO and the acute phase response in UA.

Methods: Plasma levels of sCD14 and C-reactive protein (CRP), and interleukin-6 (IL-6) production by circulating MO after in vitro stimulation of whole blood with a low dose of LPS (1ng/ml), for 4 hours were compared in 44 UA patients, 35 stable angina (SA) patients and 20 healthy subjects (C).

The CD14 C(-260)T polymorphism was assessed in 26 UA, 12 SA and 12 C. Results: Data are presented as median. Plasma levels of sCD14 were significantly higher in UA (2.5 mg/ml) than in SA (2.2 mg/ml) and C (2 mg/ml) (P<0.05). LPS-stimulated production of IL-6 by circulating MO was significantly higher in UA (4.4 ng/ml) than in SA (1.9 ng/ml), and in C (0.5 ng/ml) (P<0.01). A positive linear correlation was observed between plasma levels of sCD14 and CRP (r=0.42, P<0.01), as well as between sCD14 and IL-6 production in response to LPS (r=0.38, P<0.01). TM homogenates had significantly higher sCD14 levels (2.4 mg/ml) than those of both the CC (2.1 mg/ml) and CT (1.8 mg/ml) genotypes (P<0.05). TM homogenates also showed increased production of IL-6 by circulating MO in response to LPS-challenge (4.0 ng/ml) than carriers of the other two genotypes (1.9 and 1.3 ng/ml, respectively; P<0.05). Conclusion: Circulating MO of UA patients exhibit an enhanced responsiveness to LPS-challenge, which is related to sCD14 plasma levels, the soluble form of the receptor for bacterial LPS, and to a polymorphism in the promoter of the CD14 receptor gene. Our data suggest that a genetically determined response of circulating MO to infectious stimuli may contribute to determine the inflammatory component in UA.

POSTER SESSION

1052 Acute Coronary Syndromes: Plasma Markers and Prognostic Studies

Sunday, March 16, 2001, 9:00 a.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1052-84 Cardiac Troponin I Is A Powerful Long-Term Predictor of Serious Cardiac Events: Follow-Up of 501 Patients for 35 Months

Graham Illsley, Pamela Tognetti, Lorraine Illsley, Ning Zhuo, Antoinette Mangione. Albert Einstein Medical Center, Philadelphia, PA

Background: Sensitite and specific cardiac markers are excellent predictors of early outcome in patients with chest pain. There are, however, little data regarding the relative utility of such markers in predicting the long-term outcome of such patients. The aim of the current study was to assess the relative prognostic ability of clinical factors, cardiac troponin I (cTnI), creatinine kinase Mbmass (CK-MBmass), myoglobin light chain 1 (MLC-1) and CRP. Methods: Five hundred and one patients presenting with chest pain were studied prospectively. Eligibility criteria included >15 minutes of chest pain within the prior 24 hours felt clinically to represent myocardial ischemia, but with clinico-ecg evidence of reperfusion, and subsequent troponin I greater than the assay cut-off. Results: Data are presented as mean ± SD. At baseline, patients with troponin I >0.1 microg/L had higher age (54.5±12.3 vs. 50.8±12.4 years), lower left ventricular ejection fraction (52.1±13.3% vs. 58.1±11.4%) and higher C-reactive protein (5.0±8.7 mg/L vs. 2.0±2.9 mg/L). Cardiac troponin I was the most powerful predictor of long-term cardiac events (hazard ratio of death: 4.6, 95% CI: 1.0-20.9, P<0.05). Conclusion: Cardiac troponin I remains a powerful long-term predictor of serious cardiac events in patients presenting with chest pain. In this respect it is superior to other widely available cardiac markers and most clinical parameters.

1052-86 Improved Risk Stratification of Patients With Unstable Angina Using a Lower Than Usual Cut-Off Point of Troponin T Combined With CK-MB Measurement

B. Charles Solyom, Martialis G. Bourassa, Peter C. Arnaoutakis, Pierre Theroux. Montreal Heart Institute, Montreal, PQ, Canada

Unstable angina (UA) pts with troponin T (cTnT) levels above 0.1 microg/L are considered to have higher risk of future coronary events than those with lower values. We examined, in 131 pts (Age: 65.6±11.5; Female: 45%), with 85.2% episode of UA whether a lower cTnT cut-off point, combined with CK-MB measurement, improves risk stratification. Plasma samples, obtained upon arrival and at 4, 8, and 12 to 24 hours, were analyzed with Triage (890) and the second generation of cTnT reagents. Plasma values were correlated with a composite endpoint of new episodes of cine-positive UA, myocardial infarction (MI) or death during a mean follow-up of 15 (range 13-17) months. The risk of events was evaluated using the usual cTnT cut-off point (cTnT>0.1 microg/l), and a lower cut-off point (cTnT>0.04 microg/l). cTnT positive pts were further subdivided according to CK-MB values (> or = 0.04 microg/l). At baseline, risk factors and history of MI, PCI or CABG were not different between these groups. During the follow-up, 48 pts (36.5%) underwent PCI or CABG, and significant differences in frequency between groups. Using the cTnT cut-off point, the frequency of subsequent events was 87.1% (11.3%) with negative cTnT, 42/71 (14.8%) with positive cTnT but negative CK-MB, and 11/33 (33.3%) with both markers positive (combined: P=0.007), negative vs. positive CK-MB: P<0.009). With the lower cut-off point, the respective figures were 16/66 (24.6%), 8/43 (18.6%) and 15/42 (35.7%) (overall, P=0.0004; negative vs. positive CK-MB: P=0.02). Thus, the use of a lowered cut-off point for cTnT values and the additional analysis of CK-MB further improves the risk stratification of UA pts.

1052-87 Six Month Prognosis After Hospital Discharge in Patients With Acute Coronary Syndromes: The GHAGE Project

Robert J. Goldberg, Frederick Spencer, Joel M. Gora, Imad Sadi, Cynthia Sullivan, Keith Fox, Edward Hix, Kim Flegel, Philippe Granger, Martin Leon from the University of Massachusetts Medical School, Worcester, MA

Background: The acute coronary syndromes (ACS) continue to be a major reason for hospitalization with significant attendant morbidity and mortality. While significant advances have been made in improving the hospital outcome for these patients, considerably less information is available about the long term prognosis for this group of patients. Methods: The Global Registry of Acute Coronary Events (GRACE) Registry is enrolling patients with ACS at 91 hospitals in 14 countries. In addition to detailed information on inpatient treatment and selected short-term outcomes, patients have follow-up data collected 6, 12 and 24 months following hospital discharge assessing the development of subsequent coronary events and medication adherence. Results: To date, ~2000 patients with ACS have been successfully followed since hospital discharge. This includes 1575 patients with myocardial infarction (MI)(680 with ST segment elevation (STE) MI and 995 with non-ST MI), 1006 with unstable angina, and 123 with other cardiac diagnoses. The 6 month post discharge cardiac death rates were highest in those with non-STE MI (7.3%), followed by patients with STE MI (5.6%), those with unstable angina (4.9%), and those with other cardiac diagnoses (1.1%). Renoprotection rates for noncardiac death were relatively frequent (~20%) in all patient groups. Results of a multivariable regression analysis controlling for various demographic parameters and other cardiac diagnosis categories will be presented.
and clinical characteristics rivaled that of older patient age and failure to receive ACE inhibitors at the time of hospital discharge were significantly associated with 6-month death rates in patients with AMI and unstable angina. Older patient age and failure to receive beta blockers or statins were associated with significantly increased risk of hospitalization in patients with ACS.

Conclusions: Our results from a multi-hospital, multi-country registry suggest that patients discharged from the hospital with ACE inhibitors can experience significant long-term mortality and mortality over the ensuing 6 months. Targeted interventions need to be directed to the elderly and to the increased use of evidence-based proven therapies to improve prognosis after ACS.

1052-08  Optimal Discriminative Value of Troponin-I for 6 Month Cardiac Event Rate in the Evaluation for Suspected Acute Coronary Syndromes
Vincent Roolvink, Hans E. Luijten, Marc A. Rovers, Gilles J. H. Uijen, Piet de Keijser, Tjeerd van der Vel, Freek W. A. Verheugt, Heartcenter, University Medical Center, Nijmegen, The Netherlands.

Background. Troponin-I (cTnl) has proven to be a useful prognostic marker for short-term outcome in patients presenting with a suspected acute coronary syndrome. Nevertheless, a fair amount of patients with a positive cTnl (> 0.20 ng/ml) will not develop a major ischaemic event. This study sought to assess the optimal discriminative value of cTnl with respect to long-term outcome.

Methods. Between January 1, and October 31, 1999, cTnl-levels were determined 8 hours or more after symptom onset in 100 patients presenting with acute ischemia pain at the emergency department. Clinical charts were reviewed for subsequent events: cardiac death (n=21), non-Q-waveMI, revascularisation (invasive) or recurrent angina (re/inv). cTnl-levels were assessed by univariate analysis, with respect to the optimal combination of positive- and negative predictive value (PPV, NPV), sensitivity (SN) and specificity (SP).

Results. Mean follow-up time was 833 ± 261 days. Optimal cTnl-levels for the respective clinical endpoints are given in the table. The rate of cardiac death was 2% in case of a cTnl < 0.20 ng/ml (n=112). 14% for patients with a cTnl between 0.20 and 0.36 ng/ml (n=14), in contrast to 55% in patients with a cTnl > 0.36 ng/ml (n=20).

Conclusions. According to these findings, even a cTnl level slightly higher than 0.20 ng/ml carries a markedly increased risk for death and reinfarction within 6 months after the index event.

<table>
<thead>
<tr>
<th>N (%)</th>
<th>cTnl (ng/ml)</th>
<th>PPV</th>
<th>NPV</th>
<th>SN</th>
<th>SP</th>
</tr>
</thead>
<tbody>
<tr>
<td>cardiac death</td>
<td>3 (2%)</td>
<td>0.42</td>
<td>5%</td>
<td>99%</td>
<td>67%</td>
</tr>
<tr>
<td>nonQ-wave MI</td>
<td>10 (7%)</td>
<td>0.76</td>
<td>22%</td>
<td>98%</td>
<td>80%</td>
</tr>
<tr>
<td>re/inv</td>
<td>38 (25%)</td>
<td>0.25</td>
<td>58%</td>
<td>90%</td>
<td>74%</td>
</tr>
<tr>
<td>cTnl&gt;0.36</td>
<td>62 (41%)</td>
<td>0.90</td>
<td>71%</td>
<td>86%</td>
<td>71%</td>
</tr>
</tbody>
</table>

POSTER SESSION
1053  Cardioprotection During Myocardial Infarction
Sunday, March 18, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1053-01 Aspirin Use and All-Cause Mortality Among Patients Being Evaluated for Known or Suspected Coronary Artery Disease: A Propensity Analysis
Patricia A. Gum, Maran Thamilarasan, Junko Watanabe, Eugene Blackstone, Michael S. Lauer. Cleveland Clinic, Cleveland, OH

Background: Although aspirin has been shown reduce cardiovascular morbidity, the association between its use and long-term all-cause mortality has not been well defined.

Methods: We prospectively studied 6527 consecutive adults referred for stress echocardiography at the Cleveland Clinic between 1995 and 1998 for evaluation of known or suspected coronary disease; 2455 (38%) were taking aspirin. We used propensity analysis to identify patients for whom comparisons between aspirin use and no aspirin were expected coronary disease; 2455 (38%) were taking aspirin. During follow-up there were 243 deaths (6%). Patients taking aspirin were 34% less likely to die than non-users (adjusted HR 0.68, 95% CI 0.52-0.89, p=0.005). Conclusion: In this propensity analysis, the use of aspirin among patients undergoing stress echocardiography for evaluation of known or suspected coronary artery disease was independently associated with reduced long-term all-cause mortality.

1053-05 Lipid Lowering Drug Therapy Initiated During Hospitalization for Acute MI is Associated With Lower Postdischarge 1-Year Mortality
Robert P. Giugliano, Elliott M. Antman, Susan L. Thompson, Carolyn H. McCabe, Eugene Braunwald, Brigham and Women’s Hospital, Boston, MA, Nottingham Clinical Research Group, Nottingham, United Kingdom

Background – The benefit of commencing lipid lowering drug therapy (LLRx) during hospitalization for acute myocardial infarction (AMI) is controversial. Two major clinical trials (UNITED 2, IBIS-4) which have attempted to examine the efficacy of Mg in AMI have produced conflicting results with respect to mortality. Experimental studies have however shown that intravenous Mg started before reperfusion produces beneficial effects by decreasing infarct size and suppressing free radicals.

Methods: We randomly divided 96 patients with a first AMI (antero or inferior location) into two groups, an Mg group (n=48) and a control group (n=50). All patients were successfully reperfused by primary PTCA. Before reperfusion, Patients in the Mg group received a bolus injection of 8 mmol Mg sulphate followed by an infusion of 32 mmol over 24 h. Left ventriculograms prior to discharge were used to evaluate ejection fraction (EF) and end-diastolic volume index (EDVI) by the area-length method. Regional wall motion (RWM) in infarcted segments was analyzed using the centerline method. Coronary flow reserve (CFR) in the infarct-related artery was measured to assess coronary microvascular function, using a Doppler guidewire. CFR was expressed as the ratio of maximal hyperemic average peak velocity after injection of intra coronary papaverine to the baseline value.

Results: There was no significant difference between the groups in the time to reperfusion. Distribution of culprit lesion location, depressed ejection, and collateral grade were similar between the groups. The frequency of the angiographical no reflow phenomenon was significantly higher in the control group than in the Mg group (10% vs. 0%). Left ventricular EF, EDVI and CFR were significantly better in the Mg group than in the control group (EF: 53±13% vs 53±13%, p=0.001; EDVI: 57±14 vs 72±21 ml/m², p=0.001; CFR: 0.90±0.13 vs 0.93±0.15 SD/chord, p=0.000). CFR was also significantly higher in the Mg group than in the control group (2.9±0.9 vs 2.4±0.8, p=0.036). Conclusions: Intravenous Mg sulphate started before reperfusion may preserve left ventricular systolic function and suppress dilatation, and result in better coronary microvascular function compared to reperfusion alone in patients with AMI.

1053-07 Cardioprotective Effects of Intravenous Infusion of Magnesium Sulphate in Acute Myocardial Infarction
Hisamitsu Nakashima, Toshiro Nasuyama, Yukiharu Horiha, Shin Suzuki, Department of Cardiology, Nagasaiti Citizens Hospital, Nagasaki, Japan

Background: The role of magnesium (Mg) in troponin acute myocardial infarction (AMI) is controversial. Two major clinical trials (UNITED 2, IBIS-4) which have attempted to examine the efficacy of Mg in AMI have produced conflicting results with respect to mortality. Experimental studies have however shown that intravenous Mg started before reperfusion produces beneficial effects by decreasing infarct size and suppressing free radicals.

Methods: We randomly divided 96 patients with a first AMI (antero or inferior location) into two groups, an Mg group (n=48) and a control group (n=50). All patients were successfully reperfused by primary PTCA. Before reperfusion, Patients in the Mg group received a bolus injection of 8 mmol Mg sulphate followed by an infusion of 32 mmol over 24 h. Left ventriculograms prior to discharge were used to evaluate ejection fraction (EF) and end-diastolic volume index (EDVI) by the area-length method. Regional wall motion (RWM) in infarcted segments was analyzed using the centerline method. Coronary flow reserve (CFR) in the infarct-related artery was measured to assess coronary microvascular function, using a Doppler guidewire. CFR was expressed as the ratio of maximal hyperemic average peak velocity after injection of intra coronary papaverine to the baseline value.

Results: There was no significant difference between the groups in the time to reperfusion. Distribution of culprit lesion location, depressed ejection, and collateral grade were similar between the groups. The frequency of the angiographical no reflow phenomenon was significantly higher in the control group than in the Mg group (10% vs. 0%). Left ventricular EF, EDVI and CFR were significantly better in the Mg group than in the control group (EF: 53±13% vs 53±13%, p=0.001; EDVI: 57±14 vs 72±21 ml/m², p=0.001; CFR: 0.90±0.13 vs 0.93±0.15 SD/chord, p=0.000). CFR was also significantly higher in the Mg group than in the control group (2.9±0.9 vs 2.4±0.8, p=0.036). Conclusions: Intravenous Mg sulphate started before reperfusion may preserve left ventricular systolic function and suppress dilatation, and result in better coronary microvascular function compared to reperfusion alone in patients with AMI.

1053-11 Lipid Lowering Drug Therapy Initiated During Hospitalization for Acute MI is Associated With Lower Postdischarge 1-Year Mortality
Robert P. Giugliano, Elliott M. Antman, Susan L. Thompson, Carolyn H. McCabe, Eugene Braunwald, Brigham and Women’s Hospital, Boston, MA, Nottingham Clinical Research Group, Nottingham, United Kingdom

Background – The benefit of commencing lipid lowering drug therapy (LLRx) during hospitalization for AMI has been established.

Methods: We analyzed baseline characteristics, concomitant treatments, inhospital complications, and 1 yr mortality among 14,124 patients with AMI surviving the index admission in INTIME-I, a randomized double-blind trial comparing IPR and nPA. The association between the use of LLRx with 1 yr mortality, adjusted for baseline character idios and inhospital complications (recurrent MI, CHF, shock, stroke), was explored in a multivariate model.

Results: 34.3% of patients who survived to discharge received LLRx inhospital. Unadj usted 1-yr mortality post-discharge was 33% lower among patients receiving inhospital LLRx (3.0% vs. 4.5%, p = 0.0006). After multivariate adjustment, inhospital LLRx was associated with 29.9% lower 1-year post-discharge mortality.

Prior LL Rx In hospital Lipid Rx CR 95% CI p-value
No No 1.0 referent group
Yes No 1.09 0.61-1.83 0.91
No Yes 0.86 0.63-1.22 0.57
Yes Yes 0.49 0.29-0.87 0.03
1053-92 Lower Myocardial Infarction Risk in Users of Selective Serotonin Reuptake Inhibitors
William H. Sauer, Jesse A. Berlin, Stephen E. Kimmel. University of Pennsylvania School of Medicine, Philadelphia, PA

Background: Depression is an independent risk factor for myocardial infarction (MI). Selective serotonin reuptake inhibitors (SSRIs) may reduce this risk via treatment of depression and attenuation of serotonin-mediated platelet activation.

Methods: A case-control study of patients with MI to smokers and non-smokers was conducted among all inpatients in an 8-county area during a 24-month period. Cases were smokers hospitalized with a first MI, and controls were randomly selected smokers from the same geographic area. Uptake rate, analysis, smoking history, and other clinical and demographic data were obtained by telephone interview. Analytic use served as an alternate exposure group to assess the potential for selection and recall bias.

Results: 630 cases and 2,990 controls participated. After adjustment, using multivariable logistic regression, for age, gender, race, education, smoking, body mass index, aspirin use for MI prevention, family history, and history of coronary disease, diabetes, hypertension, and hypercholesterolemia, the odds ratio (OR) for MI among SSRIs users compared with non-antidepressant users was 0.96 (95% CI: 0.56, 1.66; P = 0.89).

Conclusion: There is a significant association between SSRIs use and MI protection. The pattern of ventricular remodeling differed between aspirin and captopril, despite causing similar reductions in ventricular weights. Both interventions reduced the pro-inflammatory cytokine TGF-β, which elicited the anti-inflammatory cytokine interleukin 10, and only captopril reduced the pro-inflammatory cytokine TNF. A graph showing the distribution of TGF-β and TNF levels in different groups is included. The addition of NEP inhibition to those of ACE inhibition does not result in significant further benefit.
**Methods:** To study the temporal relationship between progression of acute coronary syndromes and activation of cellular immune responses, we compared lymphocyte activation and differentiation towards Th1 or Th2 in patients without coronary artery disease (n=7), with unstable angina (n=14), and with acute myocardial infarction (n=10). Lymphocyte activation was assessed using 3-color flow cytometry to quantify CD3+ cells producing IFN-γ (Th1), IL-4 (Th2) or both signature cytokines (Th0).

**Results:** In patients without coronary artery disease, 7.2±2.1% of peripheral CD3+ cells stained positive for IFN-γ. The proportion increased significantly in stable angina (39.3±13.8%, p<0.001 versus control) and unstable. In marked contrast in patients with acute myocardial infarction, the frequency of IL-4+CD3+ cells declined to 7.3±1.6% (p<0.001 versus unstable). The frequency of IL-4+CD3+ (p=0.04) or IFN-γ+IL-4+CD3+ (p=0.07) cells did not differ significantly between the different groups.

**Conclusion:** The current findings suggest that IFN-γ-producing Th1 cells, but not Th2 or Th0 cells, mediate the progression of acute coronary syndromes. The transient imbalance of circulating Th1 cells seen with unstable angina may result from the instability program in the development of acute myocardial infarction strongly supports the assumption that lymphocyte activation occurs as a result of the progression of plaque instability.
1083 Stable Ischemic Syndrome: Oxidative Stress, Inflammation and Insulin Resistance

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1083-75 Treatment With Folic Acid and Cobalamin Improves Coronary Endothelial Function in Hyperhomocysteinemic Patients With Symptomatic Coronary Artery Disease

Frank F. Willems, Wim R.M. Aengevaeren, Godfried H.J. Boars, Henk J. Blom, Freek W.A. Verheugt, University Medical Center, Nijmegen, The Netherlands, Rijnstate hospital, Arnhem, The Netherlands

Background: Hyperhomocysteinemia is an independent risk factor for coronary artery disease. It is unclear whether lowering homocysteine (Hcy) with folic acid and cobalamin improves coronary endothelial function in patients with hyperhomocysteinemia and coronary artery disease. Aim of this study was to evaluate the effect of folic acid and cobalamin on coronary endothelial function in patients with symptomatic coronary artery disease.

Methods: 17 patients scheduled for elective PTCA with Hcy levels above 16 μmol/l were randomised for treatment with folic acid 0.5 mg and cobalamin daily or placebo. Coronary endothelial function was evaluated in a non-PTCA model using acetylcholine infusion in an dosage of 10-8M, 10-7M, 10-6M and nitroglycerin 200μg/kg. Each infusion was followed by coronary angiography. After 8 months of treatment a second procedure was performed using the same method. Endpoints were the mean changes in minimal obstruction diameter (MODO) and mean segment diameter (MSD) of the investigated coronary vessel as compared to the initial procedure. Results: Mean Hcy level was 19±4 μmol/l (SD). The mean difference in MODO (SD) before and after treatment with folic acid and cobalamin was 100.6% compared to 90.9% in the placebo treated group (p<0.05). The mean difference in MSD (%: before versus after treatment with folic acid and cobalamin was 100.6% compared to 90.9% in the placebo treated group (p<0.05).

Conclusion: This is the first randomised placebo controlled intervention study evaluating coronary endothelial function in hyperhomocysteinemic patients with symptomatic coronary artery disease. Our results suggest improvement of coronary endothelial function following treatment with folic acid and cobalamin.

1083-76 Evidence of Oxidative Stress in Patients With Angina and Normal Coronary Arteries: Role of Statins and ACE-Inhibitors

Carminie Pizzi, Giulia Maria Costa, Barbara Brescioni, Milena Gentile, Carlo Tumolo, BUGRAN, Naples, Italy

Background: It is well known that the endothelial dysfunction plays a key role in the pathophysiology of the angina with normal coronary angiograms. The endothelial dysfunction is associated with increased oxidative stress (OS) and loss of nitric oxide availability. Aim of study was to evaluate the influence of the therapy with statins and ACE-inhibitors on OS production in this setting. Methods: We studied 40 normocholesterolemic pts with effort angina. We performed exercise and resting intracoronary ultrasound determination of endothelial function in order to evaluate whether OS were modulated by chronic statin intake. Results: Baseline plasma levels of malondialdehyde (MDA), a marker of lipid peroxidation, by high pressure liquid chromatography (HPLC); superoxide dismutase (SOD) and CoQ10 were measured. Changes in OS were correlated with clinical response. Results: Baseline characteristics (age, gender, risk factors of coronary artery disease) were similar in the 2 groups. At T1 MDA, SOD and CoQ10 showed no differences in G1 vs G2 (MDA 2.5±2.8 μmol/l vs. 2.4±2.0 μmol/l, SOD 120±87 vs. 117±85 U/mg Hb, CoQ10 1.4±0.2 μmol/l vs. 1.3±0.2 μmol/l). At T2 MDA was significantly reduced in G1 vs G2 (1.2±0.2 μmol/l vs. 2.3±0.2 μmol/l, p<0.001). At T2 exercise stress test were a significant increase in the exercise time and maximal work capacity and a significant decrease in the maximum ST segment depression in G1, no myocardial perfusion assessed by defect Thallium tomography (SPECT) in 16 pts of G1 and only 3 pts of G2. Conclusion: Our data support the hypothesis that oxygen free radicals production may be an important role in the pathophysiology of angina pectoris with normal coronary angiograms, independently of plasma total cholesterol levels.

1083-77 Effects of Insulin Resistance and Thiazolidinedione on Effort-Induced Angina Pectoris of Type-2 Diabetes Mellitus

Tatsuhiko Murayama, Masateru Chikama, Fukai Cardiovascular Center, Fukai, Japan

Background: insulin resistance is thought to be highly involved in atherosclerotic processes. The effects of thiazolidinedione on an insulin sensitizer on coronary heart disease have masked attention, but few investigations evaluated effects of thiazolidinedione, and an insulin sensitizer, on ischemic heart disease. This study investigated whether insulin resistance and its reversal by thiazolidinedione have impacts upon clinical manifestations of effort-induced angina pectoris (EA). Methods: Type-2 diabetic patients (n=22) with EA and ischemic change on treadmill exercise test were enrolled into this study of thiazolidinedione, and randomized where they received thiazolidinedione for 4 months (T-group, n=11) or they were followed without thiazolidinedione (C-group). At baseline and at 4 months after medication, we assessed changes of exercise tolerance (appearance time of ischemic ST segment change) and noninvasively measured the reactive changes in lumen diameter of right brachial artery following transient occlusion for 5 minutes (FMD: flow mediated endothelium dependent vasodilation), and after sublingual administration of 0.6mg nitroglycerine (TNG: endothelium-independent vasodilation). Results: Exercise time (minutes) were significantly extended after medication in T-group (p=0.01) but not in C-group. HOMA index (a product of fasting glucose and fasting insulin) and FMD (% improvement after medication in T-group (p=0.01)) but not in C-group. TNG remained unchanged in both groups. Extension time was correlated to improvement of FMD (Extension of exercise time (y) vs. improvement of FMD (x); p=0.02), and improvement of HOMA index (y) vs. HOMA index (x); r=0.54). Conclusion: These findings suggest that thiazolidinedione reverses exercise intolerance partly related to endothelial dysfunction and insulin resistance in patients with effort-induced angina pectoris.

Baseline T Follow-up T Baseline C Follow-up C
Exercises Time 4.9±1.6 6.7±3.0 4.2±2.6 4.4±2.0
FMD 4.0±1.6 6.7±3.0 4.2±2.6 4.4±2.0
HOMA 2.0±1.4 2.1±1.1 2.6±1.2 2.5±1.2

1083-78 Effect of Cholesterol Synthase Inhibitor Treatment on Interleukin-6 and CRP in Patients After Myocardial Infarction

Stephan H. Holmer, Christina Hengstenberg, Hanns-Helmut Loewel, Susanne Engel, Wolfgang König, Guenter A. J. Rieger, Heribert Schunkert, University of Regensburg Medical School, Regensburg, Germany, and GSF Institute of Epidemiology, Munich, Germany

Background: Levels of cytokines (e.g. Interleukin 6 (IL6) and acute phase proteins (e.g. C-reactive protein, CRP) may indicate inflammatory activity in coronary lesions in patients with coronary artery disease and have been associated with prognosis. Chronic medication with ACE-inhibitors (atypically) improves the prognosis of such patients. It was suggested that this treatment may modulate the inflammatory process.

Methods: We tested in stable patients with previous myocardial infarction (MI) whether IL6 and CRP levels are modulated by chronic statin intake (astrazeneca statin, Merck). Plasma from the MONICA-MI-register, Augsburg (n=642, 557 men) were examined 1-10 years (mean 5.6 years) after MI with a standardized interview (intake of prescribed medication), anthropometry, CO2 excerise stress test and blood tests (e.g. IL6 high sensitive ELISA). None of the patients had signs of acute coronary syndrome.

Results: Of all patients, 51% were on statin treatment. Patients with statins showed significantly lower IL6 levels compared to those without lipid-lowering drugs (2.8±0.1 μg/ml vs. 2.8±0.1, p=0.0001). This was most evident in men (2.1±0.2 vs. 2.8±0.1, p=0.0001). Similarly, CRP was lower in patients on statins (2.3±0.3 mg/l vs. 3.1±0.1, p=0.0001). Neither IL6 nor CRP were related to cholesterol levels. The association of statin treatment with IL6 and CRP levels was also highly significant in multivariate regression models that included age, body mass index, left ventricular function (EF) and cholesterol level as covariates (p=0.001 and 0.017, resp.). In the small number of patients with MI no such association of IL6 or CRP levels with statin treatment was observed. Other medication such as ACE-inhibitors, beta-blockers, or vasodilators had no apparent effect on IL6 or CRP levels in this population.

Conclusion: In this observational study, statin therapy is strongly and independently associated with lower IL6 and CRP levels in male patients after MI. This further supports the concept that statin therapy attenuates the inflammatory process in autologous/eicosanoids independently of its cholesterol lowering effect.

POSTER SESSION

1084 Advances in Cardiopulmonary Resuscitation

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1084-79 Early Defibrillation Through First Responders Doubles Sudden Cardiac Arrest Survival in an Italian Community

Alessandro Capucci, Daniela Acheri, Massimo F. Pepoli, Ettico Dini, Maurizio Arvedi, cardiology department, Piacenza, Italy

Background: The concept that non medical individuals must be allowed to perform early defibrillation has been largely endorsed. To improve out-of-hospital survival we developed the Piacenza Progetto Vita project i.e. the first European experience of public access early defibrillation. Methods and Results: Thirty-five non-automated external defibrillators (Heartstart FR) were placed in this large city (200,000 inhabitants in the surrounding region): 15 fixed places, 12 ambulances (12 paramedics), 12 police cars. One thousand and twenty-five "Blue Codes" were dispatched: in only 95 of such cases a defibrillator was started. During the first year 187 sudden deaths occurred in the city. During this lane 186 "Blue Codes" were dispatched. In only 90 of such cases a true sudden death (48%) was found. The defibrillator was applied by volunteers in 63 cases: 36 asystole, 3 pulse less electrical activity, 4 bradycardia, 1 supraventricular...
Background: Almost one-half of postresuscitation syndrome deaths that occur take place within 24 hours of the event caused by microcirculatory dysfunction from the multi-focal hypoxia. There are no convincing clinical data to evaluate the stress response hormones and coagulative fibrinolytic parameters in patients with acute coronary syndrome (ACS) complicated by out-of-hospital cardiac arrest. Methods: Three of 275 patients whose ACS-related artery could be identified by emergency coronary angiography and whose blood test before administration of drugs could be obtained were chosen for this study. The stress response hormones and coagulative fibrinolytic parameters of 50 patients with ACS complicated by out-of-hospital cardiac arrest were compared with those from 107 patients with ACS without this complication.

Results

- **Dopamine** (μg/ml): cardiac arrest without cardiac arrest
  - Cardiac arrest: 131 ± 56
  - Without cardiac arrest: 18.8 ± 19.3

- **Noradrenaline** (μg/ml):
  - Cardiac arrest: 1843 ± 913
  - Without cardiac arrest: 2066 ± 280

- **Angiotensin II** (ng/ml):
  - Cardiac arrest: 47 ± 9
  - Without cardiac arrest: 47 ± 9

- **Brain natriuretic peptide** (pg/ml):
  - Cardiac arrest: 127 ± 163
  - Without cardiac arrest: 127 ± 163

- **Von Willebrand factor (VWF):**
  - Cardiac arrest: 257 ± 253
  - Without cardiac arrest: 257 ± 253

- **Free tissue factor pathway inhibitor (TFPI):**
  - Cardiac arrest: 46 ± 56
  - Without cardiac arrest: 46 ± 56

- **Preprothrombin fragment 1 + 2 (F1 + 2):**
  - Cardiac arrest: 3.5 ± 1.6
  - Without cardiac arrest: 3.5 ± 1.6

- **Tromboneadulin (F1 + 2):**
  - Cardiac arrest: 3.4 ± 3.0
  - Without cardiac arrest: 3.4 ± 3.0

- **Activated protein C (%):**
  - Cardiac arrest: 68 ± 68
  - Without cardiac arrest: 68 ± 68

- **1 PD-1 complex**
  - Cardiac arrest: 27 ± 15
  - Without cardiac arrest: 27 ± 15

- **FDP** (μg/ml):
  - Cardiac arrest: 26 ± 7
  - Without cardiac arrest: 26 ± 7

- **D-dimer** (μg/ml):
  - Cardiac arrest: 8.5 ± 5.3
  - Without cardiac arrest: 8.5 ± 5.3

**Conclusion:** Pumping increases in the levels of circulating vasoconstrictor hormones and systemic thrombus formation were observed in patients with ACS complicated by out-of-hospital cardiac arrest. It was suggested that the management of hypervasoconstriction and hypercoagulability in survivors with ACS complicated by out-of-hospital cardiac arrest are needed for prevention of postresuscitation syndrome.

**1084-82 Utilization of the Emergency Medical System Among Patients With Myocardial Infarction in the Reperfusion Era: Results From The NRMI 2**


Background. National practice guidelines strongly recommend that patients with symptoms consistent with an acute myocardial infarction (MI) activate the 911 Emergency Medical Service (EMS). Data for the NRMI 2 are needed to ascertain the factors which may influence their use. Methods. From April 1994 to March 1998, the NRMI 2 has enrolled 772,566 patients. We excluded patients who presented in cardiogenic shock, <6 hours from symptom onset, or who were transferred-in. We then compared the baseline characteristics and initial management for patients presenting by ambulance versus self-transport.

Results

- **Ambulance**
  - Age, years
    - Mean: 66.1
    - Standard deviation: 11.0
  - Sex
    - Female: 46.1%
    - Male: 53.9%

- **Self-Transport**
  - Age, years
    - Mean: 63.7
  - Sex
    - Female: 53.0%
    - Male: 47.0%

**Conclusion:** Only 1 of every 2 patients with MI was transported to the hospital by ambulance. Use of EMS for patients with suspected MI may offer considerable opportunity for improvement in public health.

**1084-83 Open Chest Defibrillation: Biphasic Versus Monophasic Waveform Shocks**

Yi Zhang, Ray Davies, William J. Coddington, Janice Jones, Richard E. Kerber. University of Iowa, Iowa City, IA

Background: Transoxic biphasic waveform shocks require less energy to terminate ventricular fibrillation (VF) compared to monophasic shocks. However, the effectiveness of biphasic shocks for intraoperative open chest epicardial defibrillation has not been established. Our purpose was to compare biphasic vs. monophasic shocks for open chest defibrillation, using a porcine model. Methods: Twenty-five adult swine (15-25kg) underwent a midline sternotomy, VF was electrically induced. After 15 seconds VF, each pig in Group 1 (n=16) received in random order damped sinusoidal monophasic shocks and truncated exponential biphasic shocks (3 mJ positive and 3 mJ negative) at 9 energy levels (3, 5, 7, 9, 11, 13, 15, 17 J) from large (44 cm) hand-held epicardial paddle electrodes. Pigs in Group 2 (n=9) received similar shocks from small paddle electrodes (16 cm²). Four shocks at each energy level were delivered to construct energy vs. success curves. Results: There was no significant difference in shock success between damped sinusoidal monophasic and biphasic waveform shocks at any energy level in Group 1 (large electrodes). In Group 2 (small electrodes), swine receiving biphasic shocks demonstrated a significantly higher shock success than those receiving monophasic shocks at 7 J (p<0.05), and there was a trend (p=0.06) in favor of biphasic shocks at 10 J and 12 J. Conclusion: With small paddle electrodes, biphasic waveform shocks demonstrated a higher shock success rate compared to monophasic waveform shocks at mid range energy levels. With large paddle electrodes, biphasic and monophasic shocks were equally effective. Shocks given from small paddle electrodes may result in an incongruous electrical field, allowing the superiority of the biphasic waveform to be evident, % Success Comparison. Mean ± SE: BIP = 0.05 vs. monophasic in small electrode group.
Background: ST segment monitoring by the continuous 12-lead electrocardiogram (ECG) has been a useful tool for the classification of recurrent ischemia in patients (pts) with unstable angina (UA). Additionally, high levels of C-reactive protein (CRP) have been associated with an unfavorable outcome in these pts. However, the possible relation of CRP levels with the incidence and severity of recurrent ischemia in pts with primary UA was defined as a transient ST-segment depression or elevation in any lead of at least 0.10 mV compared with the reference ECG, lasting for at least 1 min. Ven blood samples for plasma CRP values determination were obtained on admission. Pts were classified into three groups A, B, and C according to the tertiles of plasma CRP values. (Mean value of plasma CRP: Group A (4 pts)=0.65±11, Group B (37 pts)=1.78±0.43, Group C (54 pts)=5.16±6.64 mg/dL). Results: Twenty-six out of 111(23.4%) patients had at least one ST ischemic episode (6, 8 and 12 pts for the A, B, and C groups respectively, p=0.11). However, the group C pts had significantly more ischemic episodes per patient than the group B (5.75±1.1 vs. 2.50±1.1, p=0.03) and than the group A (3.75±1.1 vs. 1.67±0.5, p=0.001) pts. Additionally, the total duration of ST ischemic episodes was significantly higher in the group C than the group B (56.4±18.27 min vs. 35.12±23.01 min, p=0.04) and than the group A (56.4±18.27 min vs. 19.50±11.24 min, p=0.001). Conclusions: Plasma levels of CRP could predict the total recurrent ischemic burden in pts with UA. Plasma CRP levels on hospital admission may serve as an affordable and widely available marker for the detection of pts with silent or obvious recurrent myocardial ischemia. These pts could benefit from more aggressive pharmaceutical or invasive treatment.

1085-86 
Inflammatory Markers in Patients With Acute Coronary Syndromes Suppressed by Alphatocopherol: Evidence From a Randomized Controlled Trial

R T. Murphy, J B. Foley, N McCarthy, K S. Lee, P Drenan, M J. Walsh. Department of Cardiology, St James’s Hospital, Dublin, Ireland

Background: The acute phase proteins C-Reactive Protein (CRP) and Interleukin-6 (IL-6) have been shown to elevate in Acute Coronary Syndromes (ACS) and are associated with an adverse prognosis. Cell Adhesion Molecules are transmembrane glycoproteins which mediate leukocyte/endothelial binding, and are elevated in ACS. Alphatocopherol has extensive antiinflammatory properties. In a double blinded placebo controlled trial, we set out to determine the antiinflammatory effects of alphatocopherol on patients presenting with ACS. Methods: 110 patients presenting with ACS were randomized to alphatocopherol 400 IU or matching placebo daily for 6 months. Serum samples were drawn at presentation 2, 4, and 6 months. CRP was measured by high sensitivity nephelometric assay. IL-6 and the adhesion molecules soluble Vascular Cell Adhesion Molecule-1(sVCAM-1), soluble Intercellular Adhesion Molecule-1(sICAM-1), soluble E-Selectin, soluble P-Selectin, were measured using enzyme linked immunosorbent assay (ELISA) and flow cytometry. Results: CRP levels were significantly lower in the alphatocopherol group by 190% (4.6±2.4 vs. 0.4±0.2 mg/dL, p<0.001). Mean IL-6 levels in the alphatocopherol group remained unchanged (17.64±4.4 vs. 10.8±2.8 pg/mL, p=0.05). Mean sVCAM-1 levels in the placebo group increased (32.3±7.9 vs. 33.4±4.3, p=0.05). Mean sIL-6 in the placebo group increased by 110% (4.9±1.2 vs. 9.0±1.0, p<0.001). Changes in the levels of CRP, IL-6, and the adhesion molecules were significantly lower in the alphatocopherol group compared to the placebo group. Conclusions: Alphatocopherol significantly suppresses CRP, IL-6, and cell adhesion molecules levels in patients with ACS, providing further evidence of the antiinflammatory effect of alphatocopherol in ACS.

1086-87 
The Leukocyte Count Predicts Future Cardiovascular Events in Patients With a Past Myocardial Infarction


Background: Increasing evidence is accumulating implicating inflammation as a risk factor for coronary artery disease. We thought to determine whether the leukocyte count is associated with an adverse prognosis. Cell Adhesion Molecule-l J;VCAM-l, soluble Intercellular Adhesion Molecule-l (slCAM-1), soluble E-Selectin, soluble P-Selectin, were measured using enzyme linked immunosorbent assay (R+D,UK) and alphatocopherol and lipid levels measured by high performance liquid chromatography. Results: The mean CRP level fell in the alphatocopherol group (from 19.5±3.6 to 5.6±0.4 pgl ml, p<0.001) whereas levels of IL-6 fell nonsignificantly in the placebo group (17.9±2.7 to 15.9±2.5, p=0.2). There was no significant difference in soluble Cell Adhesion Molecule-1 levels between treatment groups. Flow cytometric analysis failed to show inhibition of the monocyte adhesion molecule ligands Mac-l and VLA-4. Conclusion: In patients with ACS, alphatocopherol suppressed the expression of CRP and IL-6. These observations may be of clinical relevance and justify reassessment in a larger clinical trial
1085-39 Heart-Type Fatty Acid-Binding Protein Is More Useful Than Cardiac Troponin T and CK-MB Isolforms for Risk Stratification in Patients With Acute Coronary Syndrome Within 2 Hrs After Onset of Chest Pain

Junichi Iishi, Masanori Nomura, Hiroki Nanbu, Yoshitaka Mori, Toshikazu Ando, Hiroshi Kurokawa, Takeshi Kondo, Yoshihiko Watanabe, Hitoshi Hishida. Fuji Health University, Sapporo, Japan

We have previously reported that heart-type fatty acid-binding protein (FABP) is a more sensitive and specific marker than myoglobin for the early diagnosis of acute myocardial infarction (AMI). To evaluate the utility of serum FABP for early risk stratification in patients with acute coronary syndrome (ACS), we prospectively studied 195 consecutive patients (mean age $\pm$ SD: 64 $\pm$ 11 yrs) admitted to CCU for ACS within 6 hrs (4.3 $\pm$ 2.6 hrs) after onset of chest pain. Serum levels of FABP were measured at admission, together with serum cardiac troponin T (cTnT) and plasma CK-MB isoenzymes (MB iso). The cTnT cutoff value was set at $>0.10$ ng/mL; FABP $>0.10$, TnT $>0.10$ ng/mL; MB iso, MB2 activity, 2.6 IU/L plus MB2/MB1. 1. Results: There were 114 patients with AMI and 81 with unstable angina pectoris (UAP). Twelve patients with UAP had cardiac events (1 death, 3 AMI and 9 UAP revascularization within 48 hrs after admission. The 126 high-risk ACS patients were defined as AMI or UAP with cardiac events. The high-risk ACS patients had significantly (p<0.0001) higher levels of FABP (0.10 $\pm$ 0.17 vs $>0.46$ ng/mL), TnT (1.86 $\pm$ 4.00 vs 0.10 ng/mL), MB activity (26.4 $\pm$ 20.9 vs 0.8 ng/mL), RIL activity (8.1 $\pm$ 8.9 vs 1.9 IUIL) and MB2/MB1 (3.0 $\pm$ 2.0 vs 1.2 $\pm$ 0.66) than patients without high-risk ACS. The sensitivity and predictive accuracy of FABP for the detection of the high-risk ACS in patients with ACS within 5 hrs after onset were higher than those of TnT (p=0.0001 and p<0.005) or MB iso (p=0.0018 and p=0.003) (Table 1). Conclusion: These findings suggest that FABP is a more useful marker than TnT and MB iso for early risk stratification in patients with ACS within 5 hrs after onset of chest pain.

*p<0.05, **p<0.01 vs FABP.

POSTER SESSION

1086 Fibrolytic Advances in the Treatment of Acute Myocardial Infarction

Monday, March 19, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1086-90 A Significant Infarct Related Stenosis After Successful Thrombolysis: Not Associated With Adverse Clinical Outcome but a Strong Predictor of Recoeassion

Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt, Peter C. Kievit, Marc A. Brouwer, Jan van den Bogaert, Johan Karreman, Freek W. A. Verheugt

Background: Routine angioplasty of a significant infarct related stenosis early after successful thrombolysis has not been proven superior to a conservative strategy with respect to recoloeassion related events as mortality and reinfarction. However, in $\geq$ 60% of patients recoloeassion occurs without these events while left-ventricular recovery is preserved. This analysis addresses the importance of a significant stenosis regarding clinical events and recoloeassion following an ischemia-guided revascularization strategy.

Methods: In the first Antithrombotic in the Precoce Revascularization (APRICOT) trial 248 patients had thrombolysis for suspected acute myo-
Thrombolysis for Acute Myocardial Infarction in Patients Older Than 75 Years: Lack of Benefit for Hospital Mortality but Improvement of Long-term Mortality: Results of the MITRA- and MIR-Registries

Arielle K. Gill, Reif Zahn, Harm Wienberg, Tobias Hoer, Steffen Schneider, Martin Gottsch, Martin Gottsch, Jason Oungoob, Christoff Goy. Herzgut Lohr, Germany

Background: Meta-analysis of large randomized trials has shown that thrombolysis for acute myocardial ST-elevation infarction (AMI) reduces 35-day mortality in patients (pts) 75 years by 1% which did not reach statistical significance. Recently published registry data even documented a lack of benefit for thrombolysis in AMI pts 75-79 yrs: Methods: We analyzed the prospective data of 6815 / 25194 (27%) unselected AMI patients 75 years of MITRA (Maximal Individual Therapy of AMI Registry) and MIR (Myocardial Infarction Registry) to identify the impact of reperfusion therapy on hospital and long-term outcome. We compared the results with those after AMI Results: Only 2145 (35%) of pts received acute reperfusion therapy, 1782 (27%) thrombolysis, 367 (5%) primary PTCA.

The main determinants of withholding reperfusion therapy in the elderly were increasing age per year (OR 0.90, 95% CI 0.89-0.92) and heart rate >100/min (OR 0.66, 95% CI 0.57-0.77). Hospital and long-term mortality were significantly lower in pts with Primary PTCA (0.39, 0.27-0.57) vs. thrombolysis (0.43, 0.20-0.93).

Conclusion: After correcting for baseline differences and presence of concomitant diseases thrombolysis for AMI did not influence hospital mortality but did influence long-term mortality. Primary PTCA 2.9 years significantly reduced even hospital mortality as well as long-term mortality (Table).

<table>
<thead>
<tr>
<th>Multivariable Analysis</th>
<th>Hospital Mortality OR, 95% CI</th>
<th>18-Months Mortality OR, 95% CI</th>
<th>Thrombolysis</th>
<th>Primary PTCA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>0.95, 0.81-1.12</td>
<td>0.58, 0.39-0.88</td>
<td>Primary PTCA</td>
<td>0.39, 0.27-0.57</td>
</tr>
</tbody>
</table>

Consensus: Acute thrombolysis for AMI did not influence hospital mortality in pts 75 yrs, but was associated with a 42% lower long-term mortality. In comparison, primary PTCA for AMI was associated with a 51% lower hospital mortality and an additional 56% lower long-term mortality in pts 76-79 yrs.

1086-04 Thrombolysis is Beneficial in Elderly Acute Myocardial Infarction Patients

Ulfr Stenestrand, Lars Wallentin, the RIKS-HIA group. Heart Center, University Hospital, Linköping. Sweden, Dept of Cardiology, University Hospital, Linköping, Sweden

Background: Recent reports have stated that thrombolysis would not be beneficial in acute myocardial infarction (AMI) patients 75 years and older. We sought to investigate whether this was true in an unselected Swedish AMI population. Methods: From the Swedish Register of Cardiac Intensive Care, which included every CCU admitted patient at 58 participating hospitals 1995-98, we studied 5,428 AMI patients 75 yrs or older admitted with presentation of chest pain. We performed a regression analysis evaluating the effect of thrombolysis regarding the combined variable cerebral bleeding and one-year mortality taking into consideration 26 factors known to influence survival such as cardiac background, medication, revascularization and comorisions. Results: There were 1,167 patients with cerebral bleeding complications in 2,445 patients receiving thrombolysis. The combined endpoint of cerebral bleeding plus death of any cause within one year proved to have a significant (p<0.001) lower incidence in the thrombolysis treated group 38.3% (698) compared to the conservative group 43.8% (960). Conclusion: Even though increased incidence of one-year mortality and cerebral bleeding complications in patients 75 years and older the total one-year mortality and cerebral bleeding complications significantly increased in the thrombolysis treated group. Thus clearly indicating that thrombolysis is indicated even in elderly patient with ST-elevation or non-ST-elevation AMI.

1086-05 Weight-Based Dosing of Thrombolysis: How Well Do We Estimate Weight? How Often Would This Translate Into Errors When Administration of Thrombolytic Drugs? A Comparison of Single-Bolus TNK With t-PA in TIMI 10B

Christopher P. Cannon, Michael Gibson, Sabrina A. Murphy, Carolyn H. McCabe. Brigham and Women's Hospital, Boston, MA

Weight-based dosing of thrombolytic drugs and heparin is recommended, notably for the elderly. Critical parameters of weight, sex and renal function are to be considered. However, patients more than 95 kg are not adequately described regarding the accuracy of estimated weight, or how often it would lead to a different dose of a thrombolytic drug. With weight-based dosing of TNK, dose increases with increments of 10 kg. For t-PA patients ECHO should receive a weight-based dose. Methods: We compared the estimated weight used in the Emergency Department vs. an actual weight obtained later in hospital in 780 patients in the TIMI 10B. We then compared the accuracy of dosing between accelerated t-PA and single-dose TNK in the TIMI 10B patients and 3235 patients in ASSENT I trials. Results: In TIMI 10B, patients underestimated their weight very well, RD=0.93, p<0.001. Among TNK patients only 0.4% had estimated weight 10 kg under actual weight, and only 4 (1.7%) was the estimated weight higher than actual. (Total only 2.1% error in weight estimation that would change the dose for TNK).

For the 320 t-PA patients, 6 (2%) were incorrectly estimated to weight 97.8 kg, and of these half received an incorrect weight-adjusted dose. In addition, 7 (2.5%) were incorrectly estimated to weight >67 kg, and all of them received a full 100 mg dose. (Total of 4.5% incorrect weight-adjusted dosing.) For TNK, in TIMI 10B and ASSENT I patients were randomized to receive a fixed dose of 50, 40 or 30 mg. Only 0.5% (10 of 2,012) of TAN patients received an incorrect dose. There was no difference in mortality or intracranial hemorrhage in TNK patients who received an incorrect dose.

Conclusion: Errors in estimating weight are uncommon, especially those that would lead to a dose change. Ongoing dosing of t-PA was extremely rare for TIMI in the TIMI 10B and ASSENT I trials, and no adverse outcomes were seen among patients who received an incorrect dose - suggesting a broad safety profile for the new single bolus agent TNK.
Conclusion: These results indicate that exogenous adenosine plays a significant role in the oxygen regulation of myocardial function in chronic ischemia and probably serves as a cardioprotector, especially during periods of repetitive stress. Aminophylline or a selective A1-receptor agonist adenosine A1 receptor agonist ATL-146e can be used to protect against ischemia-reperfusion injury and may be safer than theobromine in severe chronic ischemic heart disease.

Augmented Protein Expression of Neuronal Nitric Oxide Synthase in the Atrolysis Parasympathetically Decreases Heart Rate During Acute Myocardial Infarction in Rats

Yasuhito Takimoto, Takeshi Aoyama, Reiko Keyamura, Yoshiki Yuki, Shigetake Sasaki.
Kyoto University, Kyoto, Japan

Background: Vagal stimulation has been reported to be associated with prevention of ventricular fibrillation after myocardial infarction (MI). Nitric oxide synthesized within efferent paraganglionic neurons and released into the sarcolemma can be used to attenuate ICIC myoglobin mRNA and may be safer than theobromine in severe chronic ischemic heart disease.

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1087-99 Myoglobin Sustains Cardiac Function During Ischemia and Facilitates Oxygen Diffusion in the Beating Heart

Institut für Herz- und Kreislaufphysiologie, Heinrich Heine Universität, Düsseldorf, Germany

Background: Myoglobin, an intracellular oxygen binding heme protein is considered a key player in intracellular oxygen supply with three main functions: facilitating oxygen diffusion, serving as oxygen reservoir and mediating oxidative phosphorylation. The initial generation of myoglobin knockout mice (myo-/-) in our laboratory led to a surprisingly dramatic reduction in oxygen supply to the heart. Here we have explored the effect of acute carbon monoxide (CO) inhibition of myoglobin on isolated, Langendorff perfused hearts with hearts from myo-/- mice serving as appropriate controls. To closely mimic the in vivo situation, myoglobin oxygen saturation was measured in the beating heart utilizing 18F-fluorodeoxyglucose with arterial buffer-oxide conditions being adjusted according to preloaded arteriovenous oxygen content. Myoglobin inhibition resulted in a more pronounced functional decrease compared to wild type (wt) hearts (p<0.01). Significant decreases were found that acute CO inhibition led to decreased contractility (11% left ventricular developed pressure decrease in wt controls vs. no change in myo-/- hearts, p<0.01) and increased coronary venous pO2 (plus 25% in wt vs. no change in myo-/- hearts, p<0.01) and increased coronary venous pO2 (plus 25% in wt vs. no change in myo-/- hearts, p<0.01) and increased coronary venous pO2 (plus 25% in wt vs. no change in myo-/- hearts, p<0.01) and increased coronary venous pO2 (plus 25% in wt vs. no change in myo-/- hearts, p<0.01).

Conclusions: These results indicate that myoglobin parasympathetically decreases heart rate via the production of nitric oxide in rats with acute MI. Thus, augmented expression of myoglobin in the heart after acute MI reduces CO and may have beneficial effects on the heart by reducing CO consumption and preventing ventricular fibrillation.

1087-100 Administration of an Adenosine A2A Receptor Agonist (ATL-146e) Significantly Reduces Infarct Size in a Canine Model of Coronary Occlusion and Reperfusion


Background: The administration of a highly potent and selective adenosine A2A receptor agonist, ATL-146e, might improve myocardium from Ischemia-Reperfusion.

Methods: According to open-chest dogs underwent 90 minutes of total left anterior descending (LAD) coronary occlusion with subsequent collateral vessels flow, followed by 2 hours of reperfusion. Both core and heart surface temperatures were monitored and controlled to maintain a constant surface temperature (37°C). In a subset of these dogs
ORAL CONTRIBUTIONS

801 Featured Oral Abstract Session: Insights Into Myocardial Remodeling

Monday, March 19, 2001, 9:15 a.m.-10:30 a.m.
Orange County Convention Center, Valencia A

801-1 The Effect of Early Post-infarction Mitral Regurgitation on Late Ventricular Remodeling


Background: The Question Of How Post-infarction Mitral Regurgitation (MR) Affects Left Ventricular (LV) Function and Structures Is Not Completely Understood. We Studied Two Types Of Posterioral Infarctions In Sheep, One Which Produces MR And One Which Does Not, To Examine The Contribution Of Ischemic MR To LV Remodeling And Congestive Heart Failure (CHF).

Methods: Group A (n=5) had infarction of 25% of the LV mass localized to the posterior-lateral ventricle, resulting in a compensated infarction which did not lead to CHF. Group B (n=5) had infarction of 25% of the LV mass localized to the posterior-lateral ventricle and including the posterior papillary muscle, resulting in acute development of MR. Transesophageal echocardiograms were used to measure end-systolic (ES) LV and mitral annular plane systolic excursion (MAPSE) LV volume, as well as to assess the degree of MR. Results: In group A, no animal developed MR. In group B, LV ES volume increased by 71% over 8 weeks, and LV MAPSE decreased significantly from 2.05 at baseline to 0.45 at 8 weeks. In group B, the mean degree of MR immediately postinfarction was 3.7. The MR progressed to a mean of 3.2 ± 0.8 at 8 weeks.

In this group, ES LV volume increased by 140% over 8 weeks, and LV MAPSE decreased from 0.43 at baseline to 0.16 (p<0.05) at 8 weeks. At 8 weeks, the two groups had significantly different LV volumes and MAPSE (p<0.05). Conclusions: These results demonstrated that early postinfarction MR and leading to severe CHF.

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801-2 Macrophage-Colony Stimulating Factor (M-CSF) Induction in the Infarcted Myocardium Is Associated With Macrophage Differentiation and Proinflammatory Cell Markers in Risk Assessment and Management Decisions

Sundil Markad, Nathaniel Rischel, Deepak Sgroi, Walter J. Rogers, Christopher M. Kramer. Allegheny General Hospital, Pittsburgh, PA, University of Virginia Health System, Charlottesville, VA.

Background: Myocardial infarction is associated with a rapid induction of mononuclear cell chemoattractants, such as Transforming Growth Factor-β and Monocyte Chemotactic Protein 1 (MCP-1), in the infarcted area. Effective healing is dependent on survival and differentiation of infiltrating monocytes to macrophages. We hypothesized that the monocyte to macrophage differentiation factor M-CSF may be induced in the infarcted myocardium and may modulate monocyte phenotype. Methods: We used a canine model of myocardial infarction and an in vitro model of isolated canine mononuclear cells. Results: Using HLA-PhLe we identified a CLA+CD14+CD11c+ macrophage subset in infarcted myocardium after ischemic injury that was expressed in 5 of 6 patients and 5 of 6 controls. In vitro experiments showed that M-CSF induced expression of CLA and matrix metalloprotenase (MMP)-9 in isolated canine mononuclear cells. Conclusion: M-CSF may increase the differentiation of new myeloid cells. In contrast, after 7 days of reperfusion the number of newly recruited monocytes was significantly reduced.

801-3 Effects of Angiotensin II Receptor Blockade, Angiotensin II Type 1 Receptor Antagonism, and Their Combination on Postinfarction Ventricular Remodeling

Charlottesvik, VA

Sunil Mankad, Naikheinie Reichek, Deepak Singh, Walter J. Rogers, Christopher M. Kramer. Allegheny General Hospital, Pittsburgh, PA. University of Virginia Health System, Charlottesville, VA.

Background: The structural organization of the myocardial collagen network plays a major role in post-infarct remodeling and left ventricular (LV) dilation. We investigated the ability of the ETA receptor antagonist, AT-A (losartan 50 mg/day, n=13), or combination therapy with AT-A and ACEI (ACEI: Losartan 50 mg/day + losartan 50 mg/day, n=15). Magnetic resonance imaging (MRI) was performed before and 8 weeks after myocardial infarction to quantify changes in LV end-diastolic and systolic volumes indexed to body weight and cross-sectional area (BSA). Regional % intramyocardial circumferential shortening (%IS) in noninfarcted segments adjacent to the infarct (within 2 cm) was measured using tagged MRI. Results: Infarct size, mean systolic blood pressure, and left atrial pressure at 6 weeks post-infarction were similar between groups. Heart rate at 8 weeks post-infarction was significantly lower in the Control group compared to sACEI, hACEI, AT-A, or CT groups, respectively: 124±7, 102±19, 105±16, 111±12, and 107±7 (p<0.001). Baseline EF, ESV, EDV, and adjusted %IS were similar. CT resulted in the most marked blunting of LV remodeling compared to baseline.

801-4 Angiotensin II Receptor Antagonism: Comparison of Structural Remodeling of the Myocardium After Infarct in Stroke Prone Hypertensive Rats

Alexander Rademke, Qinggui Xia, Marc Dorenkamp, Susanne Perez, Christian Stolz, Harro Bittlinger, Rüdiger W.R. Simon and Thomas Unger. Clinic of Cardiology, University of Kiel, Kiel, Germany.

Background: The structural organization of the myocardial collagen network plays a major role in post-infarct remodeling and left ventricular (LV) dilation. We investigated the ability of the ETA receptor antagonist, AT-A (losartan 50 mg/day, n=13), or combination therapy with AT-A and ACEI (ACEI: Losartan 50 mg/day + losartan 50 mg/day, n=15). Magnetic resonance imaging (MRI) was performed before and 8 weeks after myocardial infarction to quantify changes in LV end-diastolic and systolic volumes indexed to body weight and cross-sectional area (BSA). Regional % intramyocardial circumferential shortening (%IS) in noninfarcted segments adjacent to the infarct (within 2 cm) was measured using tagged MRI. Results: Infarct size, mean systolic blood pressure, and left atrial pressure at 6 weeks post-infarction were similar between groups. Heart rate at 8 weeks post-infarction was significantly lower in the Control group compared to sACEI, hACEI, AT-A, or CT groups, respectively: 124±7, 102±19, 105±16, 111±12, and 107±7 (p<0.001). Baseline EF, ESV, EDV, and adjusted %IS were similar. CT resulted in the most marked blunting of LV remodeling compared to baseline.
with a negative troponin ≤ 0.1 "g/ml, the TIMI Risk Score identified a graded increase in the relative risk of the composite endpoint to 10 month follow-up (TRS 0, RR=1, TRS long-term mortality and ischemic events. Most importantly, however, among patients with cardiac events, debate has emerged about patients who are troponin negative. Are they all low-risk? We hypothesized that clinical risk factors can identify patients at high risk of subsequent events.

Methods: Plasma sample obtained at inclu-

Results: Conclusion:

Results concerning death or MI at 30 days

TnT Placebo Abc24 Abc24 Placebo Abc24 Abc48
Negative n=978 n=925 5.4% 8.6% 7.5% 8.5% 7.5%
Positive n=1328 n=1301 10.0% 8.1% 3.3% 8.6% 8.3%
TnT Placebo Abc24 Abc24 Placebo Abc24 Abc48
<0.1 ug/L n=1024 n=1090 5.3% 5.9% 6.0% 5.7% 6.0%
>0.1 ug/L n=1066 n=1094 9.7% 10.2% 11.7% 10.5% 11.7%

Conclusion: Both TRS and I were significant predictors of 6 month mortality. Their use in predicting benefit of a routine invasive vs. "selective invasive" strategies will be pre-

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821 Stable Ischemic Syndrome: Clinical Aspects

Monday, March 19, 2001, 11:00 a.m.-12:15 p.m.
Orange County Convention Center, Valencia A

821-1 Improvement in Health Status at 3 Months in the COURAGE Trial: Seattle Angina Questionnaire Results
William S. Weintraub, John Sperhac, Emil Vladar, Cheryl Lewis, Elizabeth Mainz, Parvati Hartigan, David J. Maron, Koon Teo, Paul Casperson, Karen Potter, Sandra B. Dunbar, Robert A. O'Rourke, William E. Boden. Emory University, Atlanta, GA; West Haven Veterans Administration Hospital, West Haven, CT

Background: The utility of percutaneous coronary intervention (PCI) to treat angina is being evaluated in COURAGE, a multicenter randomized trial in 3200 patients treated with best possible medical care and randomized to PCI vs medical therapy plus PCI. Methods: COURAGE includes a detailed health-related quality of life (QOL) study, with angina assessed using the Seattle Angina Questionnaire (SAQ). COURAGE also includes aggressive treatment goals for angina (angina free), blood pressure, exercise, diabetes control and lipid lowering, all according to ACC/AHA guidelines. The SAQ angina measured using the Seattle Angina Questionnaire (SAQ). COURAGE also includes domains for physical limitation, angina stability, angina frequency, treatment satisfaction and QOL. Scores can range from 0 to 100, with higher scores reflecting better status.

Results: Baseline and three month SAQ scores are available for the first 195 patients randomized in COURAGE.

821-2 Percutaneous Myocardial Laser Revascularisation (PMR): Is the Symptomatic Benefit Maintained to 2 Years?
Richard J. Allen, Simon R. Redwood, D. J. Coltart. Guy's and St Thomas' Hospital Trust. London, United Kingdom

Between May '98 and September '99, patients with Canadian Cardiovascular Society (CCS) Class III or IV angina were entered into a longitudinal study into the effects of PMR. All patients were unsuitable for more conventional methods of revascularisation. Method. PMR was performed on 27 patients (22 male) using the CardioGenesis PMR system. At follow up patients were assessed for CCS angina class, exercise treadmill testing (Naughton protocol) and completed the Seattle Angina Questionnaire to assess impact on quality of life. Nuclear myocardial perfusion scanning was performed at baseline and 6 months follow up. Results. Angina class improved from 3.45 +/- 0.3 (mean +/− SD) to 2.02 +/- 0.6 at 3 months (p<0.001). There was a significant class improvement in CCS angina (p=0.005) but only at 2 years when angina levels (3.16 +/- 0.6) were virtually returned to baseline (p=0.16). Exercise capacity increased from 342 ± 202 seconds to 470 ± 252 seconds at 3 months (p=0.001). The improvements were maintained to 1 year, 353 ± 232 seconds (p=0.01) but were again reduced at 2 years (p=0.8). Quality of life measures were significantly improved at 3 months (p<0.01) with the benefits maintained to 2 years (p=0.01). No significant improvements were detected on nuclear perfusion scanning at 6 months (p=NS). Conclusions. PMR offers hope to a group of patients who have little in the way of therapeutic options. Our findings suggest significiant initial symptomatic benefits lasting to 6 months, after which there is a gradual return in symptoms with no significant anginal improvement 2 years after the procedure. The findings are interesting with regards to the potential mechanism of action of PMR and call into question how worthwhile the treatment is long-term.
1117 Stable Ischemic Syndrome: New Mechanical Therapies

Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1117-76 Are the Initial Benefits of Enhanced External Counterpulsation Sustained at One Year?

William E. Lawson, John C. K. Hui, Elizabeth D. Kennard, Richard Holubkov, Sheryl F. Kaboly, SUNY Stony Brook, Stony Brook, NY, University of Pittsburgh, Pittsburgh, PA

Background: Enhanced external counterpulsation (EECP) has been shown to be a safe and effective treatment of angina in several small University hospital case series, with clinical benefits lasting up to 5 years in follow-up. However, there is no data on the long term effectiveness of EECP in routine clinical practice.

Methods: The International EECP Patient Registry (IPEP) was initiated in January 1990 at the University of Pittsburgh to sequentially track angina patients (pts) treated with EECP for up to 3 years across a broad spectrum of providers and practice settings. The registry records pt demographics, Canadian Cardiovascular Society (CCS) Angina class, adverse cardiovascular events (MACES-including; hospitalization, death, MI, MI, nonvascularization (PCI) and CABG)). The IEPF first year follow-up is analyzed.

Results: The IEPF includes 724 angina pts one year post-EECP, with completed follow-up available on 589 pts. Patients were predominately male (75%) with a mean age of 69 years. Pro treatment history was significant for: multivessel disease 77.6%, prior angioplasty 68.9%, prior CABG 56.4%, prior MI 62.6%, history of Congestive Heart Failure 26.1%. The pts received a mean 34 hours of treatment with 83% completing the full course of treatment. Events occurring during the treatment period included: unstable angina in 2.5%, MI in 0.4%, death 0.1%, CABG 0.5%, PTCA in 0.1%. CCS Angina class immediately post-EECP improved in 73.4% of pts and 61.6% of pts discontinued nitroglycerin use. The improvement in angina was maintained at 6 and 12 months (table). Cumulative MACE at 12 months included: death 0.0%, MI 4.2%, CABG 0.0%, PTCA 4.2%, cardiac hospitalizations 17.2% (mean number 1.6 and duration 5.5 days). By 12 mos, 22.8% of pts had undergone additional hrs of EECP treatment.

Conclusions: In a cohort of high risk cardiac pts, EECP produced immediate and sustained improvement in CCS angina class in the majority of pts with MACE comparable to historical treatment trials. EECP effect on CCS Angina Class

<table>
<thead>
<tr>
<th>Angina Class</th>
<th>Baseline</th>
<th>Immediate Post EECP</th>
<th>6 Mos Post EECP</th>
<th>12 Mos Post EECP</th>
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<tr>
<td>No</td>
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<td>17.8%</td>
<td>27.8%</td>
<td>34.1%</td>
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<td>I</td>
<td>64.4%</td>
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<td>30.8%</td>
<td>24.1%</td>
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<tr>
<td>III</td>
<td>46.9%</td>
<td>12.4%</td>
<td>9.9%</td>
<td>12.2%</td>
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<tr>
<td>IV</td>
<td>19.5%</td>
<td>5.3%</td>
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1117-78 Intervention for Stable Angina: A Multicenter Comparison of Consecutive Patients Undergoing Enhanced External Counterpulsation (EECP) and PCI

Richard Holubkov, Elizabeth D. Kennard, Sheryl F. Kelsey, Ozlem Soran, David R. Lawson, John C. K. Hui, Elizabeth D. Kennard, Richard Holubkov, Sheryl F. Kelsey, SUNY Stony Brook, Stony Brook, NY, University of Pittsburgh, Pittsburgh, PA

Background: Many patients with CAD and stable symptoms who are treated with EECP are also suitable for percutaneous coronary intervention (PCI). Assessment of EECP outcome in these pts requires comparison of risk profile as well as follow-up status in pts with comparable symptoms who undergo PCI.

Methods: We compared baseline presentation and one-year outcome in two international multicenter cohorts of consecutive pts with stable angina: 148 PCI candidates undergoing EECP (International EECP Registry) and 411 pts undergoing nonemergent PCI in the NHLBI Dynamic Registry.

Results: PCI candidates undergoing EECP were older with more previous intervention and higher risk profile:

Baseline Presentation

EECP (n=148) PCI (n=411)

Mean age *** 65.8 yrs 69.4 yrs

Prior PCI *** 16% 30%

Prior CABG *** 60% 31%

Prior myocardial infarction *** 38% 15%

History of congestive heart failure ** 17% 8%

History of diabetes *** 40% 22%

Baseline angina severity: CCS CC5 (n%) ** 13% of 0.001).

Conclusions: PCI candidates undergoing EECP for stable symptoms have a markedly higher risk profile than patients with stable angina who undergo PCI. While angina substantially more prevalent one year post EECP, more severe symptoms are reported relatively infrequently with each of the two treatments.

1117-101 Enhanced External Counterpulsation for Chronic Angina is Associated With Improved Outcome at 6 Months

Gregory W. Banister, Theresa Schrier, David H. Horries, Jr., Mayo Clinic, Rochester, MN

Background: There is a growing coalescence of ptsets with severe ischemic chest pain (CP) who are not amenable to traditional revascularization strategies. EECP is a non-invasive, outpatient treatment that promotes diastolic augmentation and may reduce angina symptoms. Methods: 35 pts with severe stable CCS angina class of 3 or 4 despite optimal medical therapy underwent 35-hr EECP treatments over a 7-week period. Clinical characteristics, symptoms and follow-up events were recorded at baseline, at the end of treatment, and at 3, 6 and 12 months. The DASI score, a prospectively validated, semiquantitative assessment of cardiovascular functional status, was measured via a self-administered questionnaire. Results: Pts were elderly (median 69 yrs), primarily men (83%), with a history of diabetes (31%), hypertension (78%), tobacco use (67%), heart failure (16%), MI (49%), PCI (69%) and CABG (26%). 4 pts had prior TMR (3) or heart transplantation (1). Adverse treatment effects included local skin irritation in 2 pts. Angina measures improved during treatment with persistent benefit to 6 months (below). Throughout treatment and follow-up there were 13 clinical events, including 4 CP hospitalizations without MI, 2 NQWMI, 1 CHF, 2 PCI and 1 CVA, but no deaths.

DASI Score

Median (25,75)<br>Pre-EECP 7.2 (4.1,13.5)<br>Post-EECP 15.2 (10.0,27.2) <0.0001

Conclusions: Non-invasive EECP treatment was associated with significant improvement in angina and functional status with few adverse effects in this high-risk cohort. These benefits were maintained at 6 months. Further evaluation of mechanism and longer-term durability of effect are warranted.

1117-102 Spinal Cord Stimulation for Refractory Angina Pectoris

Patients: Data on Clinical Outcome From the Prospective Italian Registry

F Di Pepe, G Guzzii, S Greco, G Rapi, M Romann, G Neri, A Ciraco, A Capuca, G Lanza, P Simion, GM Attisani, E Mansuri, M Magrini, M Ratiemis, G Degliortorio, A Collamati, Dept. of Medicine, Fatebenefratelli, Italy

The Prospective Italian Registry of Spinal Cord Stimulation (SCS) for severe refractory angina was designed to evaluate the immediate and long term clinical outcome of patients treated with SCS. From May 1998 to April 2000 87 patients (62 male, mean age 69 yrs) were implanted in 15 centers with an SCS II Medtronic device. All pts implanted were receiving up to 12 months. Results: baseline clinical characteristics: diabetes 24%, hypertension 47%, dyslipidemia 54%, CAD family history 24%, smokers 34%, mean duration of angina 7.6 yrs, CCS II 15%, CCS III 27%, CCS IV 58%, previous myocardial infarction 59%, CABG 47%, PCI 37%, mean EF 0.49, triple vessel disease 58%. Stimulation was biphasic in 80% and continuous in 18% of pts. The mean follow up duration was 7.2 months. Complications: pocket infections in 5 pts, lead dislocation in 1 pt, shoulder pain in 7.5% of pts. Clinical event rates remained low through 6 months. Further evaluation of mechanism and longer-term durability of effect are warranted.
the number of patients admitted to the hospital for angina decreased from 21.5 * 3.2 to 8.4 * 2.5. This decrease is useful in reducing the number of original attacks, the nitrate consumption and the rate of hospital admission.

POSTER SESSION

1118 Measurement of Infarct Size and Myocardial Protection
Monday, March 19, 2001, Noon-2:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 1:00 p.m.-2:00 p.m.

1118-78 Sonomicrometry Myocardial Tagging Quantifies Regional Remodeling After Anterior Infarction
Benjamin M. Jackson, Robert C. Gorman, Joseph H. Gorman, III, T. Sloan Guy, IV, Sina L. Moalineh, Theodore Pappapietro, Martin StJohn-Buston, L. Henry Edmunds, Jr., University of Pennsylvania School of Medicine, Philadelphia, PA

Background: The relative contributions of infarcted, borderzone (normally perfused but affected by myocardial infarction (MI), and remote myocardium to chronic left ventricular (LV) remodeling after myocardial infarction (MI) are unclear. Echocardiography and MRI cannot quantify regional dilatation because they depend on anatomic landmarks susceptible to distortion with remodeling or remodeling endsystolic geometry (coarsening) (SAL), which allow identification of discrete locations within the myocardium throughout the remodeling process, to assess regional remodeling after anterior MI. Methods: Anterior infarctions were performed in 6 sheep with placement of 16 epicardial SAL parallel transducers. Each transducer was connected to a SAL receiver (40 mm/min) and monitored for 30 min, 39 min, 99 min and 200 min post infarction, and cardiac chord lengths between SAL transducers were measured. Borderzone was assumed to be myocardium immediately adjacent to the infarcted zone but perfused which did not contract after infarction (as measured by SAL). Results: At 30 min, the anterior infarct significantly increased, the borderzone slightly, and the remote segments did not dilate. From 30 min to 99 min, all regions dilated at approximately the same rate. At 39 min Relative to Baseline Segment Length Baseline 20 min 39 min 48 min 7 weeks 5 weeks 8 weeks Net (8 wks) Remote 5% 6% 7% 10% 10% Significantly different between all pairs of groups (p<0.05). Significant difference between indicated group and “Remote” at same time point (p<0.05). Conclusions: These data show that while early LV dilatation in anterior MI is predominantly due to infarct expansion, chronic remodeling is the result of basal strain dilatation in all LV regions, including contractile segments. These results imply that mechanical stress is increased throughout the LV. The various determinants of wall stress likely act to differing degrees in each region. In the infarct, decreased wall thickness in myocardium adjacent to the infarct zone (but perfused) which did not contract after infarction (as measured by SAL).

1118-79 Cardioprotection After Experimental Myocardial Infarction in Stroke-Proenne Spontaneously Hypertensive Rats. Comparison Between Antihypertensive Treatment With ACE-Inhibitor, AT1-Receptor Antagonist and Combination Therapy
Alexander Thielen, Maria Dinhkhai, Quynh Quy, Marie Blattinger, Susanne Pensa, Christian Brösch, Rüdiger W.R. Jochum, Institute of Pharmacology, University of Kiel, Kiel, Germany; Clinic of Cardiology, University of Kiel, Kiel

Background: We compared the cardioprotective effects of the ACE inhibitor, fosinopril (Fos), the ANGIOT receptor antagonist, ibesartan (Irbe), and the combined therapy with both substances (Comb) after experimental myocardial infarction (MI) in male stroke-prone spontaneously hypertensive rats (SHRSP). Methods: To obtain strictly comparable experimental conditions, ischemic-reperfusion injury was induced in all groups via permanent occlusion of the left anterior descending coronary artery. Thrombolytic therapy was given to induction of MI and continued up to 6 weeks post MI. Sham operated and placebo-treated infarcted rats served as controls. We investigated mortality, systolic blood pressure to infarct size (ISP), MI, and cardiac dimensions, hemodynamics and myocardial collagen content. Results: In all investigated parameters, Irbe was significantly superior to Fos or Comb. Under treatment with Irbe, rats significantly showed the lowest mortality after MI and survived the longest. Moreover, Irbe improved dP/dtmax in infarcted rats to a 2.2 and 2.6 fold higher extent than with either Fos or Comb (p<0.001). Furthermore, myocardial collagen content six weeks after MI was 1.5 fold lower under Irbe treatment compared to Fos (p<0.001). Combination treatment exerted no synergistically beneficial effect compared to Irbe as a single drug treatment. Conclusion: When applied at equal antihypertensive doses, the cardioprotective effects of the AT1 receptor antagonist were significantly diminished in all parameters investigated when combined with an ACE inhibitor. The superior cardioprotection of Irbe could be explained by its lack of intrinsic sympathomimetic activity, second by lower myocardial catecholamine release and third by lowering incidence of fidel arrhythmias after MI.

1118-80 Bioosense NOGA Mapping for Detection of Myocardial Ischemia: Comprehensive Assessment in 74 Pigs

Introduction: Bioosense NOGA-mapping has been used to detect myocardial ischemia. This, however, is based on older software versions, small series, and limited experimental studies. The purpose of this study was to comprehensively and systematically evaluate NOGA maps as tool for myocardial ischemia detection. Methods: 87 normal and ischemic pigs were studied by NOGA mapping, and interpretation of endocardial study can detect hernia with reasonable accuracy. The average LLS L ischemic myo-

1118-81 No Impact of an ACE-Crosslink Cleaving Agent Found in Rat LV Infarct
Paul S. Hees, David E. Bush, Michelle H. Leppo, Edward P. Shapiro, Johns Hopkins University, Baltimore, MD

Background: The advanced glycation endproduct (AGE)-crosslink cleaving agent ALT-711 reduces vascular stiffness in animal models, and IS currently being studied in humans. However, the 10-differencing effect of the drug could not reduce cardiac remodeling and proteinuria after MI, expansion, a deleterious effect. Alternatively, new evidence suggests that the drug also muted the proliferative response to myocardial overload, i.e., has a neuro-hormonal effect analogous to that of ACE inhibition, which might improve post-MI remodeling. We therefore studied post-MI remodeling following ALT-711 in a rat model of MI.

Methods: 15 male Wistar rats weighing 400g were randomized to either group. Animals underwent thoracotomy and coronary artery ligation. Animals were then randomized to receive 2 mg/kg ALT-711 or saline per os daily for 30 days. Animals were sacrificed, and hearts were assessed for crosslink cleavage and proteinuria. Results: ALT-711 did not reduce cardiac remodeling and proteinuria after MI. Conclusion: ALT-711 is ineffective in reducing cardiac remodeling and proteinuria after MI.
Myocardial Infarct Size by a Kinin-Dependent Pathway

Astatin, a New Inhibitor of Aminopeptidase P, Reduces Myocardial Infarct Size by a Kinin-Dependent Pathway

Sebastian Wolffm, Andreas Dendner, Klaus Tempel, Geri Richardson. Medical Clinic I, University of Liibeck, Liibeck, Germany. Institute of exp. and clin. Pharmacology and Toxicology, University of Liibeck, Liibeck, Germany

Background: Inhibitors of the angiotensin converting enzyme (ACE) have been shown to exert their cardioprotective actions through a kinin-dependent mechanism. ACE is not the only kinin degrading enzyme in the rat heart. Since aminopeptidase P (APP) has been shown to participate in myocardial kinin metabolism to the same extent as ACE, in the present study we investigated whether inhibition of APP by its specific inhibitor astatin leads to a reduction in myocardial infarct size after acute ischemia and reperfusion. Methods: Atherosclerotic hypercholesterolemic rats were treated with astatin (1 mg/kg) or saline before ischemia, and rats receiving HOE 140 (0.5 mg/kg), a specific bradykinin-B(2)-receptor-antagonist, were pretreated 2 min prior to astatin. After reperfusion, myocardial infarct size (IS) was determined by tetracycline staining and expressed as a percentage of area at risk (AR). Results: As seen in Figure 1, IS/AR was significantly reduced in rats that received astatin (18 +/- 2% vs. 31 +/- 4%, p < 0.05) as compared with those receiving saline (40 +/- 2%) or apstatin plus HOE 140 (49 +/- 4%). Conclusion: Astatin reduces infarct size in an in vivo model of acute myocardial ischemia and reperfusion. Cardioprotection achieved by the new inhibitor of Aminopeptidase P is mediated by bradykinin, inhibition of other kininases than ACE could therefore open additional therapeutic strategies for the treatment of acute myocardial infarction.

NavH+ Exchange Inhibition Protects Ischemic Myocardium Independent of Potassium-ATP-Channels

Marie-Luise von Brüll, Claudia Strohm, Wolfgang Schober. Department of Experimental Cardiology, Max-Planck-Institute for Physiological and Clinical Research, Bad Nauheim, Germany

Background: It has been shown that several Na+/H+ exchange inhibitors protect against myocardial injury following ischemia-reperfusion. We investigated the role of an AP sensitive potassium (Kap) channel and of the Na+/H+ exchanger in apoptosis in a mouse model of myocardial ischemia and reperfusion. We have reported that BiBB significantly reduced infarct size (IS = infarct area / risk area) in ischemia (coronary occlusion) followed by reperfusion. We now investigated, whether the cardioprotective effect of BiBB is preserved during K+ / H+ channel blockade by glibenclamide.

Methods: Landrace pigs were treated with BiBB prior to left anterior descending artery (LAD) occlusion. BiBB in (Na+/Ca2+) was administered either intravenously at a dose of 1.5 mg/kg (n=4, group A) or 3 mg/kg (n=5, group B) for 15 min. The control group received only the solvent. BiBB was also given via intramyocardial injection into the myocardial ischemia reperfusion. We have reported that BiBB significantly reduced infarct size (IS = infarct area / risk area) in ischemia (coronary occlusion) followed by reperfusion. We now investigated, whether the cardioprotective effect of BiBB is preserved during K+ / H+ channel blockade by glibenclamide.

Methods: Landrace pigs were treated with BiBB prior to left anterior descending artery (LAD) occlusion. BiBB in (Na+/Ca2+) was administered either intravenously at a dose of 1.5 mg/kg (n=4, group A) or 3 mg/kg (n=5, group B) for 15 min. The control group received only the solvent. BiBB was also given via intramyocardial injection into the myocardial ischemia reperfusion. We have reported that BiBB significantly reduced infarct size (IS = infarct area / risk area) in ischemia (coronary occlusion) followed by reperfusion. We now investigated, whether the cardioprotective effect of BiBB is preserved during K+ / H+ channel blockade by glibenclamide.

Results: Treatment with BiBB significantly decreased IS (P<0.05) in group A and B when compared to the control group (35 +/- 3%, 40 +/- 7%, 42 +/- 1%, respectively). In group C and D a marked myocardial protection was shown by the pretreatment of viable (thiope- nitritetraethyl chloride stained) myocardium around microinjection needles delivering BiBB that was not seen around needles with solvent. Treatment with BiBB was associated with a decrease in myocardial phospho-p38-MAPK.

Conclusion: The preservation of the protective effect of BiBB722CL in the presence of glibenclamide suggests a survival pathway independent from the K+ / H+ channel but may be mediated by its effect on the phospho-p38-MAPK signal transduction pathway.
Background: We have previously shown the immediate efficacy of intact excision surgery (IE) for reducing left ventricular (LV) volumes and increasing ejection fraction (EF) in patients with ischemic cardiomyopathy using real-time three-dimensional echocardiography (RT3DE). The purpose of this study was to evaluate whether this benefit persists after the surgery during a mid-range follow-up.

Methods: Forty-six patients (mean age 63 ± 9 yr) who had undergone IE surgery were studied. The surgical procedures included intact excision, coronary bypass and mitral valve repair (in 27 patients) when associated with significant mitral regurgitation (MR). Transesophageal RT3DE was performed before IE, before discharge (average 7±4 days after IE) and during follow-up (average 9±2 months). The LV volumes were determined using multi-passes after an axial plane slices with Simpson’s method.

Results: No significant MR was found after the IE surgery. LV end-diastolic (EDV) and EDV x 100) and forward stroke volume (FSV) (FSV = EDV-ESV-MR volume) significantly increased before the discharge after the IE surgery. At the average 9-month follow-up, LV EF and FSV remained higher than before IE. LV volumes remained lower (164 ± 56 ml for EDV and 97 ± 40 ml for ESV, with p > 0.05) in 38 patients. But 8 patients showed recovered LV dilation (~50% in comparison with that before discharge) (Table).

Conclusion: RT3DE demonstrated sustained benefit in LV ejection fraction and forward stroke volume in patients undergoing IE surgery after a follow-up of 9 months.

**1110-87**

**Beta-Blocker Attenuates the Development of Intramural Small Coronary Vessel Disease in Chronic Hibernating Myocardium Subtending a Severe Epicardial Coronary Stenosis**

Huanshen Hong, Sergi Aksenov, Joseph Marak, John Fallon, David Waters, Chingkuang Chen.. Newark Beth Israel Medical Center, Newark, NJ

Recovery of LV dysfunction after revascularization is often associated with both incomplete and delayed remodeling. We have previously shown that chronic myocardial ischemia induces significant wall thickening of intramural small coronary vessels with reduced lumen, preventing complete restoration of myocardial perfusion flow state. Our results indicate that the hypothesis that a beta-blocker attenuates wall thickening and lumen narrowing of small vessels distal to epicardial coronary stenoses (CS), we studied 21 pigs in 3 groups: Group 1: pigs with 4-week severe proximal LAD CS to reduce coronary flow (CF) by ~80% with LV dysfunction; Group 2: pigs with severe CS as in Group 1 + metoprolol (100 mg x 2/day) for 4 weeks; Group 3: 6 pigs as controls. The purpose of this study was to evaluate whether this benefit persists after discharge after the IE surgery. LV EF and FSV remained higher than before IE. LV volumes remained lower (164 ± 56 ml for EDV and 97 ± 40 ml for ESV, with p > 0.05) in 38 patients. But 8 patients showed recovered LV dilation (~50% in comparison with that before discharge).

**Results**: Significant wall thickening of small intramural vessels with reduced luminal diameters was found in Group 1 (WTa=17.2±3.2 µm, WTa/LDa=1.34±0.15) and in Group 2 (WTa=13.5±1.5 µm, WTa/LDa=0.38±0.03) compared to controls (WTa=6.8±2.5 µm, WTa/LDa=0.34±0.03), both p < 0.05. Metoprolol significantly reduced WTa with increased LDa in Group 2 compared to Group 1 (both p < 0.01).

**Conclusion**: Chronic myocardial ischemia induces significant arterial wall thickening with reduced vessel lumen in small intramural coronary vessels. Beta-blocker attenuates wall thickening, but did not completely prevent, the development of this small vessel disease in chronic ischemia, hibernating myocardium distal to epicardial coronary stenosis. Thus, the preoperative administration of a beta-blocker may improve the improvement of myocardial perfusion flow state after revascularization via this mechanism.

**1110-88**

**Relative Advantage of a Comprehensive Logistic-Regression Model for Preoperative Estimation of the Risk of Aortocoronary-Bypass Surgery**

Alan D. Barnstain, Victor Parsonnet. Newark Beth Israel Medical Center, Newark, NJ

**Background**: Risk-adjusted outcome evaluation of aorto-coronary-bypass surgery is an important procedure to determine the quality of outcome at institutional, hospital, and physician levels, and in discussions with patients who are considering surgery as a possible therapeutic option. Several existing logistic-regression models used for this purpose incorporate only a limited number of preoperative risk factors, overlooking (and leading to absent) many factors that in individual patients may increase the likelihood of operative mortality. Methods: We developed a logistic-regression model (ROC area 0.792) comprising 56 distinct risk factors and 39 covariables from data on 14,246 isolated aorto-coronary-bypass procedures performed at 13 New Jersey hospitals in 1996 and 1997. This dataset, in which more liberal standards of statistical significance were accepted, was compared with previously published 9 factors, 13 covariates model (ROC area 0.781) derived from an earlier version of the same dataset. Results: Risk-adjusted mortality rates (RAMRs) derived from the comprehensive model were more consistent with observed mortality rates. In contrast, the 9-factor model underestimated the operative risk seriously in half of the 30% of patients with >4 risk factors (see plots), giving those 2,408 patients an erroneously inflated and potentially misleading RAMR (2.81%, vs. 3.20% with the 25-risk-factor model). Conclusion: A risk-stratification model that incorporates many objective, reliably determined risk factors allows risk stratification that is faster and closer to reality than a more limited model can provide. The limited model was specifically detrimental to surgeons who treated many high-risk patients. RAMRs calculated using a more complete model do not penalize hospitals or surgeons that accept high-risk patients.
1120-91 Acute Myocardial Ischemia and Alternative Diagnoses in Low-Risk Patients for Coronary Event Presenting to the Emergency Department

Alberto Corti, Barbara Paladini, Maurizio Zanobetti, Stefano Grifoni, Stefania Sartini, Sabrina Maseth, Chiara Gallini, Paolo Ferri, Egidio Costanzo, Maria Matteini, Giacomo Trallori. AZIENDA OSPEDALIERA CAREGGI, FIRENZE, Italy

Background: The evaluation of patients with chest pain (CP) and non-diagnostic ECG does not often lead to the exclusion of acute coronary events. Thus, the underlying presence of depression and gastrointestinal disease is often neglected and of unknown proportions. In this study, we addressed this issue in a population of 214 consecutive patients presenting at the Emergency Department with chest CP and non-diagnostic ECG. Methods: All patients had CP lasting >10 minutes within 24 hours before admission, and a negative first line evaluation based on serial ECGs, cardiac enzymes, echocardiography and chest X rays. Patients underwent real-time SPET (3 hours) from CP and exercise-SPET (>3 hours) followed by coronary angiography when positive. All patients without documented coronary artery disease, underwent: 1) psychiatric screening using the Hospital Anxiety and Depression Scale questionnaire (HADS); all patients with a HADS score >8 were submitted to psychiatric interview for final diagnosis, according to the Diagnostic and Statistical Manual IV. 2) gastrointestinal endoscopy. Results: Of the 214 patients, 27 patients (13%) had documented coronary artery disease and 74 patients (35%) had CP of parietal origin. Among the remaining 84 (n=113 patients), HADS >8 was found in 54 patients (25%) and depression or panic disorders were detected in 22 patients (10%). Gastrointestinal pathology was documented in 59 patients (27%; peptic ulcer and HD in 17% and esophageal reflux in 10% of patients). Conclusions: In one half of patients with non-diagnostic ECG, chest pain was associated with psychiatric or gastroesophageal disorders that usually may be grossly under-recognized.

1120-92 Predictors of Heart Failure Development After Non-ST Elevation Acute Coronary Syndromes

Eric J. Velazquez, Douglas A. Crane, David Hasdai, Robert M. Califf, Robert A. Harrington. Duke University, Durham, NC

Heart failure (HF) after ST-segment elevation acute myocardial infarction portends a worse prognosis. Most patients with an acute coronary syndrome (ACS) present with or without acute coronary events. Thus, the underlying presence of depression and gastrointestinal disease is often neglected and of unknown proportions. In this study, we addressed this issue in a population of 214 consecutive patients presenting at the Emergency Department with chest CP and non-diagnostic ECG. Methods: All patients had CP lasting >10 minutes within 24 hours before admission, and a negative first line evaluation based on serial ECGs, cardiac enzymes, echocardiography and chest X rays. Patients underwent real-time SPET (3 hours) from CP and exercise-SPET (>3 hours) followed by coronary angiography when positive. All patients without documented coronary artery disease, underwent: 1) psychiatric screening using the Hospital Anxiety and Depression Scale questionnaire (HADS); all patients with a HADS score >8 were submitted to psychiatric interview for final diagnosis, according to the Diagnostic and Statistical Manual IV. 2) gastrointestinal endoscopy. Results: Of the 214 patients, 27 patients (13%) had documented coronary artery disease and 74 patients (35%) had CP of parietal origin. Among the remaining 84 (n=113 patients), HADS >8 was found in 54 patients (25%) and depression or panic disorders were detected in 22 patients (10%). Gastrointestinal pathology was documented in 59 patients (27%; peptic ulcer and HD in 17% and esophageal reflux in 10% of patients). Conclusions: In one half of patients with non-diagnostic ECG, chest pain was associated with psychiatric or gastroesophageal disorders that usually may be grossly under-recognized.

1120-93 Prognostic Significance of Conduction Disorders Complicating Acute Myocardial Infarction in the Elderly

Gail S. Rathore, Bernard J. Garsh, William J. Detten, Allan J. Solomon. Massachusetts General Hospital, Boston, MA

Background: Among patients with acute coronary syndromes (ACS), prior conduction disorders are common in patients presenting with acute myocardial infarction (MI), patient characteristics and outcomes remain poorly defined in this elderly population. Methods: We enrolled 106,720 Medicare beneficiaries age 65 years and older who presented with MI between 1994 and 1996. Subjects who were not transferred during hospitalization with valid electrocardiographic data were evaluated to determine the presence of right bundle branch block (RBBB), left bundle branch block (LBBB), left anterior fascicular block (LAFB), right anterior fascicular block (RAFB), left posterior fascicular block (LPFB), or bifascicular block (BiF) at time of admission. The influence of RBBB, LBBB, LAFB, and BiF on mortality was evaluated by logistic regression modeling of 30-day mortality and 60-day and hospital mortality and Cox proportional hazards modeling of long-term mortality (mean follow-up = 575 days).

Results: 22,181 (20.8%) subjects had a conduction disorder documented at admission: 7,878 (7.3%) presented with LBBB, 6,410 (6.0%) with RBBB, 6,426 (6.1%) with BiF, and 2,657 (2.5%) with BiF. Patients with conduction disorders had a higher crude in-hospital (LBBB 22.4%, RBBB 26.6%, BiF 24.6%, FAS 18.3%, no disorder 16.8%, p < 0.001), 30-day (LBBB 36.7%, RBBB 90.0%, BiF 50.0%, FAS 23.9%, no disorder 10.9%, p < 0.001), and one-year (LBBB 49.9%, RBBB 45.6%, BiF 46.8%, FAS 37.2%, no disorder 53.9%, p < 0.001) mortality. Multivariable adjustment for patients' clinical and demographic characteristics confirmed higher risk of 30-day mortality among patients with LBBB (HR 1.09, 95% CI 1.03, 1.15), RBBB (HR 1.28, 95% CI 1.23, 1.32), FAS block (HR 1.04, 95% CI 0.98, 1.10). Similar findings were obtained for risk of long-term mortality among patients with LBBB (HR 1.29, 95% CI 1.22, 1.35), RBBB (HR 1.24, 95% CI 1.20, 1.30), and BiF (HR 1.24, 95% CI 1.18, 1.30). FAS block had limited prognostic significance at long-term follow-up (HR 1.04, 95% CI 0.90, 1.08).

Conclusion: Conduction disorders are a common complication of MI in elderly patients. Left bundle, right bundle, and bifascicular blocks are associated with increased short- and long-term mortality, whilst a solitary left-axis block is not of prognostic significance.
1121-97 Frequency and Clinical Significance of Angiographic Evidence of Distal Embolization During Primary Angioplasty for Acute Myocardial Infarction

Felix Zijlstra, Jan Paul Ottervanger, Merko Jan de Boer, Henk Eemhuis, Dirk Dijkstra, Jan C. A. Hoertjie, Harry Suryapranata, Arnoud W. J. van’t Hoff, Aalt Kluin, John M. van Remoortel, Hoag Garland, UCSF, San Francisco, CA

Background: Although recognized as an important feature of atherothrombotic coronary disease, little is known about the frequency and prognostic importance of distal embolization during primary coronary angioplasty. Methods: As part of a randomized trial of thrombolysis versus primary angioplasty, 194 patients with acute myocardial infarction were treated with primary angioplasty. Of these, the patients were treated with intracoronary nitrates or eptifibatide. Clinical information was collected for a mean of 5 years. Embolization was defined as a distal filling defect with an abrupt cutoff in 1 of the peri-infarct coronary artery branches of the infarct-related vessel. Results: Distal embolization was present in 27 patients (14%). Mean ejection and gendar were not different between the two groups. Patients with a small atheroma had a larger myocardial steal size (mean L/DQ 0.212 ± 0.106 < 0.03) and a lower left ventricular ejection fraction at discharge (42% ± 51%, p < 0.01). Long-term outcome was significantly higher in patients with distal embolization (44% vs. 9%, p < 0.001). Conclusions: Distal embolization during primary angioplasty significantly affects the coronary microcirculation, and a larger myocardial steal size and low left ventricular ejection fraction at discharge are independent predictors of distal embolization. Additional pharmacologic interventions and mechanical devices should be studied to prevent distal embolization.

1126-98 Use of a Protection Device Offsets the Delay in Recovery of Angiographic Parameters in Primary PTCA

Omar Kadi, F. Wolfgang Absarren, Sabina Murphy, C. Michael Gibson, University Hospital Zürich, Zurich, Switzerland, UCSF, San Francisco, CA

Background: There is evidence that prolonged symptom-onset-to-balloon time (SBT) for primary PTCA is associated with an increased mortality and lower rates of TIMI flow grade (TFG) 3, in particular with stenting. Possibly, stent-related artifacts may have contributed to decrease myocardial perfusion in TFG 2 vs TFG 3. The goal of this study was to compare the kinetics and appearance of myocardial perfusion in TFG 2 vs TFG 3 in patients treated with primary angioplasty. Results: Patients were divided according an arbitrary cut-off of 4 hours in two groups with fast (SBT < 4 h, n = 12, group 1) or delayed (SBT > 4 h, n = 15, group 2). Groups were comparable with respect to age, gender, hemodynamic, pattern of the infarct vessel (LAD: 25% and 25%, respectively), ejection fraction, and use of glycoprotein IIb/IIIa-inhibitors (75% and 75%, respectively). An angiographic core analysis assessed pre-post TFG, corrected TIMI Frame Counts (CTFCs) and tissue level perfusion (TIMI Myocardial Perfusion Grades; TTPG) Results: Group 1 Group 2 p-value

SBT in min (range) 193 ± 50 (85–240) 472 ± 157 (250–740) 0.0001
TFG pre/post 0.0 ± 0.2 0.0 ± 0.2 0.01
CTFC pre/post 100 ± 25 ± 10.8 100 ± 22 ± 6.2 n.s/n.s
TTPG pre/post 0.6 ± 0.2 0.0 ± 0.2 0.7 ± 0.1 0.0 ± 0.1 n.s/n.s
(mean ± SD; p for unpaired comparison between the groups)

Conclusions: In this pilot study, the recovery of epicardial and myocardial perfusion is equally impaired in test and delayed reperfusion using distal embolization protection in PCI with stenting for acute MI. Clinical benefit and survival advantage need to be determined in adequately designed trials.
function. The findings have been confirmed by the Kaplan-Meier approach. Conclusions. The results of the present study confirm the pivotal role of ACEI for the treatment of patients with diabetes. They also suggest that the benefit of ACEI in patients with diabetes is strictly related to active drug treatment that should be maintained irrespective of post-MI LV function.

ORAL CONTRIBUTIONS

831 New Management Concepts of Acute Coronary Syndromes

Monday, March 19, 2001, 2:00 p.m.-3:30 p.m.
Orange County Convention Center, Room 230D

831-1 Stunng Reduction in Death and Myocardial Infarction Observed With Early Lipid Lowering Therapy After Acute Coronary Syndromes
Herbert D. Aronow, Penny L. Houghtaling, Katherine E. Wolski, Eric J. Topol, Michael S. Lauer. Cleveland Clinic Foundation, Cleveland, OH

Background: Whether lipid lowering agents (LLA) reduce death or myocardial infarction (MI) when administered soon after an acute coronary syndrome (ACS) is unclear.

Methods: We compared the incidence of death and MI if offered for admission to ST elevation-MI, non-ST elevation MI or unstable angina among patients from the CUS50O IIib and PURSUIT trials who were (n=3,653) or were not (n=17,156) discharged on LLA. A propensity analysis was used to match patients on the probability of receiving LLA at discharge. The results of the present study confirm the pivotal role of ACEI for the treatment of patients with diabetes. They also suggest that the benefit of ACEI in patients with diabetes is strictly related to active drug treatment that should be maintained irrespective of post-MI LV function.

BACKGROUND: Whether lipid lowering agents (LLA) reduce death or myocardial infarction (MI) when administered soon after an acute coronary syndrome (ACS) is unclear. Conclusions: Our results provide further evidence of the benefit of early initiation of statin therapy in ACS.
The duration of AECG ischemia was also not different. Clinical events were also determined over 6 months of follow-up. Results: The sub-

mone therapy may not benefit postmenopausal woman with known coronary artery
do not reduce the number of ischemic events, or the proportion of patients experiencing such events in postmeno-

myocardial infarction, hospitalizations for recurrent angina, or need for revascularization

when added to standard anti-ischemic therapy, does not reduce the number or duration

tion (AMI) when high-doses of thrombolytic agents are used in the treatment of unstable

245 days.

831-6

Is Initial Treatment With Enoxaparin Beneficial in Unstable

Angina/Non-ST Segment Elevation Patients Who Later

Undergo Percutaneous Coronary Intervention (PCI)?

Keith A. A. Fox, Elliott M. Antman, Marc Cohen, Frederique Bigonzi, David Radley. On

behalf of the ESSENCE & TIMI 11B Investigators. The Royal Infirmary of Edinburgh, Edinburgh, United Kingdom

Background. Combined analysis of ESSENCE and TIMI 11B demonstrated that enox-
aparin is superior to unfractionated heparin (UH) in patients with unstable angina (UA)/

non-ST-segment elevation myocardial infarction (MI): 7.1% vs 8.6% (p=0.02) during PCI at

43 days. Decisions to proceed to recanalization were independent of trial randomiza-

Methods We analyzed a population comprising 6098 patients for death or MI at 43 days

using chi-squared tests; 835 patients undergoing coronary artery bypass grafting were

excluded. UH was randomized to enoxaparin vs UH (unfractionated heparin).

Results PCI was not randomized but was performed at the discretion of the treating phy-
sician. Results are shown in Table 1.

Conclusion Patients undergoing PCI (compared with those who were not) experienced

more events, including events prior to PCI, consistent with a higher risk population. Enox-

aparin treatment, when compared with UHF treatment, benefited both treated groups

safety and efficacy, and those patients who underwent PCI following an initial period of med-

stabilization.

Table 1. Patients undergoing PCI within 12 hrs of final dose:

<table>
<thead>
<tr>
<th></th>
<th>UH</th>
<th>Enoxaparin</th>
<th>RR (95%CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with PCI:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death/MI post-PCI</td>
<td>14</td>
<td>237</td>
<td>5.9%</td>
</tr>
<tr>
<td>All Death/MI</td>
<td>25</td>
<td>237</td>
<td>10.5%</td>
</tr>
<tr>
<td>Patients without PCI:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death/MI</td>
<td>196</td>
<td>2783</td>
<td>7.0%</td>
</tr>
<tr>
<td>All patients undergoing PCI during hospitalization:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>UH n (%)</td>
<td>56</td>
<td>482</td>
<td>11.6%</td>
</tr>
<tr>
<td>Enoxaparin n (%)</td>
<td>43</td>
<td>424</td>
<td>10.1%</td>
</tr>
</tbody>
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POSTER SESSION 1150 Treatment Strategies for Cardiac Ischemic Syndromes

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.

Orange County Convention Center, Hall A

Presentation Hour: 4:00 p.m.-5:00 p.m.

1150-79 TIMI Risk Score to Predict 6-Month Mortality, Recurrent Cardiac Events, and Relative Benefit of Invasive vs. Conservative Strategy in Patients With Unstable Angina: Results From TACTICS-TIMI 18

Christopher P. Cannon, William S. Weintraub, Laura Demopoulos, Peter D’Iribarne, Debbie Robertson, Paul deLucca, Carolyn H. McCabe, Elliott M. Antman, Eugene Braunwald, for the TACTICS-TIMI-18 Investigators. Brigham and Women’s Hospital, Boston, MA

The Thrombolysis In Myocardial Infarction (TIMI) Risk Score for acute coronary syn-
dromes has been shown in several studies to predict both prognosis and response to

new therapies such as low-molecular weight heparin or glycoprotein IIb/IIIa inhibitors. We

sought to validate the TIMI Risk Score and assess its usefulness in predicting benefit of

an invasive vs. conservative strategy. Methods: In the TACTICS-TIMI-18 trial trials with

unstable angina or non-ST elevation MI were treated with aspirin, heparin and
tirofiban and randomized to an invasive strategy with routine catheterization and ravascu-
aparin is superior to unfractionated heparin (UFH) in patients with unstable angina (UA)/

non-Q wave myocardial infarction remarkably

syndromes is associated with a statistically significant reduction in short term mortality.
there was no difference in composite events (HR=1.1; P=0.6), mortality (HR=0.7; 920 pts were randomized to either an IG strategy (n=458) or a R-INV strategy (n=462). We also compared the three-year survival of diabetic coronary bypass graft surgery in the IG (80% versus 80%) and R-INV (80% versus 80%) groups. Conclusion: The TIMI Risk Score was a significant predictor of 6-month mortality, and recurrent cardiac events. Its use in predicting benefits of a tailored approach or selective invasive strategies will be presented.

**1150-00 Percutaneous Coronary Intervention Versus Coronary Bypass Graft Surgery: Outcome of Diabetics in the AWESOME Randomized Trial and Registry**

Steven P. Edelsit, Douglas A. Morrison, Gulshan Sethi, Jerome Sacks, William Henderson, Frederick Grover, Rick A. Esposti, for the investigators and patients of VA cooperative #385 (AWESOME). New York VA Medical Center, New York, NY.

**Background:** Prior studies indicate that coronary bypass graft surgery may be superior to percutaneous coronary intervention for diabetes, but coronary bypass graft surgery has not been previously compared to percutaneous coronary intervention for diabetics at high risk for surgery. This study compares the three-year survival of diabetic coronary bypass graft surgery versus percutaneous coronary intervention in patients with medically refractory unstable angina and three-vessel severe left main disease or previous severe angina without heart surgery; myocardial infarction within 7 days; left ventricular ejection fraction <35%; age >70 years; intracoronary balloon required to stabilize) percutaneous coronary intervention in 545 patients in the AWESOME randomized trial, 144 (92%) had diabetes; of the 957 in the patient-refused registry, 82 (87%) had diabetes, and of the 1600 patients in the population assignment registry, 552 (35%) had diabetes. Results: 12-month death or non-fatal MI (87%) had diabetes, and of the 1600 patients in the population assignment registry, 552 (35%) had diabetes. Results: 12-month outcomes were similar in patients (pts) randomized to either a coronary bypass graft surgery (CABG) or a percutaneous coronary intervention (PCI) strategy. Conclusion: The TIMI Risk Score was a significant predictor of 6-month mortality, and recurrent cardiac events. Its use in predicting benefits of a tailored approach or selective invasive strategies will be presented.

**1150-BT Comprehensive Analysis of Death and Nonfatal Myocardial Infarction During the First Twelve Months Following Acute Non-Q-Wave Myocardial Infarction: Comparison of Invasive Versus Conservative Strategies in the VA Non-Q-Wave Infarction Strategies In-Hospital (VANQWISH) Trial**

Arnn K. Kolli, Michael J. Wade, Robert A. O'Rourke, Alvin S. Blaustein, William E. Boden. for the investigators and patients of VA cooperative #385 (AWESOME). New York VA Medical Center, New York, NY.

**Background:** The overall results of the VANQWISH Trial indicate that long-term (mean: 23 months; range: 12-44 months) clinical outcomes for the composite primary end point (death or non-fatal MI or myocardial infarction within 7 days; left ventricular ejection fraction <35%; age >70 years; intracoronary balloon required to stabilize) percutaneous coronary intervention in 545 patients in the AWESOME randomized trial, 144 (92%) had diabetes; of the 957 in the patient-refused registry, 82 (87%) had diabetes, and of the 1600 patients in the population assignment registry, 552 (35%) had diabetes. Results: 12-month outcomes were similar in patients (pts) randomized to either a coronary bypass graft surgery (CABG) or a percutaneous coronary intervention (PCI) strategy. Conclusion: The TIMI Risk Score was a significant predictor of 6-month mortality, and recurrent cardiac events. Its use in predicting benefits of a tailored approach or selective invasive strategies will be presented.

**1150-02 The Effect of Clopidogrel vs Aspirin on Recurrent Clinical Events and Total Vascular Mortality: Results From the CAPRIE Study**

James J. Ferguson, Rollo P. Villareal, Edward K. Massin. Texas Heart Institute, Houston, TX.

**Background:** The CAPRIE study compared the thienopyridine clopidogrel with aspirin in patients with atherosclerotic disease; the primary outcome cluster was a composite of new first events. However, since recurrent events are also a significant contributor to subsequent overall clinical outcomes, we analyze all events (initial and recurrent) and total vascular mortality (total MI, total stroke, and other vascular death) in CAPRIE. Methods: A retrospective analysis of the CAPRIE patient cohort (n=18,965), including both initial events (death/non-fatal MI, death/non-fatal stroke, other vascular death) and subsequent vascular events.

Results: initial Events: Total Events: 1021 1264
MI 43 33
Stroke 94 119
Other vascular death 35 34
Total 361 354
Subsequent Events: Recurrent vascular death 57 42
Total vascular death 278 350
The net reduction in total events (both initial and recurrent) with clopidogrel was 14 events/1000 patients; the net reduction in total vascular death (both initial and recurrent) was 9/1000.

Conclusions: In CAPRIE, clopidogrel was significantly superior to aspirin in preventing both initial and subsequent vascular events. The total events prevented (14/1000 patients) and total vascular deaths prevented (9/1000) may be more representative of the potential clinical benefits of clopidogrel over aspirin.

**Safety of Abciximab in Addition to the Low Heparin Doseparin as the Primary Treatment of Acute Coronary Syndromes (ACS)**


The combination of aspirin and low-dose heparin is at present the routine initial treatment of acute coronary syndromes in many patients. So far the safety and efficacy of the addition of abciximab to low-dose heparin or the primary medical treatment in acute coronary syndromes (ACS) has not been evaluated. Methods: As a substudy within the multi-national multicenter prospective double-blind trial of the efficacy of abciximab as the primary medical treatment in ACS without early revascularization 974 of the 7800 patients used subcutaneous treatment with dalteparin 2000 I.U. b.w. (max. dose 10 000 I.U.) instead of the routine 46 hours heparin infusion. The patients were randomized to bolus injection followed by 24 hours (n=315) or 48 hour (n=331) infusion of abciximab or corresponding placebo (n=330). The primary endpoint was set at 30 days follow up. In the main trial there were no significant differences in efficacy by the addition of abciximab.

Results: 1288 + 372
Any stroke 1.2% 1.1%
Major stroke (TIMI) 0.4% 0.3%
Ischemic stroke 1.2% 0.4%
Any bleeding (non-CABG) 0.7% 0.9%
Major (TIMI) 0.2% 0.2%
Minor 1.1% 4.0%
Platelet count <500/mL 0% 0.8%
*p<0.05; **p<0.01; ***p<0.001

Conclusion: Combination of abciximab with full dose LMWH (doseparin) seems as safe as its combination therapy with reduced dose standard heparin. In both cases there is a slight excess in bleeding with combination therapy.
Regulation of Angiogenesis and Coronary Flow in Myocardial Infarction

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1151-84 Angiogenesis Converting Enzyme Inhibitor Reduces VEGF Expression by Cardiac Myofibroblasts in Healing Infarct: Scar Tissue and Attenuates Ventricular Remodeling

Samuel A. Wolkfine, Gunghee Zhu, Heather Lewis, Christopher Hall, John Auer, Michael Scott, Gregory Lancz. Washington University, St. Louis, MO

To define the time course of expression of VEGF in cardiac remodeling after infarction, the cell types involved, and the role of the renin-angiotensin system in VEGF regulation, we performed experiments to determine: 1) the timeframe for expression of VEGF by cardiac myofibroblasts, which are well established as mediators of cardiac remodeling, relative to that observed for the renin-angiotensin system (RAS) by immunostaining for VEGF and p-smooth muscle actin (p-SMA), a marker for myofibroblasts, indicated that the majority of myofibroblasts expressing VEGF at all times were fibrocellular myofibroblasts, which was confirmed by double immunostaining for VEGF and p-SMA. We conclude that: 1) VEGF expression in healing infarct scars is faster and is regulated by the renin-angiotensin system; 2) myofibroblasts are the predominant cell types that express VEGF in chronic cardiac wound healing after infarction; and 3) ACE inhibitors coordinate the reduction in remodeling and scar tissue VEGF expression independent of infarct size. These data suggest that ACE inhibitors alter the natural history of scar tissue wound healing after infarction, including obligate angiogenic responses attributable to cell types such as the myofibroblast.

Cardiomyoplasty Improved Left Ventricular Function and Myocardial Revascularization After Myocardial Infarction in Rats

Karla L. D. Da Anaglia, Maria Claudia Itoyo, Adolfo A. Leiner, Idigene A. Costtari. Bending Division, Heart Institute (Inocv), Medical School, Federal University of Sao Paulo, Sao Paulo, Brazil

Background: Myocardial infarction can cause complex architectural changes that have an important bearing on ventricular function. We tested the hypothesis that cardiomyoplasty (CDM) combined with VEGF treatment in the setting of experimentally induced myocardial infarction (MI) would stimulate angiogenesis and reduce the hemodynamic deficit. Methods: Male Wistar rats were divided in five experimental groups: C (n=6), CDM (n=6), MI (left coronary artery ligation; n=5), MI+CDM performed 14 days after MI and sham-operated (R) (n=6). Recombinant human VEGF165 was infused (25 mg) into the left latissimus dorsi (LD) main artery immediately before CDM. End-diastolic pressure (EDP) was obtained by left ventricular catheterization. Regional blood flow (CF) from LD to the myocardium (CF LD-M) was determined by the ratio of blue microspheres counted in LD to that counted in the myocardium. Left ventricular hypertrophy (LVH) and end-diastolic pressure (EDP) were reduced after CDM in MI rats. No differences were found between groups in UJ and coronary flow. VEGF treatment was associated with an increase in the CF LD-M in MI rats submitted to CDM. MI+CDM was greater in VEGF group compared to CDM and MI+CDM.

C   COM   MI   MI+COM   MI+COM+VEGF
LVH/5 2.5±0.05  2.8±0.08  3.4±0.12*  2.9±0.08*  3±0.14*  p<0.05 vs. COM and MI
CF (mL/min) -0.14±0.5  -0.41±0.2  1.5±0.4  2.7±1.6  3.7±1.6  2±0.02  p<0.05 vs. C and MI
CO (mL/min) 62.5±6.6  74.6±6  49.5±4.5  71.5±1.8  76±9  6

Conclusion: Cardiomyoplasty improved left ventricular function after myocardial infarction. In this setting, VEGF treatment may offer an alternative route to myocardial revascularization.

1151-85 Effects of Angiotensin II Type 1 Receptor Blockade and Angiotensin Converting Enzyme Inhibitor on the Ventricular Remodeling After Myocardial Infarction: With References to Sarcoplasmic Reticulum and its mRNA

Elchi Gashi, Takashi Katagai. Third Department of Internal Medicine, Showa University School of Medicine, Tokyo, Japan

We clarified the role of renin-angiotensin system and its relation with ventricular remodeling after myocardial infarction with the influences of Ca-ATPase activity of the sarcoplasmic reticulum (SR) and its mRNA (SRCa2a) using angiotensin II type 1 receptor blockers (ATII and ACEI) and treatment with recombinant human VEGF in the setting of experimentally induced myocardial infarction. Treatment with ATII and ACEI significantly reduced VEGF expression at later time periods (p<0.05 for each). ACE inhibitors altered the natural history of scar tissue wound healing after infarction, including obligate angiogenic responses attributable to cell types such as the myofibroblast.
Pharmacokinetics and Efficacy of Intravenous Vascular Endothelial Growth Factor (rhVEGF) in Porcine Hibernating Myocardium

Shankha S. Bhowmik, Patrick W. Domkowski, Luis H. Diodato, Amme M. Pippin, Kevin P. Landolfi, Brian H. Amrex, Duke University Medical Center, Durham, NC

Background: In porcine hibernating myocardium, we have demonstrated changes in myocardial blood flow (MBF) and function with laser and angiogenic therapies. The purpose of this study was to examine the pharmacokinetics (PK) and long-term efficacy of intravenous (IV) rhVEGF (total 30 g/kg) in hibernating myocardium. Methods: Eight mini-pigs with 90% left circumflex artery (LCX) stenosis and documented hibernating myocardium by positron emission tomography (PET) and dobutamine stress echocardiography (DSE) were randomized to IV rhVEGF (30 ng/kg/min for 200 minutes at 3-7 day intervals, n=6) or IV vehicle (n=2). As an additional control, 6 pigs had 30 intramyocardial vehicle (IM) injections. PK parameters were calculated using non-compartmental analysis and compared to published human data. After 3 and 6 months, PET and DSE were repeated. Results: There was no ischemic change by DSE detected by changes in regional wall motion score index (WMSI) = 1 normal, 2 hypokinetic, 3 akinetic, and 4 dyskinetic. Results: The plasma clearance (14.8 ml/min/kg) was biphasic with a large volume of distribution (Vss 1530 ml/kg) and a terminal half-life of 71 minutes after IV rhVEGF. The rapid clearance and large Vss suggest extensive tissue binding and is similar to the PK parameters reported in humans (Cl 22 ml/min/kg; t1/2 77 men; Vss 1690 ml/kg). With IM and IV vehicles, MBF did not increase significantly over baseline at 3 months (1.7±0.2% and 0.6±0.5%, respectively). With rhVEGF, MBF increased by 4.7±3.8% over baseline at 3 months (p<0.05), and by 22.0±5.8% at 6 months (p<0.001). As an additional control, 6 pigs had 30 intramyocardial vehicle (IM) injections. PK parameters were calculated using non-compartmental analysis and compared to published human data. After 3 and 6 months, PET and DSE were repeated. Results: There was no ischemic change by DSE detected by changes in regional wall motion score index (WMSI). However, repeated DSE detects ischemia by changes in regional MBF. In conclusion, IV rhVEGF significantly improved regional MBF, as well as resting and stress-induced ischemia in porcine hibernating myocardium.
CAGD before six using a following 6 minutes of treatment: PWV was evaluated using a computer system COMPLIOR. In each patient carotid-femoral PWV was measured. For automatic measurement of PWV pressure waveforms were digitized at rate 500Hz for carotid-femoral distance to healthy volunteers constituted a control group. Results: After 6 months the plasma cholesterol level was 205±13 mg/dl in Group 1 and 168±15 mg/dl in Group 2 (p<0.01). Results of PWV are shown in the table. *p<0.01

Pulse wave velocity m/s

<table>
<thead>
<tr>
<th>Group</th>
<th>Initial</th>
<th>After 6 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>12.1±3</td>
<td>8.9±0.7</td>
</tr>
<tr>
<td>II</td>
<td>12.4±2</td>
<td>7.2±0.4</td>
</tr>
</tbody>
</table>

After 6-month therapy with statin a significant decrease of PWV was observed. This result may be explained by beneficial effect of statins on the degree of plaque growth. The alternative explanation may be the influence of statins on vascular remodeling.

1152-94 Relation Between Self-Efficacy and Diet/Exercise Adequacy in Coronary Rehaufiliation

Sammy Chan, Kori Kingsbury, Frances Johnson, Anita Brozek, Wolfgang Lindner, Sandra Barr, Jim Frisch. Alfred Krassiewicz, University of British Columbia, Vancouver, BC, Canada

Background: Self-efficacy (SE) has been shown to influence health behavior. To determine the role of SE in cardiac rehabilitation (CRP), we correlated SE with measures of diet/exercise compliance in participants of CRP Methods: 47 subjects (age 61±13, 19% female, 60% CAD were evaluated. SE was subbed in 2 domains (diet, exercise) with a 6 item questionnaire (SEQ) using Likert scales. Adequacy of diet was measured with body mass index (BMI). Adequacy of exercise was assessed with age adjusted fitness classification (FTT) (1-7, most to least fit) based on treadmill results. SEQ was tested prior to CRP and 6 months later in response to the CRP. All subjects completed a 4 month CRP with supervised exercise conditioning and outpatient diet counseling.

Results: Subjects were divided into 2 groups based on their SE scores. At initial evaluation, subjects with high dietary SE had a significantly lower BMI (figure). The indices did not change in either group at completion. Exercise SE was evaluated in subgroup with negative stress test. At start of CRP, subjects with high exercise SE were significantly more fit (figure). However, subjects with low SE improved significantly during CRP while there was no change in FTT in subjects with high exercise SE scores. Conclusions: (1) diet and exercise SE scores correlate with Initial BMI and FT suggesting that these scores are useful in predicting behavior in an ambulatory setting; (2) a supervised exercise CRP improves FT especially in subjects with low SE; (3) dietary counseling only has a minimal impact on BMI regardless of SE.

1153 Time to Treatment in Acute Myocardial Infarction

Monday, March 19, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1153-95 The Importance of Time to Treatment in Acute Myocardial Infarction

Peter Hansen, Yukiko Koyama, Michael Ward, Hege Rasmussen, Greg Nelson, Royal North Shore Hospital, Sydney, Australia

Background: Time to treatment in acute myocardial infarction (AMI) has long been recognized as a critical determinant of outcome. In recent years, the importance of immediate and effective treatment has been emphasized. The aim of this study was to evaluate the importance of time to treatment in patients with AMI. Methods: We retrospectively reviewed the charts of all patients with AMI admitted to our hospital from January 1, 1999, to December 31, 2000. The primary endpoint was the time from symptom onset to the start of treatment. Results: The median time from symptom onset to the start of treatment was 3 hours (95% CI: 2.5-3.5). Conclusions: The importance of time to treatment in the management of AMI cannot be overstated. Early and effective intervention is critical to achieving optimal outcomes.

1153-96 Relation Between Time-to-Pharmacologic Reperfusion and the Probability of Achieving Complete ST-Segment Resolution in ST Elevation Myocardial Infarction

Howard A. Cooper, James A. de Lemos, Sabina A. Murphy, Carolyn H. McCabe, Kristin C. Schuler, Elliott M. Antman, Eugene Braunwald, Brigham and Women’s Hospital, Boston, MA

Background: ST-segment resolution reflects myocardial reperfusion and predicts mortality following ST elevation MI. The relation between time-to-pharmacologic reperfusion and ST-segment resolution is unknown.

Methods: Data was pooled for 544 patients randomized to various combinations of reteplase, alteplase, and abciximab (TIMI trial) and 763 patients randomized to full-dose tirofiban or placebo (TIMI 14 trial). Univariate logistic regression was used to assess the independent relation between time from symptom onset to the start of pharmacologic reperfusion and the probability of achieving complete ST-segment resolution at 90 minutes. Subsets in the model were the initial infarct location (anterior-posterior), abciximab use in TIMI 14 (yes/no), and fibrinolytic agent (reteplase/alteplase/tirofiban).

Results: Time-to-treatment was inversely related to the probability of achieving complete ST-segment resolution at 90 minutes (per hour OR 0.84, 95% CI 0.79-0.90, p<0.03). Patients with non-anterior infarcts were more likely to achieve complete ST-segment resolution (TIMI 14 trial). However, the propensity of achieving complete ST-segment resolution was not significantly different among the fibrinolytic agents (p=NS), but was greater if abciximab was part of the reperfusion regimen (OR 2.65, 95% CI 1.51-4.20, p=0.007).

Conclusion: While the effects of abciximab and infarct location predominate, time-to-treatment also has a significant impact on the probability of achieving reperfusion at the myocardial artery. This may be one mechanism by which early pharmacologic reperfusion results in reduced mortality in ST elevation MI.

1153-97 Prehospital Infarction Angioplasty Triage (PHIAT): Results From the Zwolle Myocardial Infarction Study Group


Background: Time from onset of symptoms to reperfusion therapy is of paramount importance for the clinical outcome in patients (pts) with acute myocardial infarction (AMI). Prehospital identification of pts with AMI may result in a reduction of total ischemic time when considering primary angioplasty (PA) treatment. Methods: Between November 1998 and July 2000, 17 ambulances were equipped with 12-lead ECG computers using an algorithm to Identify large AMI. When pts were Identified as having large AMI, immediate transport and preparation of cath lab and personnel were initiated. Results: During the study period in 213 pts the indication for PA treatment was made. The mean age was 69.4 years (range 16-90). One patient died before arrival in the hospital.

Clinical characteristics (n=212):
1153-98 Delayed Is Better Than Early Elective Intervention After Acute Myocardial Infarction Treated With Thrombolytic Therapy


Background: Optimal timing of elective percutaneous coronary intervention (PCI) after acute myocardial infarction (MI), especially those treated with thrombolytic therapy (TT), is unknown. Aim: We compared the results of early (<6 hours) and delayed (6-24 hours) elective PCI after acute MI (AMI) patients with 12 hours of RR compared with TT. Methods: We performed a retrospective analysis of 231 consecutive pts with acute MI undergoing elective PCI after successful TT (pts undergoing emergency PCI or hemodynamic instability were excluded). Group 1 = <6 hours; Group 2 = >6 hours. Each group was analyzed according to TT. All major adverse cardiac events (MACE: death, non-fatal MI, and re-intervention) were recorded.

<table>
<thead>
<tr>
<th>Group (24-hour Times)</th>
<th>From TT+</th>
<th>From TT</th>
<th>From TT-</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (%)</td>
<td>12</td>
<td>74</td>
<td>115</td>
</tr>
<tr>
<td>Age (YRS)</td>
<td>57±13</td>
<td>56±12</td>
<td>58±14</td>
</tr>
<tr>
<td>DM (%)</td>
<td>3 (25%)</td>
<td>25 (34%)</td>
<td>31 (37%)</td>
</tr>
<tr>
<td>1-Vessel disease (%)</td>
<td>10 (83%)</td>
<td>53 (72%)</td>
<td>22 (74%)</td>
</tr>
<tr>
<td>Anterior MI (%)</td>
<td>3 (25%)</td>
<td>52 (34%)</td>
<td>33 (36%)</td>
</tr>
<tr>
<td>Female (%)</td>
<td>7 (58%)</td>
<td>30 (41%)</td>
<td>29 (97%)</td>
</tr>
<tr>
<td>GP IIb/IIIa (%)</td>
<td>3 (25%)</td>
<td>38 (51%)</td>
<td>7 (21%)</td>
</tr>
<tr>
<td>In-hospital death (%)</td>
<td>1 (8.2%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>In-hospital MACE (%)</td>
<td>3 (25%)</td>
<td>5 (7%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Conclusion: Early (6-24 hours) elective PCI after acute MI is associated with higher rate of in-hospital MACE especially when thrombolytic therapy was given.

1153-99 Influence on Outcome of Time From Myocardial Infarction Onset to Primary Angioplasty

Thierry Lefebvre, Christophe Loubeyre, Marie-Claude Morice, Padma Kaul, Frans Van de Werf, Thierry Lefevre, Christophe Loubeyre, Marie-Claude Morice, Yves Louvard, Franck Robert, Anthony H. Hu, Stephen E. Kimmel, Joseph M. Merlis, Paul W. Armstrong, for the ASSENT2 Investigators. University of Alberta, Edmonton, AB, Canada

Background: Proximal angina occurring shortly before the onset of acute myocardial infarction is associated with favorable outcome by the mechanism of ischemic preconditioning. However, little is known about impact of diabetes on ischemic preconditioning. Aim: We studied 830 consecutive patients with a first anterior wall acute myocardial infarction who underwent emergency catheterization with <12 hours after the onset of chest pain. Proximal angina was defined as angina episode(s) occurring within 24 hours before the onset of acute myocardial infarction. Serial contrast left ventriculograms were obtained in 505 patients at the time of acute and pre-discharge catheterization. Results: In 490 patients without diabetes, proximal angina was associated with lower peak creatinine kinase (3,382±2,521 U/L vs 3,233±2,412 U/L, p=0.037), absence of left ventricular ejection fraction reduction (9.7±13.2% vs 5±13.6%, p=0.0005) and lower in-hospital mortality (3.4% vs 9.3%, p=0.015). On the contrary, in 130 diabetic patients, there was no significant difference in peak creatinine kinase value (3,392±2,501 U/L vs 3,373±2,412 U/L, p=0.73), the change in left ventricular ejection fraction (7.2±14.0% vs 8.2±15.1%, p=0.76) and in-hospital mortality (8.8% vs 11.0%, p=0.68) between patients with and those without proximal angina. Conclusion: Proximal angina occurring shortly before the onset of acute myocardial infarction was associated with limited infarct size, enhanced recovery of left ventricular function and improved survival. However, such beneficial effects of proximal angina were not observed in diabetic patients, suggesting that diabetes might prevent ischemic preconditioning in patients with acute myocardial infarction.

1154 Specific Clinical Risk Markers in Acute Coronary Syndromes

Masaeharu Ishihara, Hikaru Sato, Taiji Kikawai, Yuki Shimetani, Satoshi Kurisu, Kenji Nakahiko, Yosukeik Koura, Takeshi Umemura, Shuji Nakamura, Hirohisa City Hospital, Hiroshima, Japan

Background: Proximal angina occurring shortly before the onset of acute myocardial infarction is associated with favorable outcome by the mechanism of ischemic preconditioning. However, little is known about impact of diabetes on ischemic preconditioning.

Methods: We studied 830 consecutive patients with a first anterior wall acute myocardial infarction who underwent emergency catheterization with <12 hours after the onset of chest pain. Proximal angina was defined as angina episode(s) occurring within 24 hours before the onset of acute myocardial infarction. Serial contrast left ventriculograms were obtained in 505 patients at the time of acute and pre-discharge catheterization. Results: In 490 patients without diabetes, proximal angina was associated with lower peak creatinine kinase value (3,382±2,521 U/L vs 3,233±2,412 U/L, p=0.037), absence of left ventricular ejection fraction reduction (9.7±13.2% vs 5±13.6%, p=0.0005) and lower in-hospital mortality (3.4% vs 9.3%, p=0.015). On the contrary, in 130 diabetic patients, there was no significant difference in peak creatinine kinase value (3,392±2,501 U/L vs 3,373±2,412 U/L, p=0.73), the change in left ventricular ejection fraction (7.2±14.0% vs 8.2±15.1%, p=0.76) and in-hospital mortality (8.8% vs 11.0%, p=0.68) between patients with and those without proximal angina. Conclusion: Proximal angina occurring shortly before the onset of acute myocardial infarction was associated with limited infarct size, enhanced recovery of left ventricular function and improved survival. However, such beneficial effects of proximal angina were not observed in diabetic patients, suggesting that diabetes might prevent ischemic preconditioning in patients with acute myocardial infarction.
were in CRI patients. Patients with CRI were older and had more prior congestive heart failure, diabetes, hypertension and myocardial infarction (table). CRI patients had longer hospital stays, were less likely to have a normal angiogram and were more likely to have a failed procedure if coronary intervention was attempted. CRI was an independent predictor of inhospital mortality. Conclusions: CRI is prevalent in patients presenting with an acute coronary syndrome and is an under-appreciated independent risk factor for in-hospital mortality. Recognition of the increased risk burden of CRI identifies a patient subset at substantially higher risk of adverse cardiovascular outcome.

ABSTRACTS - Myocardial Ischemia and Infarction 341A

Cardiovascular Risk Index (CRI): Non-Invasive Invasive

Regarding ST-segment deviation (>0.2mV) and the summed ST-segment elevation in 11 leads (except aVR) was calculated. Patients with bundle branch block, fascicular block and left ventricular hypertrophy constituted a separate subgroup of 514 patients.

Non-ST-segment elevation MI

ST-segment

strategy

Death, MI 1 year

Death, MI 1 year (Child)

up/Lower Median 2SD or 3SD values

0.2mm

9.3%

11.7%

0.45

0.09

43.8%

0.005 or *p<0.001 compared with group above. Results: An invasive treatment strategy reduced the risk of death or AMI by 1 year risk significantly in the subgroup of patients with <50% of high-risk stenosis. There was a gradual increase in Troponin T values by 5% at the beginning of ischemic burden as well as the patients with the ST-segment deviation had more severe coronary artery disease by 5.7 days angiography. Conclusion: In patients with unstable coronary artery disease this ischemic burden determined by ECG is related to poor outcome in patients treated non-invasively. An invasive treatment strategy provides a significant risk reduction in these patients. In addition, ischemic burden in the ECG is also correlated to Troponin T level and to the severity of coronary artery disease by angiography.

1154-101 Emergency Department Non-Mycocardial Perfusion Imaging Results in More Effective Utilization of Coronary Angiography in Low Risk Chest Pain Patients

Michael C. Kortos, Rafael K. Shin, Kristin L. Schmidt, Robert L. Joseph, Joseph P. Oronas, James L. Isman, MCV/VCU, Richmond, VA

Background: Previous studies have shown that using myocardial perfusion imaging (MPI) with stress testing in Emergency Department (ED) patients with chest pain is cost effective. This may result from more effective utilization of invasive testing, with a reduction of coronary angiography in low-risk patients. Methods: We compared a conservative group of ED patients prospectively evaluated according to a protocol using MPI in low risk patients (ACT) to a control group (CON) evaluated during the year prior to implementation of the protocol. CON patients were retrospectively assigned a pre-defined risk level based on the ED admission record and ECG. High risk (high risk stable angina pts were compared to major risk pts (Low), who underwent MPI in the ACT group but not in the CON group, to assess the relationship of MPI to the use of coronary angiography (Con], presence of significant disease (Siz Dz >70% stenosis)), and revacculation (Rev) in tests performed within 30 days of ED evaluation. Results: There was no difference in the proportion of pts who were High and Low risk between the two groups (Table). High risk CON pts underwent stress testing more frequently (p<0.05) than did High risk ACT pts. Cath was performed as frequently in High risk CON and ACT pts with no difference in the incidence of Siz Dz and Rev in tests performed within 30 days of ED evaluation. Conclusion: There was no difference in the proportion of pts who were High and Low risk between the two groups (Table). High risk CON pts underwent stress testing more frequently (p<0.05) than did High risk ACT pts. Cath was performed as frequently in High risk CON and ACT pts with no difference in the incidence of Siz Dz and Rev in tests performed within 30 days of ED evaluation. Pts with appropriate invasive test utilization in Low risk chest pain pts. ED MPI improves cost effectiveness of low risk pts by increasing the yield of invasive testing.

<table>
<thead>
<tr>
<th>% Pts</th>
<th>Stress</th>
<th>Cath</th>
<th>Siz Dz</th>
<th>Rev</th>
</tr>
</thead>
<tbody>
<tr>
<td>CON, High (n=175)</td>
<td>27</td>
<td>45</td>
<td>72</td>
<td>59</td>
</tr>
<tr>
<td>CON, Low (n=136)</td>
<td>32</td>
<td>50</td>
<td>60</td>
<td>46</td>
</tr>
<tr>
<td>ACT, Low (n=114)</td>
<td>73</td>
<td>21</td>
<td>31</td>
<td>22</td>
</tr>
</tbody>
</table>

* p<0.05 ** p<0.005

1154-102 Outcome of Patients With Acute Coronary Syndromes With and Without Prior CABG: Results From the PURSUIT Trial


Coronary Artery Bypass Grafting (CABG) significantly improves the morbidity and mortality of patients (pts) with advanced coronary artery disease. However, it is unclear whether prior CABG protects pts presenting with acute coronary syndromes (ACS) from adverse events. Furthermore, the effect of glycoprotein (GP) IIb/IIIa blockade in pts with prior CABG presenting with ACS is also unknown. The purpose of this study was to evaluate the baseline characteristics and outcomes of pts presenting with ACS with and without prior CABG. Methods: PURSUIT randomized pts presenting with ACS to 72 hrs of therapy with the GP IIb/IIIa inhibitor epti and placebo as an active control. Results: PUR- 

SUIII 1134 pts (12.0%) had prior CABG. Pts with prior CABG were older, heavier, had significantly more cardiac risk factors, more prior MI, stroke, PVD and PTCA compared to pts without prior CABG. Thus use of aspirin, beta-blockers, clopidogrel, thienopyridines, ACE inhibitors and nitrates were higher in the 2 pts prior to presentation in pts with prior CABG. The incidence of death and death/MI in prior CABG compared to non-prior CABG at 7 days was 5.2 vs 4.3% and 15.7 vs 14.8% and at 6 months it was 8.1 vs 6.1% and 20.7 vs 18.1%. The table showed adjusted event rates (% and CI) for death and death/MI by prior CABG. Comparing epti vs placebo in pts with prior CABG, the 30 day mortality was 4.1 vs 6.3%, 30 death/MI was 15.0 vs 18.6%. Conclusions: Pts presenting with ACS and prior CABG have significantly worse baseline characteristics than non-prior CABG pts. Prior CABG pts have significantly higher mortality at 30 days and 6 months.
combination therapy, and without the routine use of GP IIb/IIIa inhibitors. Methods: To determine the optimal reperfusion strategy in AMI, 2,082 pts of any age with AMI <12 hrs without out cardiogenic shock were randomized at 76 sites to primary PTCA alone (n=516), PTCA + Abx (n=529), stenting alone (n=512), or stenting with Abx (n=525), and followed for 12 mos. The primary clinical endpoint was the 6 month composite incidence of death, recurrent ischemia, and reinfarction compared to PTCA alone, significantly reduced ischemic TVR within 6 months in all pts with diabetes (31% relative risk reduction) and non-diabetes (51% reduction). A potential benefit of abciximab in reducing MACE at 6 months was evident in non-diabetic pts, but not in those with diabetes.

6 Month Events

<table>
<thead>
<tr>
<th></th>
<th>PTCa</th>
<th>Stent</th>
<th>Stent + Abciximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4.3%</td>
<td>2.3%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>0.2%</td>
<td>0.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>1.6%</td>
<td>2.1%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Ischemic TVR</td>
<td>14.0%</td>
<td>11.9%</td>
<td>7.2%</td>
</tr>
<tr>
<td>MACE</td>
<td>10.4%</td>
<td>14.0%</td>
<td>12.5%</td>
</tr>
</tbody>
</table>

**Conclusions.** Compared to primary PTCa alone, MultiLink stent implantation during AMI results in a marked reduction in ischemic TVR and MACE at 6 mos, without adversely affecting TIMI flow or survival. The outcomes trend to be further improved with abciximab, especially in pts undergoing PTCa alone. Complete 12 mo follow-up, and 6 mo angiographic data will be presented for the first time in March.

**ORAL CONTRIBUTIONS**

**838 Combination Strategies for Managing Acute Myocardial Infarction**

Monday, March 19, 2001, 4:00 p.m.-5:30 p.m.
Orange County Convention Center, Room 230D

**ABSTRACTS - Myocardial Ischemia and Infarction**

Does Stenting and Glycoprotein IIb/IIIa Receptor Blockade Improve the Prognosis of Diabetics Undergoing Primary Angioplasty in Acute Myocardial Infarction? The CADILLAC Trial


**Background.** Although the prognosis of pts with AMI and diabetes mellitus (DM) is improved with primary PTCa compared to thrombolysis therapy, long-term outcomes are still poor compared to non-DM. Patients with DM undergoing elective PCI may benefit by stent implantation (reduced TVR and abciximab; Abx; prolonged survival). Methods. To examine whether similar benefits of stents and Abx are conferred in an AMI population, we examined the CADILLAC database, in which 2,082 pts of any age with AMI <12 hrs in duration without cardiogenic shock were randomized to primary PTCa, PTCa + Abx, stenting with the MultiLink or MultiLink Duet stent, or stenting + Abx. DM was present in 346 pts (16.5%). The primary clinical endpoint was the 6 month composite incidence of death, disabling stroke, myocardial infarction (MI), and ischemia requiring TVR. Results. Compared to non-DM pts, the 6 month rate of MACE was increased in the diabetic (17.1% vs. 12.3%, p=0.02). Considering the individual components of the primary endpoint, death occurred in 4.4%, of pts with DM vs. 2.9% of pts without DM (p=0.03); disabling stroke occurred in 3.0% vs. 0.2% respectively (p=0.0058), infection 5.6% vs. 1.7% (p=0.07); and ischemic TVR 11.9% vs. 10.2% (p=0.037). The outcomes in DM and non-DM stratified by treatment appear in the table.

**6 Month Results**

<table>
<thead>
<tr>
<th></th>
<th>PTCa</th>
<th>Stent</th>
<th>Stent + Abciximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>3.9%</td>
<td>2.7%</td>
<td>2.0%</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>0.5%</td>
<td>0.5%</td>
<td>0.5%</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>1.7%</td>
<td>0.7%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Ischemic TVR</td>
<td>12.1%</td>
<td>10.4%</td>
<td>7.1%</td>
</tr>
<tr>
<td>MACE</td>
<td>15.0%</td>
<td>12.1%</td>
<td>12.1%</td>
</tr>
</tbody>
</table>

**Conclusion.** This is the first report of the CADILLAC trial, which examined combined therapy with stents and Abx in pts with DM, and demonstrated a significant reduction in MACE at 6 months in pts with DM. A similar benefit was observed in non-DM pts who received primary PTCa. Further follow-up and analysis of the angiographic data will be presented for the first time in March.

**839-l A Prospective, Multicenter, International Randomized Trial Comparing Four Reperfusion Strategies in Acute Myocardial Infarction: Principal Report of the Controlled Abciximab and Device Investigation to Lower Late Angioplasty Complications (CADILLAC) Trial**

Gregg W. Stone, Cindy L. Gines, David A. Cox, Giulio Guagliumi, Barry Rutherford, Gary Johnson, Mark Effron, Paolo Esente, Alexandra J. Lansky, John Gregg W. Stone. The Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York, NY; Orange County Convention Center, Room 230D

**Background.** Prior studies have shown that stent implantation in AMI, while reducing recurrent ischemia and restenosis compared to PTCa alone, may degrade antegrade blood flow and result in increased mortality. These studies were done with first generation stent technology, and without the routine use of GP IIb/IIIa inhibitors. Methods: To determine the optimal reperfusion strategy in AMI, 2082 pts of any age with AMI <12 hrs without cardiogenic shock were randomized in a 2x2 factorial design to primary PTCa alone (n=516), PTCa with abciximab (n=529), stenting alone (n=512), or stenting with abciximab (n=525), and followed for 12 mos. The primary endpoint was the Multilink and Multilink Duet. Angiographic inclusion criteria included native ref. vessel dia. >2.5 mm or <4.5 mm, length ~65 mm, non-ostial location, and absence of major side branch involvement. The primary endpoint was the 6 mos composite incidence of death, disabling stroke, reintervention, and ischemic TVR. Protocol 6 mos angiographic follow-up was performed in a 962 pt subset to assess myocardial recovery and restenosis. Results: Mean age was 60 ± 12 yrs (range 21-95), 27% were female, 17% had diabetes, and 37% had anterior MI. Median time from symptom onset to ER was 1.8 hrs, and from ER to PTCa 2.9 hrs. By core lab analysis, TIMI-3 flow was restored in 95.2% of pts after PTCa, 96.2% after PTCa + abciximab, 94.6% after stenting, and 96.1% after stent + abciximab (all p=NS). The primary clinical endpoint data appear in the table.

**6 Month Results**

<table>
<thead>
<tr>
<th></th>
<th>PTCa</th>
<th>Stent</th>
<th>Stent + Abciximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>4.3%</td>
<td>2.3%</td>
<td>2.7%</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>0.2%</td>
<td>0.6%</td>
<td>0.6%</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>2.1%</td>
<td>2.3%</td>
<td>2.3%</td>
</tr>
<tr>
<td>Ischemic TVR</td>
<td>14.0%</td>
<td>11.9%</td>
<td>7.2%</td>
</tr>
<tr>
<td>MACE</td>
<td>10.4%</td>
<td>14.0%</td>
<td>12.5%</td>
</tr>
</tbody>
</table>

**Conclusion.** This is the first report of the CADILLAC trial, which examined combined therapy with stents and Abx in pts with AMI, and demonstrated significant reduction in MACE at 6 months in all pts with diabetes.

**E33 Effect of Stent Implantation and Glycoprotein IIb/IIIa Receptor Blockade on TIMI Flow and Mortality After Primary PCI in Acute Myocardial Infarction: Final Results of the CADILLAC Trial**

Cindy L. Grines, David A. Cox, James E. Tcheng, Giulio Guagliumi, Thomas Stubley, John Lansing, unacio usagam, stacy numero, wino ishii, wylie cardillo, James E. Tcheng, John Gregg W. Stone, The Cardiovascular Research Foundation and Lenox Hill Heart and Vascular Institute, New York, NY; William Beaumont Hospital, Royal Oak, MI

**Background.** Long-term mortality after reperfusion therapy in AMI is directly related to the early achievement of TIMI-3 flow. In the randomized Stented PAMI Trial, post procedural TIMI-3 flow rates were reduced in Palmaz-Schatz stented pts compared to those undergoing PTCa only, which resulted in a strong trend toward increased mortality after stenting, offsetting the benefit of reduced restenosis. However, GP IIb/IIIa inhibitors were rarely used in Stent PAMI and lower profile. Better performing stents have since been introduced. Methods: To determine the optimal reperfusion therapy strategy in AMI, 2,082 pts of any age with symptom duration <12 hrs without cardiogenic shock were randomized at 76 international centers in a 2x2 factorial design to primary PCI alone (n=1616). PCI + abciximab (n=529), stenting with the MultiLink or MultiLink Duet stent (n=512), or stenting + abciximab (n=525). Results: By core lab analysis, TIMI-3 flow was restored in 95.6% of pts. TIMI-2 flow was present in 3.0%, and TIMI-0 flow was present in 1.4%. Mortality at 6 months occurred in 68 pts (3.3%); 2.9% of pts with PCI flow died, vs. 6.7% with TIMI-2 flow and 7.1% with TIMI-0 flow (p<0.04). TIMI flow rates and 6 mos mortality by treatment arm appear in the table.

**6 Month Results**

<table>
<thead>
<tr>
<th></th>
<th>PTCa</th>
<th>Stent</th>
<th>Stent + Abciximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>95.3%</td>
<td>95.8%</td>
<td>96.1%</td>
</tr>
<tr>
<td>Disabling stroke</td>
<td>3.2%</td>
<td>3.0%</td>
<td>3.0%</td>
</tr>
<tr>
<td>Reinfarction</td>
<td>3.0%</td>
<td>3.0%</td>
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</table>

**Conclusion.** Coincident with improved stent technology, post procedural TIMI flow rates are no longer reduced by stent implantation in AMI, and survival is excellent with all mechanical reperfusion strategies in patients without cardiogenic shock.
ABSTRACTS - Myocardial Ischemia and Infarction 344A

**Background:** Abciximab (ABX) improves clinical outcomes in pts undergoing elective percutaneous intervention. We hypothesized that the adjunctive use of ABX during primary PTCA and stenting would improve the early safety profile of the procedure and reduce late adverse events. **Methods:** In the CADILLAC trial, 2082 pts of any age who presented within 12 h post MI with non-ST elevation ACS were prospectively randomized in a 2x2 factorial design to primary PTCA or Multilink stenting, and to ABX or no ABX. The primary endpoint was the 6 month composite occurrence of death, disabling stroke, reinfarction, or ischemia requiring TVR. **Results:** A total of 1,054 pts were assigned to ABX (550 to PTCA and 500 to stent), and 1,089 pts were assigned to no ABX (516 to PTCA and 512 to stent). By core lab analysis, TIMI-3 flow was restored in 96.2% of pts assigned to ABX vs. 96.4% assigned to no ABX (p=0.18). Results by intention to treat appear in the table.

<table>
<thead>
<tr>
<th></th>
<th>No Abciximab</th>
<th>Abciximab</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 day death</td>
<td>23 (2.2%)</td>
<td>19 (1.8%)</td>
<td>0.48</td>
</tr>
<tr>
<td>30 day disabling stroke</td>
<td>2 (0.2%)</td>
<td>2 (0.2%)</td>
<td>0.99</td>
</tr>
<tr>
<td>30 day reinfarction</td>
<td>6 (0.6%)</td>
<td>7 (0.7%)</td>
<td>0.01</td>
</tr>
<tr>
<td>30 day ischemic TVR</td>
<td>43 (4.2%)</td>
<td>25 (2.4%)</td>
<td>0.02</td>
</tr>
<tr>
<td>30 day MACE</td>
<td>69 (6.7%)</td>
<td>45 (4.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>30 day severe bleed</td>
<td>4 (0.4%)</td>
<td>6 (0.6%)</td>
<td>0.75</td>
</tr>
<tr>
<td>6 month MACE</td>
<td>448 (14.4%)</td>
<td>125 (13.9%)</td>
<td>0.09</td>
</tr>
</tbody>
</table>

The reduction in the 30 day MACE rate with abciximab was more pronounced in pts assigned to PTCA (4.3% vs. 8.1%, relative reduction [RR] 47%, p=0.01) than in those assigned to stenting (4.2% vs. 5.3%, RR 21%, p=NS). As was the reduction in 6 month MACE (14.2% vs. 18.4%, RR 22%, p=NS), and in 30 day and 6 month TIMI 0 flow (3.6% vs. 8.1%, RR 57%, p<0.05, respectively). Conclusions: In patients with non-ST elevation ACS undergoing emergency PTCA, Abciximab is associated with improved early and late clinical outcomes, especially after primary PTCA, without increasing complications.

**838-4**

**Long-term Survival after Routine Rescue PTCA for Failed Thrombolytic Therapy:** Is Similar to That of Successful Thrombolysis

Philippe G. Grig, Laurent Francois, Damien Durant, Patrick Chor, Florence Aubry, Dominique Hembert, Hakim Benamer, Laurent J Feldman, Jean-Michel Juliard, Alphaglate Paris, France

**Background:** Failed thrombolysis is associated with decreased short- and long-term survival. Rescue PTCA has been tested in small clinical trials, but no information is available on the long-term outcome after rescue PTCA for failed thrombolysis. **Methods:** 382 consecutive pts with acute myocardial infarction resistant to thrombolytic therapy for acute infarction were studied. 95% underwent 90 min angiography and 200 (60%) had TIMI 3 flow. 31 patients were treated with rescue PTCA. In 8 pts, rescue PTCA was associated with a repeat angioplasty and the rest had a single PTCA.

**Results:** All pts had a history of MI (98%), 55% had diabetes, and 75% had hypertension. Most pts (60%) were treated with abciximab. The group treated with rescue PTCA was compared with 311 pts treated with thrombolysis alone, using the chi-square test for categorical variables, and a log rank test for survival analysis.

**Conclusion:** For patients with acute MI resistant to thrombolysis, rescue PTCA did not improve survival and did not prevent reinfarction, with a similar long-term outcome compared to thrombolysis alone.
344A ABSTRACTS - Myocardial Ischemia and Infarction

patients who received lamifiban. Target concentration was achieved in 91.9 (72%); base-
line differences associated with a significant likelihood of being out of range included age, sex, and renal insufficiency (CRI). There were no significant statistical differences in the primary endpoint for a subset of troponin-positive patients, and no changes in events were seen in the >18 ng/ml group. No statistical differences were seen in bleeding.

Methods: The PURSUIT risk score was calculated for 313 consecutive Un特派ted County, MN patients presenting to our institution with non-ST elevation AMI between 1988 and 1998. The predicted mortality was then compared with the actual mortality.

Conclusions: In a community-based population with non-ST segment elevation AMI the PURSUIT risk score allowed an excellent prediction of 30-day mortality. The PURSUIT risk score can be used in non-selected patient populations with non-ST elevation AMI for accurate early risk stratification.

9:30 a.m.

346-5

Striking Heterogeneity of Responsiveness to Glycoprotein IIb/IIIa Inhibitors in Patients With Acute Coronary Syndromes and Positive Troponin

Marco Roffi, L. Kline Newby, Robert A. Harrington, Harvey D. White, Christian W. Hamm, Eric J. Topol. Cleveland Clinic Foundation, Cleveland, OH

Background: Previous trials have shown that GP IIb/IIIa are particularly beneficial in the medical management of non-ST elevation acute coronary syndromes (ACS) patients with elevated troponin. However, this benefit could not be reproduced in GUSTO IV ACS. We therefore performed a systematic overview. Methods: We included in a meta-analysis the troponin-positive populations of the 5 so far performed non-interventional GP IIb/IIIa trials assessing troponin status systematically, namely PRISM (tirofiban for 48 hours), PARAGON B (lamifiban for up to 72 hours), and GUSTO IV ACS (for 24 or 48 hours). The diagnostic threshold for troponin positivity was troponin-I level of 1.0 ng/L. In PRISM, and troponin-T level of 0.1 ng/L in PARAGON B and GUSTO IV ACS. Results: As shown in the figure, the incidence of death/MI in troponin positive patients was highly significantly reduced by GP IIb/IIIa inhibitors in PRISM and PARAGON B (p=0.001 and p=0.016, respectively) but not in GUSTO IV ACS (p=0.06). Conclusions: The impact of GP IIb/IIIa blockade was strikingly heterogeneous across the trials (as documented by Breslow-Day test p=0.001). Unlike the previous trials, in GUSTO IV ACS troponin positivity was poor as an inclusion criteria. This led to a different patient population enrollment with a cloaked lower event rate (0.7 vs. 13-19 % in the placebo group), less responsive to GP IIb/IIIa inhibition. Alternatively or additionally, the different benefits may be due to variable drug action.

9:45 a.m.

346-6

Reversibility of Platelet Inhibition Associated With Small Molecule, Competitive GP IIb/IIIa Antagonists: An In Vitro Model for Clinical Management Strategies

Richard C. Rankin, Vyo En Liu, Frederick & Sponsore. University of Massachusetts Medical School, Worcester, MA

Background: Platelet surface glycoprotein (GP) IIb/IIIa (pIIb/IIIa) receptor inhibition, by preventing fibrinogen binding, attenuates hemostatic potential. Because small molecule antagonists have relatively low GP IIb/IIIa receptor affinity (and high circulating plasma concentrations), it has been assumed that: 1) platelet inhibition may only partially restore physiologic aggregability, and 2) alternative subtypes would be required to manage hemorrhage events. Methods: Washed platelets from 24 healthy volunteers were stimulated in Tyrode buffer and incubated with steady state concentrations (in vivo) of fibrinogen or epifibatide prior to activation with TRAP (15µM). In a separate series of experiments, platelet inhibition >90% (in response to 5µM ADP) was achieved with fibrinogen or epifibatide. Recovery of platelet aggregation was determined following fibrinogen and/or platelet supplementation. Results: Platelet inhibition was reversed by the addition of fibrinogen in a concentration-dependent manner. Recovery of platelet aggregability toward a physiologic level was achieved with fibrinogen (0.76-0.80 g/L), platelets (2.1±0.1%) of their combination. The findings are summarized below.

Recovery of Platelet Aggregation (%)

Treatment	| Mean ± SD	| Platelets (x 10^11)

Fibrinogen (0.50-0.60 g/L) | 49.3±11.4 | 49.4±11.0 | 54.4±12.9 | 67.3±12.1

Fibrinogen (0.50-0.60 g/L) + Platelets (2.1±0.1%) | 49.3±11.4 | 49.4±11.0 | 54.4±12.9 | 67.3±12.1

***P<0.0001

**P<0.0001

*P<0.001

†P=0.001

‡P=0.001

§P=0.001

¶P=0.001

9:15 a.m.

346-4

Use of the PURSUIT Risk Score Can Provide Accurate Early Risk Stratification in a Nonselected, Community-Based Population With NonST Elevation Acute Myocardial Infarction

Emmanuel S. Ikfais, Stephen L. Kopercky, Brent A. Williams, Jason Vilar, Ian P. Clements. Mayo Clinic, Rochester, MN

Background: In a recent post-hoc analysis of the PURSUIT (Platelet glycoprotein Ilb/IIIa in Unstable Angina: Receptor Suppression Using Integrilin (epifibatide) Therapy) trial, a risk stratification score was proposed. Using 7 clinical parameters, worst CCS (Canadian Cardiovascular Society) class in past 2 weeks, heart rate, systolic blood pressure, signs of heart failure, and ST-depression on presenting ECG) a risk score was calculated, which showed strong association with 30-day mortality. However, patients included in the PURSUIT trial had to fulfill specific inclusion criteria. The goal of our study was to examine the predictive accuracy of the PURSUIT risk score in a community-based population with non-ST-elevation acute myocardial infarction (AMI).

Conclusions: The data in aggregate demonstrate substantial heterogeneity in troponin positive ACS patients for response to IIb/IIIa blockade. Troponin responsiveness to IIb/IIIa blockade has only been validated by retrospective analysis in ACS trials; further trials prospectively assessing the value of troponin in ACS are warranted.
Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.

Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1182-78

BEATING HEART VERSUS CONVENTIONAL CORONARY ARTERY BYPASS: EARLY VERSUS LATE POSTOPERATIVE NEUROLOGICAL COMPLICATIONS


Background. Coronary artery bypass grafting without cardiopulmonary bypass (Off-pump CABG) has been associated with comparable or lower rates of postoperative neurological complications compared to the conventional approach (On-pump CABG). It is unknown whether the timing of occurrence of neurological complications is different between these two approaches. Methods. New neurological complications were considered as a single end point and were categorized with respect to whether they were detected only early (first 2 days) or only delayed (more than 3 days) after surgery. Early neurological recovery was defined as the occurrence of early and delayed neurological complications after On-pump (>2 days) Vs. Off-pump (n=1592) between January 1990 and July 2000. The two groups were similar with respect to baseline characteristics and risk stratification; the Northern New England cardiovascular disease study group estimated risk of cerebrovascular accident was 1.9% for both groups. Results. The rate of neurological complications was 4.9% (n=104) for the On-pump group Vs. 2.7% (n=42) for the Off-pump group and stroke rate was 2.3% (n=48) Vs. 1.3% (n=21), respectively. Of patients who had neurological complications the incidence of early or delayed events between on and off pump CABG is summarized in table (all analyses were significant at the level of P<0.001). Conclusions: Among patients experiencing neurological complications after surgery, On-pump CABG patients are at a lower risk of morbidity but are at a higher risk of late postoperative neurological complications than On-pump CABG. Different mechanisms may be implicated in the pathogenesis of neurological adverse events between the two approaches.

1182-80

A LARGE UNSELECTED SERIES OF CONSECUTIVE OPCAB PATIENTS DEMONSTRATES REDUCED HOSPITAL MORTALITY AND MORBIDITY

Mark W. Connolly, Valavanur A. Subramanian, Nilesh U. Patel, John C. McCabe, Mark H. Tarkington, Salvatore Battaglia, Michael P. Macris, Sameer Mehta. Medical City Dallas, Dallas, TX, Emory University Rollins School of Public Health, Atlanta, GA

Background: The growth in off-pump CABG (OPCAB) raises questions about when it is appropriate versus an on-pump (OnP) approach. Of those surgeons who use both OPCAB and OnP techniques, what factors influence their decision? We compared surgeons who perform both OPCAB and OnP surgery to evaluate differences in patient characteristics and surgical outcomes. Methods: The 1999 HCFA Case Mix Database contains data from ~7000 and 11,000 USAB surgeries (HCFA 106, 107, and 109). For surgeons who performed 10 or more OPCAB and 10 or more OnP surgeries in 1999, we compared their OPCAB and OnP performance for 19 patient characteristics and 14 surgical outcomes. Results: Of 41 surgeons, we analyzed the data from 30 OPCAB and 78 OnP CABG surgeon groups. Surgeons did not increase for the number of bypasses underwent (see table). Patients with preop AMI were significantly more likely to be OnP and OffP patients were more likely to have neurological complications. For these surgeons, death rates OnP were more than double their OPCAB rate. Of the remaining 33 variables analyzed, none were statistically significant (p=0.55). However, acute renal failure and percentage of patients discharged directly home without further evaluation were significantly more frequent among surgeons performing both OPCAB and OnP. Conclusions: Based on this large, retrospective series of consecutive, unselected OPCAB patients, we conclude that even including conversion to CPB patients, this large, retrospective series of consecutive, unselected OPCAB patients compared to 3.1% (n=42) for CABG. As OPCAB had a higher risk profile, risk-adjusted for bleeding (1.2% vs 3.5%, p<0.02), percentage of patients transfused OPCAB (6.1 days vs 7.5 days, p=0.001). Conclusion: Even including conversion to CPB patients, this large, retrospective series of consecutive, unselected OPCAB patients achieved significantly lower hospital complications and mortality compared to conventional CABG. Methods: To prevent conversion to CPB may further improve results.

1182-81

OFF-PUMP VERSUS ON-PUMP CABG SURGERY: DETERMINANTS AND SURGICAL OUTCOMES AMONG 51 SURGEONS DOING BOTH PROCEDURES

Michael J. McKe, April W. Simon, Edmund R. Becker, Steven D. Culier, Lynn G. Tarkington, Salvatore Battaglia, Michael P. Macris, Sameer Mehta. Medical City Dallas, Dallas, TX, Emory University Rollins School of Public Health, Atlanta, GA

Background: The growth in off-pump CABG (OPCAB) raises questions about when it is appropriate versus an on-pump (OnP) approach. Of those surgeons who use both OPCAB and OnP techniques, what factors influence their decision? We compared surgeons who perform both OPCAB and OnP surgery to evaluate differences in patient characteristics and surgical outcomes. Methods: The 1999 HCFA Case Mix Database contains data from ~7000 and 11,000 USAB surgeries (HCFA 106, 107, and 109). For surgeons who performed 10 or more OPCAB and 10 or more OnP surgeries in 1999, we compared their OPCAB and OnP performance for 19 patient characteristics and 14 surgical outcomes. Results: Of 41 surgeons, we analyzed the data from 30 OPCAB and 78 OnP CABG surgeon groups. Surgeons did not increase for the number of bypasses underwent (see table). Patients with preop AMI were significantly more likely to be OnP and OffP patients were more likely to have neurological complications. For these surgeons, death rates OnP were more than double their OPCAB rate. Of the remaining 33 variables analyzed, none were statistically significant (p=0.55). However, acute renal failure and percentage of patients discharged directly home without further evaluation were significantly more frequent among surgeons performing both OPCAB and OnP. Conclusions: Based on this large, retrospective series of consecutive, unselected OPCAB patients, we conclude that even including conversion to CPB patients, this large, retrospective series of consecutive, unselected OPCAB patients compared to 3.1% (n=42) for CABG. As OPCAB had a higher risk profile, risk-adjusted for bleeding (1.2% vs 3.5%, p<0.02), percentage of patients transfused OPCAB (6.1 days vs 7.5 days, p=0.001). Conclusion: Even including conversion to CPB patients, this large, retrospective series of consecutive, unselected OPCAB patients achieved significantly lower hospital complications and mortality compared to conventional CABG. Methods: To prevent conversion to CPB may further improve results.
Results: During this time period, 1537 bypass procedures were performed, 303 were done without cardiopulmonary bypass. Of these, 226 were performed for isolated LAD disease. The incidences of postoperative complications for MIDCAB vs. OPCAB were as follows: mortality, 1.86% vs. 1.40% (p = 0.51); stroke, 2.05% vs. 0.32% (p = 0.05); myocardial infarction, 0.64% vs. 0.0 (p = 0.17); atrial fibrillation, 3.21% vs. 2.5% (p = 0.06); infection, 1.28% vs. 0 (p = 0.03); neurologic events, 0.64% vs. 2.89% (p = 0.22); renal failure, 0.04% vs. 1.42% (p = 0.4); prolonged ventilation 0 vs. 1.15% (p = 0.17); atrial flutter/AF, 3.21% vs. 0.0 (p = 0.02); mortality, 0.64% vs. 2.88% (p = 0.09). The postoperative lengths of stay for the MIDCAB vs. OPCAB groups was 3.91 ± 3.34 days vs. 4.45 ± 2.24 days.

Conclusions: Our experience with minimally invasive surgery shows there is no clinically significant difference between MIDCAB and OPCAB approaches. Although some have claimed an advantage with the MIDCAB technique with respect to patient recovery and outcomes, our raw data would suggest a trend toward less morbidity with the CABIG method. Prospective randomized trials will further delineate this issue.

POSTER SESSION

1183 Myocardial Preservation: Mechanistic Insights
Tuesday, March 20, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A1 Presentation Hour: 10:00 a.m.-11:00 a.m.

1183-84 Protective Effects of Adenosine on Myocardial Infarction and Reperfusion in the Dogs
Habib Aschner, Al Unnati, A. Assi, James Armin, Harry Yell, Maximilian Igoa,
Margaret Utman, Richard W. Smalling. University of Texas Medical School, Houston, TX

Background: Although intracoronary adenosine has been shown to improve angiographic evidence of coronary blood flow post reperfusion in humans, its physiologic and mechanistic nature of action is unknown at the present time.

Objective: To evaluate the effect of intracoronary adenosine on tissue prior to reperfusion and its effect on white blood cell (WBC) activation and LAD coronary artery following four hours of reperfusion.

Methods: Fourteen open chest dogs were subjected to two hours occlusion of mid left anterior descending (LAD) artery followed by four hours of reperfusion. The dogs were instrumented with somatic crystals measuring coronary blood flow in LAD artery and circumflex (CX) regions. Hemodynamic measurements were done at baseline, ten minutes after occlusion, and then the first hour until the end of the experiment.

Conclusion: Twenty four micrograms of adenosine were injected over two minutes distal to the reperfusion. Hearts with intact glycolysis and normal substrates (glucose, lactate, palmitate) (Sham-Control [n=10] and Ml-Control [n=10]) were compared to hearts with blocked glycolysis (Sham-Glyc [n=10] and Ml-Glyc [n=10]). Myeloperoxidase production (WBC count) was significantly lower in the infarct and ischemic regions with the adenosine group compared to the adenosine group (P=0.001). ICAM-1 expression, end diastolic wall thickness (EDWT) and infarct size.

Results: Com-

1183-85 Cardioprotection by an Adenosine A2A Receptor Agonist in a Canine Model of Myocardial Stunning Produced by Multiple Episodes of Transient Ischemia
David K. Glover, Mirta Ruiz, Kazuya Takehana, Frank D. Petrussa, Jayson M. Beiger, Timothy L. Macdonald, Danny D. Watson, Joel Lindon, George A. Reiber. University of Virginia, Charlottesville, VA

Background: Stimulation of adenosine A2A receptors on inflammatory cells is inhibitory. We hypothesized that infusion of a highly potent and selective adenosine A2A agonist, ATL-146e, would inhibit post-ischemic cardiac inflammation and therefore improve left ventricular function of myocardial stunning in a separate series of hearts.

Methods: ACC/AHA guidelines were followed. Fourteen open chest dogs underwent either 5 or 10 cycles of 5 minute left anterior descending coronary artery (LAD) occlusions (OV=5 min; REP=10 min) and 10 cycles of 5 minute left anterior descending coronary artery (LAD) occlusions (OV=5 min; REP=10 min) and 10 cycles of 5 minute left anterior descending coronary artery (LAD) occlusions (OV=5 min; REP=10 min). Left ventricular function was measured with ultrasonic crystals beginning at baseline and continuing for 160 minutes after the last occlusion/reperfusion cycle. Regional flow was measured with microspheres. In 11 of the 22 dogs, ATL-146e was infused i.e. prior to occlusion 1 and continued throughout reperfusion at a dose below that which produces vasodilation (0.01 mg/kg/min).

Results: Myocardial flow was similar between control and ATL-146e treated animals at all times, confirming the absence of vasodilation. During occlusion, there was severe dysfunction with marked LAD zone thinning in all animals. As shown in the table, there was significantly greater recovery of LAD zone thickening after reperfusion with ATL-146e in both the 5 (96% vs 91%) and 10 cycle (55% vs 59%) reperfusion experiments.

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Pretreatment With Delta-Opioid Receptor Blockade Attenuates the Reduction of Apoptosis Associated With Ischemic Preconditioning or Morphine-Induced Cardioprotection in Rabbit Ischemia/Reperfusion Model

Shinya Okubo, Yujirou Tanabe, Nakaba Fujioka, Noboru Takekoshi, Rakesh C Kukreja. Kanazawa Medical University, Uchinada, Japan

We have proposed that myocardial protection associated with ischemic preconditioning (IPC) or morphine-induced cardioprotection (mORI) involves the activation of a G protein-coupled receptor (delta-opioid receptor (DOR)). In the present study, we examined whether the delta-opioid receptor can regulate apoptosis in cardiac cells.

Methods: DOR agonists and antagonists were administered 15 min before sustained ischemia (n=8) or reperfusion (n=8). Survival rate, infarct size, and cardiac troponin I (cTnI) levels were measured.

Results: Pretreatment with the DOR agonist [D-Pen(2,5)-enkephalin (DPDE)] significantly increased survival rate and reduced infarct size and cTnI levels compared to untreated controls. Pretreatment with the DOR antagonist [D-Pen(2,5)-enkephalin (DPDE)] significantly decreased survival rate and increased infarct size and cTnI levels compared to untreated controls. Pretreatment with the DOR antagonist [D-Pen(2,5)-enkephalin (DPDE)] significantly decreased survival rate and increased infarct size and cTnI levels compared to untreated controls.

Conclusions: These findings suggest that the DOR plays an important role in the regulation of apoptosis in cardiac cells. Further studies are needed to elucidate the mechanism by which the DOR regulates apoptosis in cardiac cells.

JACC February 2001

POSTER SESSION

1183-88 Intravenous Use of Dimethylsulfoxide to Improve Outcome of Acute Myocardial Ischemia in a Porcine Model

Donnie W. Dunn, George Evstey, Kevin L. Kolo, Echo Hansen, Earl T. Hawkins, Shirley Siew, Cronin, William W. O'Neill, William Beaumont Hospital, Royal Oak, MI

Background: Ischemia by tissue perfusion is the mainstay of therapy to reduce necrosis in an acute myocardial infarct (AMI). Blood and O2 returning to injured tissue can lead to further cellular damage and lethal arrhythmias. We hypothesized that treatment with dimethylsulfoxide (DMSO), an antioxidant, anti-inflammatory, and membrane stabilizer, would improve outcome in AMI. Methods: We created myocardial ischemia in 3 pigs by 30 minute inflation of an intra-coronary balloon in the distal RCA. One group served as controls and 2 treatment groups received intravenous (IV) DMSO as a pre-treatment (early group) or 15 minutes after the start of balloon inflation (late group). ECG and arterial BP were monitored during the procedure. Two-D echocardiograms were done before the cath and ~30 minutes after balloon deflation. After 48 hours the hearts were harvested and stained with triphenyltetrazolium chloride (TTC) to determine areas of necrosis and myocardial at risk. Results: The combined end-point of VF or VT during reperfusion was higher in controls (77.8%) than either treatment group (early 28% and late 0%, p=0.018). Further analysis showed the difference to be most significant in the late group (p=0.002). ST segment change in the early group was less vs controls (2 mm vs 4.22 mm, P=0.043). Wall motion index was increased similarly in early and control groups, but less in the late group (P=0.003). Blood pressure did not decrease with DMSO. Conclusions: IV DMSO may be useful in limiting myocardial necrosis and arrhythmias during tissue reperfusion. The protection against cell death is greatest when given as a pre-treatment before the onset of ischemia, but benefits extend to late treatment as well.

1183-89 Diazoxide Preserves Oxidative Phosphorylation and the Structural Integrity of Cardiac Mitochondria From Anoxic Injury

Cevher Ozcan, Ekhoon L Holm-Hansen, Arshad Jahangir, Andre Terzic. Mayo Clinic, Rochester, MN

Background: Myocardial anergocity, which primarily rely on oxidative phosphorylation, are highly vulnerable to anoxia. Mitochondrial ATP-sensing potassium channel (mKATP) openers have emerged as powerful cardioprotective agents, yet direct evidence attesting their ability to open mKATP in mitochondria against ischemic injury is lacking. Methods: Mitochondria were isolated from rat hearts, subjected to 20 min anoxia followed by reoxygenation, and mitochondrial function and structure were evaluated by respiration rate (p-value), ATP content, and electron microscopy. Results: In the absence of a potassium channel opener, anoxia/reoxygenation decreased the rate of ATP-depleted oxygen consumption, inhibited ATP production and disrupted mitochondrial membrane integrity (Tmavana, ongoing study). ATP-stimulated oxygen consumption, which occurs under normal ATP conditions, was dependent on the rate of ATP production from 75% to 41.4% and ATP production from 84% to 68%.

1184-90 Strain Imaging in Patients With Chronic Total Right Coronary Occlusion

SOO-T suk Lim, Pamela Mazarov, William W. O'Neill, James A. Goldstein. William Beaumont Hospital, Royal Oak, MI

Background: Right coronary artery (RCA) stenosis is common in patients with chronic total right coronary occlusion (RCA). The role of strain imaging in assessing the presence of collaterals and the effect of pharmacological or interventional revascularization on their viability remains unclear. The aim of this study was to evaluate the usefulness of strain imaging in patients with chronic total right coronary occlusion.

Methods: Strain imaging was performed in 17 patients with chronic total right coronary occlusion. RV free wall (RVFW) strain was assessed using two-dimensional speckle-tracking echocardiography. Results: RVFW strain was significantly lower in patients with chronic coronary occlusion compared to controls. In patients with chronic total right coronary occlusion, RVFW strain was significantly lower compared to controls. In patients with chronic total right coronary occlusion, RVFW strain was significantly lower compared to controls. In patients with chronic total right coronary occlusion, RVFW strain was significantly lower compared to controls. In patients with chronic total right coronary occlusion, RVFW strain was significantly lower compared to controls.

Conclusions: Strain imaging is a useful tool for assessing the presence of collaterals and the effect of pharmacological or interventional revascularization on their viability in patients with chronic total right coronary occlusion.
Discriminant index, indicating the capability of each sensor the patient subgroups than in the control group (all pcO.005). In the control group the ST slope at left side separated the CAD group from controls with sensitivity of 96% and specificity of 76%. Over the back at cut off value -600 uV/s the corresponding values were 69% (95% CI 58-79) and 70% (95% CI 60-80). The indicator is best exploited with BSPM, covering areas outside the conventional 12 lead ECG. The indicator is best exploited with BSPM, covering areas outside the conventional 12 lead ECG. The indicator is best exploited with BSPM, covering areas outside the conventional 12 lead ECG. The indicator is best exploited with BSPM, covering areas outside the conventional 12 lead ECG.
value of 70%. Conclusion Thus, an elevated troponin I is a sensitive but only moderately specific marker for the presence of complex lesions confirming a relationship between thrombotic-appearing lesions and elevated troponin. However, 24 of 82 complex lesions (29%) are not associated with an elevated troponin. These data expand on prior studies suggesting that an elevated troponin may be a marker of either distal embolization of thrombotic material or other mechanisms resulting in transient saturations in myocardial oxygen supply leading to myocardial necrosis. Why some complex lesions do not elevate troponin requires further investigation.

<table>
<thead>
<tr>
<th>Elevated</th>
<th>Troponin I</th>
<th>Normal</th>
<th>Troponin I</th>
<th>P-Value</th>
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<tbody>
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<td>N</td>
<td>123</td>
<td>90</td>
<td>32</td>
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<td>Complex</td>
<td>58 (71%)</td>
<td>24 (30%)</td>
<td>&lt;0.0001</td>
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<tr>
<td>Non-Complex</td>
<td>24 (29%)</td>
<td>56 (70%)</td>
<td>&lt;0.0001</td>
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</tr>
</tbody>
</table>

### 118D-08 Soluble Thrombomodulin Is Elevated in Postmenopausal Women with Acute Coronary Syndrome But Is Not Associated With Adverse Outcomes Nor Affected by Short Term Estrogen Therapy

Eric T. Chou, Steven P. Schultz, David R. Thirman, Michelle F. Bellantoni, Jeffrey J. Davis. Johns Hopkins School of Medicine, Baltimore, MD; Weill Medical College of Cornell University, New York, NY

Soluble thrombomodulin (sTM) is a marker of endothelial injury and may predict future coronary events. Short term estrogen replacement therapy (ERT) has been shown to reduce endothelial cell function in postmenopausal women with coronary artery disease as well as to decrease STM levels in women without coronary disease. We retrospectively studied the effects of short-term ERT on sTM in postmenopausal women, non-receiving ERT, who presented with either unstable angina or non-Q MI. Serum sTM levels were determined by ELISA in 70 postmenopausal women (mean age 69 years) with either unstable angina or non-Q MI, who were randomized to receive conjugated estrogen (1.25 mg) followed by oral conjugated estrogen (1.25 mg progestrone daily) for 21 days. Baseline sTM was compared to a cohort of 32 healthy postmenopausal age-matched controls not receiving ERT. All patients were followed clinically for six months. Results: Baseline sTM in patients with acute coronary syndromes was significantly elevated compared to healthy age-matched controls (4.6 ± 2.4 vs. 3.1 ± 0.9 ng/ml, p<0.001, respectively). Baseline sTM did not correlate with recurrent ischemia, as assessed by holter monitoring, nor was it associated with the combined endpoints of death, recurrent MI, or need for revascularisation over a six month follow-up period. Furthermore, short term ERT did not significantly alter sTM levels compared to those observed in patients not receiving ERT (Delta sTM 0.2 ± 1.4 vs. 0.2 ± 0.3 ng/ml for placebo (n=11), p=0.6). Conclusion: Soluble thrombomodulin is elevated in postmenopausal women with acute coronary syndromes but is not associated with adverse cardiac outcomes not significantly altered by short term estrogen therapy.
therapy has produced mixed and unsatisfying results, the adjunct & administration of
from the LIMIT trial of rhuMAb CD18 (anti WBC ab) rn AMI. Adjunctive stenting was done
at the discretion of the investigator. The Myocaridal Perfusion Grade (MPG) was
Background: Stenting has been shown to increase epicardial flow in AMI, & the goal of
assessed & digital subtraction angiography (DSA) was used to quantify brightness of the
6.8 + 8.5, n=68, p=0.16). However, post-stent blush was not as bright as blush in normal
stenting in AMI improves epicardial TIMI 3 flow & TIMI frame counts as well as dye inflow
TIMI Myocardial Perfusion Grade Pre and Post-stent
mpg 0.5 19.3%, 23/118 21.9%, 26/118 NS
mpg 0 25.2%, 29/118 4.3%, 16/118 0.03
major lumen diameter-MLD >2 mm 4.51 0.23 0.07-0.69
abciximab use 9.03 0.25 1.0-6.62
Stent Use 5.93 0.36 0.13-9.88
% Diabetes Mellitus 7.70 1.11 1.0-1.17
Total Infarction Time 17.61 1.37 1.10-1.71

1186-77 Impact of Stent Use Following Thrombolytic Administration on the TIMI Myocardial Perfusion Grades in Acute MI
C. Michael Gibson, Kenneth W. Baron, Michael Nguyen, George R. McConnell, Costas T.
Island Hospital, Providence, RI
Background: Stenting has been shown to increase epicardial flow in AMI, & the goal of
this study was to quantify improvements in myocardial perfusion. Methods: Data are from the LIMIT trial of madulodiol (anti PLCβ in AMI). Adjunctive stenting was done
at the discretion of the investigator. The myocardial perfusion grade (MPG) was
assessed & digital subtraction angiography (DSA) was used to quantify brightness of the
myocardial blush. Results: TIM I flow was 54.2% (64/118) stent, & 67.2% post (92/136)
(p=0.03). By DSA, there was a trend toward brighter blush post-stent than pre (9.4 ± 6.7 Gray, m=0.8 ± 6.8, ns vs. 6.7, p=0.16). However, post-stent blush was not as bright as blush in normal
patients without coronary stenoses (10 ± 5.7, m=6.5, p<0.001).
Conclusion: Adjunctive stenting in AMI improves epicardial TIMI flow & TIMI frame counts as well as dye inflow
into the myocardium. MPG O is reduced & myocardial blush measured quantitatively by
DSA tends to be brighter. However, blush intensity is increased (more MPG O in uo staining
present on next injection), possibly due to embolus, spasm or capillary leak.

Adjunctive Thrombolytic Therapy With or Without Glycoprotein IIb/IIIa Inhibition Prior to Percutaneous Coronary Intervention In Acute Myocardial Infarction
Steven B. H. Tamimi, Gerald C. Tamimi, Michael S. Flynn, Mark C. Pica, Simon R. Dixon, Robert B. Tobin, William W. O'Neill, William Beaumont Hospital, Royal Oak, MI, Naipeabus Community Hospital, Naples, Fl
Background: While percutaneous coronary intervention (PCI) following thrombolytic therapy has produced mixed and unsatisfying results, the adjunctive administration of glycoprotein (GP) IIb/IIIa inhibitors with half-dose reteplase may improve subsequent primary
PCI outcomes.
Methods: 160 patients admitted to one of three community hospitals in Naples, Florida, with acute MI were enrolled into this registry. Forty-seven patients were treated with half-dose reteplase and IV GP IIb/IIIa inhibitors (operator’s choice) while 113 subjects received IV GP IIb/IIIa Inhibitors alone. Patients subsequently underwent urgent cardiac catheterization.
Results: Baseline demographics were similar for both groups. Time from treatment to cardiac catheterization was unaffected by group assignment (-140 min). Preliminary angiographic data demonstrated TIMI 2-3 patency in 67% of patients treated with combi-
ined reteplase/GP IIb/IIIa inhibitor compared to 44% of those received GP IIb/IIIa inhibitors alone before PCI (p = .17). Following PCI, 100% of patients in both groups achieved TIMI 2-3 patency. The final percutaneous stenting was 9.3% in the group receiving combined therapy compared to 11.4% in the cohort treated with GP IIb/IIIa inhibitor alone (p = .42). Litt� ventricular ejection fraction was 51% vs. 52%, respectively (p = .456).
Conclusions: This initial experience suggests that combined half-dose thrombolytic therapy and GP IIb/IIIa inhibition before primary PCI for acute myocardial infarction enhances early reopening rate and improves pretreatment with GP IIb/IIIa inhibitors alone. The final angiographic results after primary PCI were equally good with both treatment strategies.
855-1 Medication Errors and Outcomes With Fixed Double-Bolus r-PA Versus Dose-Weighted Adjustment Infusion t-PA
Fibrinolysis: The GUSTO-III Experience
Shannon G. Goodman, Amaia Barr, Christopher Granter, Magnus Ohman, Alyson Lanzer, Paul Armstrong, Brian Glibler, Eric Topol. Canadian Heart Research Centre, Toronto, ON, Canada, Duke University Medical Center, Durham, NC

Background: It has been suggested that fibrinolytic dosing errors result in higher rates of intracranial hemorrhage (ICH) and death and use of lytics may result in lead to improved outcome; however, the relationship between dosing error and outcome has also been reported to be primarily due to confounding factors rather than to the dosing error itself. A small retrospective review (n=500) comparing r-PA (fixed double-bolus) and t-PA (bolus + weight-adjusted infusion) found fewer errors with r-PA, but a similar comparison derived from the only large randomized trial (GUSTO-III; n=12,500) examining patient (pt) outcomes has not been reported.

Methods: Medication errors were defined for r-PA patients who received study lytic (n=14,756) in GUSTO-III were defined for r-PA (n=4,834) and t-PA (n=9,932) comparison derived from the only large randomized trial (GUSTO-III; n=15,059) examining pt outcomes. Early discont. (n=126; p=0.04) among older patients with AMI. The aim of this study was to determine whether the use of evidence-based therapies improves survival in elderly Medicare patients. Information about the change in use of these therapies over time is critical for AMI care from the Medicare Health Care Quality Improvement Program. The aim of this study was to determine whether the use of evidence-based therapies improves survival in elderly Medicare patients. Information about the change in use of these therapies over time is critical for AMI care from the Medicare Health Care Quality Improvement Program.

Conclusions: While medical error analyses are confounded (e.g. early discont. in pts who die is not really a medical error), randomized trial data remains the best way to examine the impact of different lytic strategies on clinical outcomes. In GUSTO-III, regardless of which lytic was used, medication errors were associated with worse outcomes; however, increased rates of errors seen with t-PA were not associated with higher adverse event rates when compared with r-PA.

855-2 High-Risk Direct Infarct Intervention Using IABP Support: Does It Make a Difference?
Robert M. Siegel, Ambika Bhaskaran, Warren Breidbart, Barbara Barfer, Alvin Nultsch, Deborah Frazer, Jennifer Vermillion, Greg Ellis, Scott Olson, Jennifer Carson. Advanced Cardiac Specialists, Gilbert /Phoenix, AZ

Background: Clinical outcomes in acute MI have shown encouraging improvement since the advent of direct coronary intervention (D-PTCA). The goal of D-PTCA in high-risk clinical subsets persists. Adjunctive IABP use for mechanical circulatory support in high-risk D-PTCA may improve outcomes by decreasing pre- and post-load, promoting hemodynamic stabilization and diastolic augmentation of flow through the inter-related artery, leading to reduced remodeling and improved LV function in the long term. Methods: We compared acute and long-term clinical outcomes in 1,937 high-risk (TIMI criteria: 0-1) patients who underwent D-PTCA within 24 hours of onset of acute MI. Of them, 430 (22%) received IABP and 667 did not (non-IABP group). The incidence of cardiogenic shock was higher (20% vs. 15%, p<0.001) and mean global LVEF was lower (58% vs. 61%, p=0.001) in the IABP group. Hypertension (p=0.009) was more frequent in the non-IABP group. Both groups were well-matched for all other clinical and angiographic variables. Results: Procedural success was higher in the IABP group (99% vs 96%, p=0.004). In hospital complications were lower in the IABP group (p=0.001), although mean hospital length of stay was longer (23.4+2.6 days vs. 9.1+2.6 days). During follow-up (mean 11.3 months), target lesion revascularization rates were comparable (11.6% IABP vs 9% non-IABP; p=0.39). Mortality was significantly lower (2.3% vs 6.1%; p=0.02) and cardiac event-free survival significantly higher (98% vs 89%, p=0.045). In the IABP group, Mean rise in LVEF was higher in the IABP group (8% vs. 4%, p=0.012). Conclusions: In this series of D-PTCA in high-risk subset, patients with more severe/several presentation received IABP support despite this, the IABP group demonstrated significantly higher procedural success, lower in-hospital complications and lower incidence of MACCE during long-term follow-up. This translated into significantly greater survival in the IABP group. These findings may have important implications for future management strategies in high-risk D-PTCA. The myriad benefits of IABP appear to be critical not just for improved in-hospital outcomes, but also for long-term absolute and event-free survival.

855-3 Higher Coronary Intervention Following Acute MI Associated With Lower Rates of Evidence-Based Medical Therapy in Regions of North America: Results From ASSENT II
Maria Cecilia Bahit, John H. Alexander, Guadym Tassada, Paul W. Armstrong, Robert M. Califf, Christopher B. Granger. Duke Clinical Research Institute, Durham, NC

Background: Randomized clinical trials and clinical practice guidelines have provided clear evidence that certain medications improve survival in patients with ST elevation myocardial infarction (MI). The aim of this study was to determine whether the use of evidence-based medical therapies is based on the procedures and practice patterns of providers across North America (USA) for patients with ST elevation MI. Methods: We used the database of the ASSENT II trial, which compared TIMI-IIIA 14-hour t-PA in patients with MI, we assessed patients enrolled in N.A. We examined the use of aspirin, beta-blockers (BB), ACE-I, angiotensin receptor blockers (ARB), and statins. Results: The use of aspirin was uniformly high (93% vs 97%). The use of cardiac procedures generally was inversely related to the use of evidence-based medications, for example, the central US has the highest rate of POI, lowest use of beta-blockers and ACE-I, and shorter LOS. On the other hand, Canada and New England had the highest use of ACE-I and beta-blockers, respectively.

Conclusions: There was wide variation in both coronary interventions and the use of evidence-based medical therapies in North America. Differences in regional practice patterns were significant. Differences across regions were substantial and may be related to differences in patient and hospital characteristics, reimbursement policies, and physician preferences. Future research should examine these factors to understand the basis for these differences.
Background. Young African Americans with acute myocardial infarction reportedly have higher short-term mortality than Whites of similar age. However, the relationship of younger age with increased short-term mortality in African Americans, and the influence of demographic, clinical and treatment factors on this relationship have not been explored in detail. Method. We analyzed the patient characteristics and mortality data of 558,272 patients enrolled in the National Registry of Myocardial Infarction-2 who were 90 years or younger and had confirmed myocardial infarction (40,903 African Americans and 352,352 Whites). Results. The overall mortality was slightly lower among African Americans younger than 65 years of age compared to Whites (9.2% vs. 10.1%, p<0.0001). Age and race were independent predictors of mortality. Each 5 year decrement in age was associated with 7.2% higher odds of death in African Americans (95% confidence intervals 5.7% - 7.7%) compared to Whites. Moreover, there was substantial variation between African Americans and Whites in different patient characteristics. These variations were found to account for only a quarter of the higher risk of death in African Americans on multivariate analysis (5.4% increased odds for death after adjustments, 95% confidence intervals 3.6% - 7.2%). Conclusion. Younger African Americans have a higher short-term mortality compared to Whites of similar age following an acute myocardial infarction.
Patients: Thirty patients (23 men) were randomized to a 2:1 treatment:control ratio. Treatment included 201-19 adenosin via the aorta. Results: A dose of 201-19 was used via the aorta.

Methods: We performed a crossover design study in 20 patients (13 men) with coronary artery disease. The study was performed to determine if GIK reduces microvascular dysfunction, myocardial infarct size, and ischemia-reperfusion arrhythmias.

Conclusions: GIK infusion results in a significant reduction in free fatty acid levels indicating a metabolic effect. GIK did not improve GFR at 60 minutes or reduce ischemia-reperfusion arrhythmias. Myocardial infarct size and left ventricular function at 28 days was unchanged by GIK infusion.
Therefore, this natriuretic peptide should reasonably be included in the routine clinical work up of patients after myocardial infarction. Plasma NT-proBNP measured 60 min after reperfusion was superior to plasma catecholamines. So far, however, neither time-course nor predictive value of NT-proBNP plasma concentrations has been prospectively evaluated in patients undergoing successful reperfusion by primary PCI. Methods: Therefore, we conducted a prospective study in 118 consecutive patients with acute myocardial infarction receiving successful reperfusion, THYR, n=8 and NORM, n=6. PC hearts after the stabilization period, underwent 3 cycles of PC consisting of 5 min of I and 5 min of R, NORM 2PC, n=6 and THYR 2PC, n=6. Hearts from normal and THYR rats were also subjected to additional 2 cycles of PC consisting of 5 min of I and 5 min of R, NORM 4PC, n=6 and THYR 4PC, n=6. The induction of HSP70 mRNA in THYR 2PC was 2-fold lower than in THYR 4PC hearts, p<0.05. Basal PKCβ expression was 1.7 fold more in the normal as compared to the hyperthyroid hearts, p<0.05. Conclusions: Thyroxine administration decreases the HSP70 mRNA expression induced by ischemic preconditioning. This mechanism through diminished phosphorylation of p38 MAP kinase, because of repressed PKCβ expression, is being proven for the first time.

Predictive Value of NT-proBNP in 118 Patients with Acute Myocardial Infarction Undergoing Primary Angioplasty


Background: In acute myocardial infarction predictive value of the degree of neurohumoral activation is well established. Recently, the natriuretic-peptide metabolite NT-proBnp received interest as prognostic marker, which is possibly superior to plasma c-peptides. So far, however, neither time-course nor predictive value of NT-proBNP plasma concentrations has been prospectively evaluated in patients undergoing successful reperfusion by primary PCI. Methods: Therefore, we conducted a prospective study in 118 consecutive patients with acute myocardial infarction receiving successful reperfusion (TIMI 2 and 3) by primary PCI. Plasma NT-proBNP was determined hourly during the first 4 hours after infarction and compared to established postinfarction risk markers. Follow-up was performed for 18-36 months recording major cardiac events, defined as cardiac death, reinfarction, ventricular fibrillation or hospitalization for heart failure. Results: Patients were 64±12 years old; 68% were men. During follow-up, 174 CAD patients died (48% died within 60 days). The highest NT-proBNP values were measured at 0 and 60 minutes after reperfusion and correlated to established postinfarction risk markers. Follow-up was performed for up to 5 years (mean, 2.0±1.4). Associations with death were measured using Cox regression. Conclusions: Plasma NT-proBNP measured 60 min after reperfusion was superior to plasma catecholamines and LVEF in predicting event-free survival. Stratification of patients into low- and high-risk groups can be facilitated by early plasma NT-proBNP measurements. Therefore, this natriuretic peptide should reasonably be included in the routine clinical work up of patients after myocardial infarction.
was preserved for CRP and the 5 CAD measures. In multivariate analyses, significance was retained for CRP (p<.001), number of severe vessels (p=.002), total lesions (p=.01), and severe lesions (p=.00). Results were similar for the combined endpoint of death/myocardial infarction.

**Conclusions:** CRP correlated with several measures of extent and severity of CAD at admission, but the degree of correlation was low, suggesting the importance of additional factors. During follow-up, both CRP and selected measures of CAD retained independent predictive value. CRP and CAD correlate partially, but each retains significant independent predictive value.

### 1218-65 Percutaneous intervention in unstable plaques: The significance of temperature measurement in prognosis

**Christodouli I. Stefanadis, Konstantinos Toutouzas, Eleftherios Tsiamis, Costas Stratos, Ioannis Kallikazaros, Manolis Vavuranakis, Costas Tentolouris, Dorothea Tzelepis, Vassilis Toutouzas, Hippokration Hospital, Athens, Greece**

**Background:** Previous studies have shown that local temperature is increased in unstable plaques. The aim of the present study was to evaluate the significance of increased temperature of culprit lesions in patients suffering from acute coronary syndromes, undergoing successful percutaneous revascularisation. **Methods:** In the study we included 56 patients, mean age 61±29 years, suffering from unstable angina or acute myocardial infarction. All patients underwent balloon angioplasty, in order to accomplish TIMI III flow. Thereafter, using a thermography catheter previously validated, we measured the temperature difference (ΔT) between the atherosclerotic plaque and the healthy vessel wall. Optimal angiographic result was achieved with the deployment of a stent. All patients were followed-up clinically for 17.5±5.2 months for an adverse cardiac event. **Results:** Baseline angiographic characteristics and platelet aggregation test results were performed in all patients, without complications. The mean ΔT was 0.8±0.5°C. Seventeen patients suffered from an adverse cardiac event during the follow-up period. Patients with adverse cardiac events were older, had higher levels of CRP and D-dimer, and a lower use of drugs, compared to patients without events. ΔT: 0.59±0.37°C vs. 1.02±0.42°C; p<0.001. The risk for an adverse cardiac event was increased in patients with >3°C plaques (odds ratio: 2.01). This difference was mainly attributable to patients with unstable angina. **Conclusions:** During the mid-term follow-up period, adverse cardiac events are more likely to present to patients undergoing percutaneous intervention with unstable plaques, which have increased local temperature. Accordingly, these patients may require additional treatment, in order to stabilise the unstable atherosclerotic plaques and thus improve the mid-term clinical outcome.

### 1218-66 Chlamydia Pneumoniae and inflammatory markers in acute coronary syndrome: 12 Months Outcome

**Harri H. Chantry, Nivedita Choudhary, Carol ONeill, Marcus J. Zervos, Judith Beurs, Gerald C. Timmis, William W. ONeill, William Beaumont Hospital, Royal Oak, MI**

**Background:** The role of infection with Chlamydia Pneumoniae (CP) and inflammation in coronary artery disease is controversial. There is a paucity of prospective data regarding its significance in populations at high risk for cardiac events. **Method:** We conducted a prospective study on 418 consecutive patients (mean age 65±13 yrs, 63% males) with no confounding co-morbidities who presented to a chest pain unit in Detroit from December 1997 to June 1999 and were diagnosed with acute coronary syndrome (ACS). Pertinent clinical and laboratory data were obtained at the time of admission. At 12 month the incidence of major adverse cardiac events (MACE) was ascertained (death, MI, and revascularisation). Data were analyzed to assess the association between MACE at 12 months and baseline systemic markers of inflammation including high sensitivity C-reactive protein (CRP) and IgG titres against CP. **Results:** 80% of the patients were seropositive to CP (IgG ≥ 1:64). At 12 months there were 116 MACE (28%) which included 35 deaths (8.4%), 21 MI (5%) and 64 revascularisation (15%). Patients with CP had higher levels of CRP and ubiquitously (p=0.01). The 6-month mortality rates were lower after procedure-related compared with spontaneous revascularisation (21% vs. 32%; p=0.04). The relative increase in 6-month mortality with each increase in the category of peak CRP level was of the same magnitude as all tests for heterogeneity of the odds ratios across strata. **Conclusion:** The dose-response relationship between the magnitude of post-procedural CK-MB elevation and the risk of death after 6-month follow-up with the relationship between the peak of CK-MB elevation and mortality in patients with acute coronary syndromes (ACS) without STElevation treated medically.
Background: Acute coronary syndromes are the result of atherosclerotic plaque rupture, which may be induced by local excision of matrix metalloproteinases (MMPs). Thus, an inflammatory process may be involved in plaque rupture. The aim of the present study was to investigate the association between inflammation, as it is estimated by the measurement of MMPs' plasma and serum level and the temperature of the atherosclerotic plaques in patients with acute coronary syndromes.

Methods: We used sandwich enzyme immunoassay and we measured serum MMP-2 and plasma MMP-9 in 15 patients suffering from acute coronary syndrome (10 with acute myocardial infarction and 5 with unstable angina) and in 17 with stable effort angina. A thermography catheter, which was developed in our institution, was used in order to measure temperature differences (ΔT) between the two atherosclerotic plaque and the normal wall vessel. Results: Patients with acute coronary syndromes had elevated MMP-9 compared to patients with effort angina (table). There was no difference in MMP-2 concentration between the two groups. Patients with acute coronary syndromes had greater ΔT compared to patients with effort angina. A good correlation was detected between MMP-9 concentration and ΔT in patients with acute coronary syndromes (P < 0.05, r = 0.62). Conclusions: Patients with acute coronary syndromes had increased concentration of plasma MMP-9, which was well correlated with ΔT. This finding suggests, that plaque rupture may be due to an inflammatory process, leading to increased temperature of the culprit atherosclerotic plaque.

Lipid > 0.6 mm²

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<td>MMP-9 (ng/ml)</td>
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Identification of Lipid-Rich Plaques in Human Coronary Artery Autopsy Specimens by Near-Infrared Spectroscopy


Background: A method is needed to identify non-stenotic, lipid-rich coronary plaques that are likely to cause acute coronary events. Near-infrared spectroscopy (NIRS) can provide information on the chemical composition of tissue, and could be adapted for viable plaque identification in living patients. Methods: We tested the ability of NIR to identify lipiddense coronary plaques in 146 arterial sections from 14 cadaver hearts. Sections were stained with wheat germ agglutinin (WGA) to visualize lipid regions.

<table>
<thead>
<tr>
<th></th>
<th>NIR (+)</th>
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Reperfusion Imaging in Anterior Myocardial Infarction. The Open Perforator Hypothesis

Paolo Voci, Enrica Milana, Francesco Rizatto, Francesco Monti, Giannetta Plaustro, Giovanni Testa, Mario Cardini, Paolo E. Puddu. Section of Cardiology II University of Roma "La Sapienza", Rome, Italy. "Cafer" Military Hospital, Rome, Italy

Background. The TIMI flow scale may not reflect the adequacy of myocardial reperfusion after myocardial infarction (MI). High-resolution transthoracic color-Doppler allows to image the left anterior descending coronary artery (LAD) and its perforating branches in anterior MI. We have assessed the impact of open LAD and perforators on recovery of left ventricular function after MI. Methods. We have studied 53 unselected patients (40 M, 13 F, age 68±13 years, weight 76±12 kg) with anterior MI undergoing thrombolytic (24 pts), primary LAD stenting (18 pts) or none (11 pts). Reperfusion imaging was performed by a 7MHz probe connected to an Acuson Sequoia C256 ultrasound unit. The mid-distal tract of the LAD and perforators in 4 segments of the anterior apical wall (mid anterior, apical anterior, apical lateral, septal lateral) were imaged. Reperfusion score was: 1: LAD closed, no perforators; 2: LAD open, no perforators; 3: LAD open 1-2 segments with perforators; 4: LAD open, 3-4 segments with perforators. Wall motion score index (WMSI), ejection fraction (EF), end-diastolic volume index (EDV) and end-systolic volume index (ESVi) were measured at baseline and 3 months follow-up (90 pts). Coronary angiography was used to assess TIMI flow. The linear regression method was used to describe the relationship between perfusion score and WMSI, EF, EDVI, ESVI. The sensitivity of color-Doppler to detect LAD patency was 97.5%, specificity 85% and diagnostic accuracy 96.1%. There was a significant correlation between perfusion score at baseline and recovery of ESVI at follow-up with an intersect corresponding to perfusion score 2 (Figure). Perfusion scores also predicted EF, EDVI and ESVI at baseline and recovery of ESVI.
Coronary Flow Velocity Reserve as a Predictor of Left Ventricular Volume and Functional Change After Acute Myocardial Infarction.


Background: It has been known that coronary flow velocity reserve (CFR) represents the degree of microvascular integrity. This study was designed to examine the value of CFR in the prediction of left ventricular volume and functional change after acute myocardial infarction (AMI).

Methods: To avoid the effect of epicardial stenosis on CFR, intracoronary adenosine-induced CFR of individual artery (iCFR) was measured by Doppler wire after successful elective angioplasty or stenting (stenting diameter stenosis<30% and TIMI flow=2) in 80 patients (74 male, mean age: 55±11 years) within 7 days after onset. To evaluate the area of ischemic injury as a whole, CFR was measured at global segment adjacent to angioplasty site. Left ventricular and diastolic volume index (LVEDVI, LVWMSI) were assessed by echocardiography before and after angioplasty (mean 17±1%). Receiver operating curve of CFR were used to determine the accuracy (area under curve; AUC) and best cut-off value (BCV) in relation to LV volume and functional change.

Results: Mean CFR was 1.88±0.58. In relation to the prediction of LVEDVI and LVWMSI, CFR showed accuracy 63.1% on the BCV of 1.7, and 68.8% on the BCV of 1.3, respectively. Patients were divided into 3 groups according to the level of CFR: LVEDVI, LVWMSI increased in group CFR<1.3, LVEDVI without improvement in group CFR 1.3-1.7, LVWMSI without improvement in group CFR 1.7.

Conclusions: Baseline CFR showed a significant decrease in LVEDVI with improvement in LV and LVWMSI. Patients with CFR<1.3 showed a significant increase in LVEDVI without improvement in LV and LVWMSI.

1219-93 Left Ventricular Electro-Mechanical Mapping in Patients Without Previous Myocardial Infarction: Comparison with Stress Perfusion Imaging

Irene Bozzi, Olen Van Langenhove, Jean Fajadet, Patrick Serruyts, Nicolas Fourquet, Catherine Klemt, Jean Marco, Claude Pauleau, Thibaut Franscois, Thierry Caderas, Alain Feldman, M-G.

Background: The Biosense Nogo is a catheter-based system for electro-mechanical mapping of the left ventricle. The combination of linear local shortening (LLS) data as test of local mechanical function and local intracardiac signals (ultrasound voltage = UV) as test of electrical function provides information about local electro-mechanical coupling. Methods: Linear local shortening and unipolar voltages were measured in 20 patients without previous myocardial infarction, with documented coronary artery disease and reversible defects at stress/rest redistribution nuclear perfusion imaging. The endocardial sites were divided into 10 anatomical regions and compared with the equivalent segments visualized isochronically. Stress nuclear images were analyzed by single photon emission tomography and perfusion defect severity was defined using a semiquantitative scoring of segments (Bonferroni perfusion, 1=moderate reduction, 2=severe reduction, 3=absent uptake). Results: A total of 176 endocardial segments had adequate scintigraphic and Nogo data for comparison. The distribution of reatts = 0.001 and according to thallium uptake is reported in Table 1. Conclusions: UV correlated significantly with the severity and extent of stress perfusion defects in patients with no previous MI. LV potentials appear able to identify regions with severe perfusion defects and preserved mechanical function.

1219-94 Advanced Age Impairs Development of Collateral Vessels to Infarct Related Artery in Patients With Acute Myocardial Infarction

Toshiya Kurotobi, Hiroshi Sato, Hideyuki Sato, Shoji Shibaoka, Eiji Hidaka, Kunihiro Kingo, Daisaku Nakatsukasa, Atsushi Hirayama, Tatsunori Kuzuya, Kaizohisa Kodama, Masatsugu Han Osaka University Graduate School of Medicine, Suita, Japan, Osaka.

Background: Animal experiments have shown that advanced age blunts angiogenesis and development of new vessels in response to angiogenic cytokines. We investigated whether the hypothesis that development of collateral vessels (Coil) to infarct related artery (IRA) is impaired with aging in patients with acute myocardial infarction (AMI).

Methods: Of consecutive 1360 patients with AMI, 652 patients who fulfilled the following criteria were enrolled in this study: 1) Coronary angiograms were obtained within 72 hrs after the onset of AMI, and 2) IRA showed complete occlusion (TIMI grade 0 or 1). Coil to IRA was evaluatated according to the Ronton score. The grades from 1 to 3 were defined as significant Coil. In random selected 50 patients, vascular endothelial growth factor (VEGF) and hepatic growth factor (HGF) were measured at chronic phase. Results: Prevalence of Coil significantly decreased with advanced age (45.6% in <60 yrs, 44.6% in 60-59 yrs, 42.6% in 60-69 yrs, 32.0% in >70 yrs, p<0.05). Serum VEGF and HGF level were not significantly different in each decade. Pre-infarction angina significantly increased the prevalence of Coil development below 70 yrs, (48.0% vs 20.9%, p=0.05), but this effect was impaired above 70 yrs. In a multivariate analysis showed that the absence of Coil was an independent predictor of in-hospital mortality in elderly patients above 70 yrs (odds ratio 2.4, 95% CI 1.5-3.8). Prevalence of Coil significantly decreased with advanced age (45.6% in <60 yrs, 44.6% in 60-59 yrs, 42.6% in 60-69 yrs, 32.0% in >70 yrs, p<0.05), and advanced age was an independent predictor of decreased collateral development to IRA (odds ratio 1.02, 95% CI 1.01-1.03, p<0.05). Serum VEGF and HGF level were not significantly different in each decade. Pre-infarction angina significantly increased the prevalence of Coil development below 70 yrs, (48.0% vs 20.9%, p=0.05), but this effect was impaired above 70 yrs. Multivariate analysis showed that the absence of Coil was an independent predictor of in-hospital mortality in elderly patients above 70 yrs (odds ratio 2.4, 95% CI 1.5-3.8). Advanced age may blunt development of Coil to IRA in patients with AMI due to lack of response against toll promoting stimuli. This abnormality may contribute to poor prognosis in elderly patients with AMI.
Background: The new consensus of The Joint ESC/AHA/WHF Committee for the Redefinition of Myocardial Infarction (AMI) on hospital outcomes is not established.

Methods: The National Registry of Myocardial Infarction 2 database was analyzed to determine hospital outcomes for thrombolytic-refractory patients admitted with AMI (Kaplan class II or III) complicating AMI.

Results: A total of 190,518 patients were identified (36,303 with CHF). Patients presenting in CHF were older (72.6±12.5 vs. 63.2±13.5 yrs.), had a longer time from symptom onset to hospital presentation (2.8±2.6 vs. 2.5±2.4 hrs.), and had a higher prevalence of anterior/left AMI (36.8% vs. 35.2%), diabetes (20.1% vs. 19.5%), use of hypertension (24.6% vs. 66.1%) (all p<0.00005). Patients with CHF were more likely to receive ACE inhibitors, but those without CHF were more likely to be treated with aspirin, beta-blockers, thrombyotically or primary angioplasty. Patients presenting in CHF had a longer length of stay (7.1±6.9 vs. 6.0±4.8 days, p<0.00005) and greater risk for adverse hospital outcomes. CHF on admission was the strongest predictor of hospital death in multivariate analysis (OR 1.89; 95%CI 1.62, 1.75).

Conclusion: Patients with CHF complicating AMI have more medical comorbidities and therefore have a greater risk for hospital mortality and adverse outcomes. Despite this, they are less likely to be treated with aggressive reperfusion strategies and therefore have a greater risk for hospital mortality and adverse outcomes.

Reperfusion Induced Bradycardia and Hypotension is Common With Proximal But Not Distal Acute RCA Occlusions: Role of the Ischemic Right Ventricle

Daniel T. Lee, Vinh D. Nguyen, William W. O'Neill, James A. Goldstein, William Beaumont Hospital, Royal Oak, MI

Background: Reperfusion of the coudally occluded right coronary artery (RCA) may result in abrupt bradycardia and hypotension, which has been attributed to stimulation of Bezold-Jarisch reflexes arising from the ischemic left ventricle (LV). Based on clinical observations in patients with LV infarction from our group and others suggesting that bradycardia and hypotension commonly occurs following reperfusion of proximal RCA occlusions, we hypothesized that reflexes arising from the ischemic RV may play a role in abrupt bradycardia and hypotension.

Methods: We retrospectively analyzed the incidence of reperfusion induced bradycardia and/or hypotension in patients with acute inferior myocardial infarction undergoing primary angioplasty of RCA lesions proximal to the RV branches (n = 144) or distal to the RV branches affecting the RV alone (n = 46). Patients in contrast, reperfusion of distal RCA occlusions rarely resulted in hypotension (6%, p = 0.001 vs proximal) or bradycardia (10%, p < 0.001 vs proximal).

Conclusion: These data demonstrate that reperfusion induced bradycardia and hypotension commonly occur in patients with proximal RCA occlusions affecting the RV and LV, but rarely occurs with distal occlusions supplying the LV alone. These findings suggest that interventions induced reflexes arising from the ischemic RV may play a role in abrupt bradycardia and hypotension.
Results: The addition of troponin-positive patients (Tn+ patients) resulted in a further increase of enzyme levels and a 1.5-fold increase compared to the traditional cardiac enzyme definition (OR 1.5, 95% CI 1.0-2.9). The odds ratio (OR) for in-hospital death was significantly higher in the Tn+ patients versus the Tn- patients (p=0.039). Urokinase plasminogen activator correlated positively with plaque area (p=0.029) and vessel areas (p=0.002), as compared to contractile and neural remodeling. Increased plasma levels of urokinase plasminogen activator were associated with plaque rupture (2.5±0.66 vs 2.5±0.87 ng/ml, p=0.029). Plasma levels of plasminogen activator inhibitor and urokinase plasminogen activator correlated positively with plaque area (p=0.027 and p=0.009) and vessel areas (p=0.010 and p=0.002). There was no correlation between the plasma levels of thrombin activation system and qualitative and quantitative plaque morphology. Conclusion: Elevated levels of parameters of the plasmin activation system, but not the increased levels of thrombin activation system are associated with signs of plaque instability in patients with unstable angina.

Elevated Plasma Levels of the Plasmin Activation System, but Not of Thrombin Activation System Correlate With the Sonographic Signs of Plaque Instability in Patients With Unstable Angina

Marinna Gyorgyori, Paul Tang, Ali Hassan, Franz Weidinger, Hans Dornannits, Anton Lagrange, Dagmar Gross, Kurt Huber. Division of Cardiology, University Vienna Medical Center, Vienna, Austria

Background: We determined the possible association between the echocardiographic signs of plaque instability (expansive remodeling, plaque rupture and thrombosis) and the increased plasma levels of plasmin and thrombin activation system enzymes in patients with unstable angina. Methods: The basal plasma levels of the thrombin activation system (thrombin-antithrombin complex, homocysteine, tissue factor pathway inhibitor, and prothrombin fragment 1+2) and the plasmin activation system (tissue-type and urokinase-type plasminogen activator, plasminogen activator inhibitor type-1) were measured in 52 consecutive admitted patients (28 male, 44±5 years old, with unstable angina). All patients underwent coronary angiography and intravascular ultrasound 3±2 hours after admission. The atherosclerotic plaque morphology assessed by intravascular ultrasound was determined as plaque composition and eccentricity, plaque disruption, visible thrombus and calcification. Quantitative intravascular ultrasound analyses involved the measurements of luminal, vessel and plaque area of the culprit lesion, proximal and distal reference segments and the types of arterial remodeling. Results: Expansive remodeling was associated with significantly larger plaque levels of plasminogen activator inhibitor type-1 (171±65 vs 97±41, 77±4428 mg/ml, p=0.039) and urokinase plasminogen activator (2.0±1.2 vs 2.1±0.6 vs 2.4±0.67 ng/ml, p=0.029) as compared to contractive and neutral remodeling. Increased plasma levels of urokinase plasminogen activator were associated with plaque rupture (2.5±0.66 vs 2.5±0.87 ng/ml, p=0.029). Plasma levels of plasminogen activator inhibitor and urokinase plasminogen activator correlated positively with plaque area (p=0.027 and p=0.009) and vessel areas (p=0.010 and p=0.002). There was no correlation between the plasma levels of thrombin activation system and qualitative and quantitative plaque morphology. Conclusion: Elevated levels of parameters of the plasmin activation system, but not the increased levels of thrombin activation system are associated with signs of plaque instability of the culprit lesion in patients with unstable angina.
Quality of Life One Year After Invasive Intervention in Unstable Coronary Artery Disease: Results From the FRISC II Invasive Trial

Magnus Jarzton, Lars-Åke Levk, Eva Swahn, FRISC II Investigators, Institution of Medicine and Care, Linköping University, Linköping, Sweden, CMRT, Center for Medical Technology Assessment, Linköping University, Linköping, Sweden

Background: Both early invasive and non-invasive treatment strategies in patients presenting with unstable coronary artery disease have been used during the acute phase of the disease. Until today there is no published study analysing the quality of life in this important and large patient group in the long-term follow-up. The aim of this study was to identify differences in quality of life between the two treatment groups.

Methods: A total of 2457 patients, median age 66 years and 70% men, with unstable angina or non-Q-wave myocardial infarction were randomised to early invasive or non-invasive treatment. The quality of life was measured with the generic quality of life instrument SF-36 (Short Form Health Survey) at time for randomisation, outpatient visits at 3 and 6 months. At one-year follow-up SF-36 was measured in a subgroup of 620 patients. SF-36 is presented in eight scales (range 0-100, where 100 corresponds to full health).

Results: In the FRISC II trial the invasive treatment showed a significant reduction in mortality (0.2% vs 0.9%, p=0.01). At time for randomisation there was no significant difference in quality of life between the groups. In six of the scales, A 5 and 6 months follow-up was significantly different (p<0.01 in all eight scales) in quality of life favouring the invasive group. The differences still remained significant at one-year follow up in six of the scales.

Conclusions: Patients with unstable coronary artery disease treated with early invasive strategy have better quality of life measured with SF-36 up to one year follow up compared to patients treated with non-invasive strategy.

Poster Session

1249 Outcome Predictors in Acute Myocardial Infarction

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

Primary Angioplasty in Acute Myocardial Infarction: Does Age Matter?
Carol Regueiro, Alison Hart, Linda Cramshaw, Shelly McCormick, Michael Arsheterich, Terry Hantschi, Richard Shannon, Allegheny General Hospital, Pittsburgh, PA

Background: Recent data suggests that there are subtle/call variations in the treatment of acute myocardial infarction (AMI) based on age, race, gender and socioeconomic status. Advanced age is associated with poorer outcomes in AMI that may benefit from acute coronary intervention. We evaluated the use of primary angioplasty (PA) in elderly patients treated in an academic referral center. Methods: We reviewed the records of a consecutive sample of 100 patients with AMI from 1997-2000. Our primary outcome was PA in AMI, defined as coronary intervention within the first 24 hours of admission. Secondary outcomes included use of post-AMI therapies such as aspirin (ASA), beta-blockers (BB), angiotensin converting enzyme inhibitors, and other anticoagulants (ACO). We collected variables including demographics, comorbidities, do-not-resuscitate status, and severity of illness using the ATLAS system. Univariate analysis was performed on the variable of interest as well as all candidate variables. Subsequent logistic regression modeling incorporated all variables significant on univariate analysis.

Results: Procedural success was comparable (97.6% women, 97.6% men; p=0.31). Women were more likely to present late (125 vs 116 minutes; p=0.05), and had a longer total duration of ST-variability during the first 4 hours 28 vs. 17.6 minutes (p=0.001). Seven patients had vectorcardiographic signs of reocclusion during the first 4 hours of observation. Early dynamic changes in the ST-segment deviation have been connected to worse outcome, intermittent recurrences and a higher thrombogenic activity.

Methods: A total of 2457 patients from 11 hospitals were included in the vectorcardiographic substudy of the ASSENT PLUS trial. Inclusion-criteria were the same as in the ASSENT-2 trial. All patients received aspirin and either heparin or dextran. An angiogram was performed on day 4-7. Patients were treated non-invasively for 24 hours. 12-hour curves were analysed blindly by two independent observers. During the acute phase, 0.4 hours, an increase in ST-vectormagnitude of 25mV for >=2 minutes was considered as a significant episode of ST-invasivity. Thirteen hours to 24 hours, vectorcardiographic signs of reocclusion were defined a ST-episode, according to our previous vectorcardiographic definitions. Patients with bundle branch block were excluded. 176 of the patients underwent an angiography, which was not done-cab-analysis by two observers.

Background: Rapid, complete and sustained reperfusion is the goal when treating an acute myocardial infarction. Continuous ST-monitoring has been shown to accurately detect reappearance with cerebrovascular. Early dynamic changes in the ST-segment deviation have been connected to worse outcome, intermittent recurrences and a higher thrombogenic activity.

Results: Procedural success was comparable (97.6% women, 97.6% men; p=0.31). Women were more likely to present late (125 vs 116 minutes; p=0.05), and had a longer total duration of ST-variability during the first 4 hours 28 vs. 17.6 minutes (p=0.001). Seven patients had vectorcardiographic signs of reocclusion during the first 4 hours of observation. Early dynamic changes in the ST-segment deviation have been connected to worse outcome, intermittent recurrences and a higher thrombogenic activity.

Conclusion: Female gender is regarded as an independent predictor of mortality following MI. We registered our data over 5 years (2002-2007) on 1,005 consecutive patients (218 female; 696 male) who underwent direct invasive intervention (d-PTCA) during 12 hours of onset of symptoms. Methods: We analyzed baseline variables, procedural characteristics between hospital and 30-month clinical outcomes compared to women in previous studies (61 vs 66 years; p<0.0001), more frequently diabetic (17% vs 25%; p=0.001) or hypertensive (46% vs 57%; p=0.005), Men were more frequently smokers (38% vs 31%; p=0.026), had higher rate of prior MI (32% vs 14%; p<0.0001) and prior CABG (12% vs 5%; p=0.001). Women took longer to arrive at the hospital (125 vs 97 minutes; p<0.0001). Women had a worse 30-month event-free survival (13 vs 16 minutes; p=0.08). Both groups had similar baseline vectorcardiographic variables and LV function (mean LVEF 60.6%).

Results: Procedural success was comparable (97.8% women, 97.8% men; p=0.31). Time to onset of symptoms was more frequent in women (6.7 vs 9; p=0.05) with longer hospital stay (1.1 vs 3.0 days; p<0.001). In hospital CABG (2%; women vs 1% men) and death (0.3% in both) was similar in both groups. The use of anti-plaister drugs, beta-blockers and ACE-inhibitors was similar in both. At 12-month follow-up, mortality (4.0% women,
Results: The mean serum creatinine and creatinine clearance on admission were 1.05 ± 0.35 mg/dL and 89 ± 34 mL/min respectively. Serum creatinine appeared not to correlate with in-hospital or six-month event rates. However, univariate analysis a creatinine clearance of 75 mL/min (mean creatinine 1.2 ± 0.4 mg/dL) was associated with hypotension in the cath lab (10.6 vs 6.5%, p=0.035), intubation (1.3 vs 0%, p=0.018), in-hospital death (5.1 vs 0.8%, p=0.001). In hospital MACE (0.6 vs 3.0%, p=0.01) and death at 6-months (7.4 vs 1.1%, p=0.001). Creatinine clearance predicted in-hospital and 6-month death in a multivariate model (excluded age and sex since these were more useful to calculate clearance). Mean contrast volume was not significantly higher for patients with events. Seven patients required dialysis post intervention; admission creatinine and creatinine clearance were less than 0.7, 1.0, 1.3, 4.1 mg/dL and 80, 55, 52, 22 mL/min in these patients respectively.

Conclusions: Creatinine clearance, but not serum creatinine, on admission is a predictor of early and late death after primary angioplasty or stenting for acute myocardial infarction. These data suggest that: routine calculation of admission creatinine clearance may better risk stratify AMI patients.
Background: Chronic renal insufficiency (CRI) has been associated with a high mortality and morbidity (715%) after coronary artery bypass grafting (CABG) with cardiopulmonary bypass (On-pump). It is unknown, however, whether left without cardiopulmonary bypass (OPCAB) may yield an improved clinical outcome over On-pump CABG in patients with preexisting CRI. Methods: We compared the perioperative outcomes of patients with CRI (baseline serum creatinine > 2.0 mg/dl) who underwent On-pump (n=121) versus OPCAB (n=1079), between October 1998 and April 2000. Only patients who received > 1 graft were included. Patients were well matched with respect to the baseline characteristics, except for a higher percentage of male patients (76.4% vs. 60.4%, p<0.008) at the On-pump vs. OPCAB group. Results: Early clinical outcome is shown (see table). No patient scheduled for OPCAB required conversion to On-pump CABG. Complete revascularization rate was attained in all patients. Conclusions: The therapeutic effect of CRI on the early clinical outcome after CABG is especially pronounced after CABG through OPCAB. Pulmonary, cardiac and further revascularization determinants in patients with preexisting CRI may explain for this phenomenon and favor OPCAB as a low risk revascularization option at this subset of patients.

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1250-82 Early Mortality And Morbidity of Bilateral Versus Single Internal Thoracic Artery Revascularization: Propensity and Risk Modeling

Demosthenes Katritsis, John Ioannidis, Ohon Galanis, Cliff P. Costanty, George Drosos, Daniel G. Giwastel, Constantine Argeonostopoulos, ATHENS EUROCENTER, ATHENS, Greece

Objective: We evaluated whether bilateral internal thoracic artery (BITA) revascularization is associated with any increased in-hospital mortality and complications compared with single internal thoracic artery (SITA) revascularization. Background: Despite proven long-term benefits, BITA revascularization has been slow to adopt because of fears of increased early mortality. Methods: We evaluated 1697 consecutive patients undergoing BITA (n=867) or SITA (n=830) revascularization. We used propensity score analyses and adjusted risk models to estimate differences between groups. Results: There were 20 (2.3%) deaths in the BITA group vs. 26 (3.1%) in the SITA group (odds ratio 0.73, p=0.039). Propensity analysis identified several factors that affected the decision to use BITA. Adjusting for propensity score and all potential risk factors, the odds ratio for death with BITA vs. SITA was exactly 1.00. BITA did not increase the number of in-hospital complications with the possible exception of deep sternal wound infections (11.13% vs. 2.4%, p=0.067). In multivariate modeling BITA increased the risk of deep sternal wound infections only in emergent cases and in older patients; the excess risk was negligible among 1205 patients (71.1% of total) who did not have emergent revascularization and were >70 years old (risk difference 9.8%, p=0.12). There was no difference in length after adjustment for propensity factors (mean 11.3 vs. 11.7 days, p=0.066). Conclusions: BITA grafting conferred no increased risk for early death and does not prolong hospital stay. The small increase in the risk of deep sternal wound infections did not affect the majority of patients.

1250-83 Clopidogrel for Prevention of Thrombotic Complications After Cardiac Surgery: A Word of Caution

Mierczyk K. C., Dullum, Benjedka O., Laidnak, Kertchak D. tt.: Am Koronar, Peter C. Hill, Danken W. Boyes, Albert J. Pfister, Ammar S. Bafi, Robert C. Lowery, Qazi Anjum, Jorge M. Garcia, Paul J. Corso. Washington Hospital Center, Washington, DC, Medical City Dallas Hospital, Dallas, TX

Background: Ciopidogrel is a relatively new platelet aggregation inhibitor, but both its benefits and risks have been insufficiently elucidated. Early thromboembolic and hemorrhagic complications were recorded in patients from both groups. Patients from the two groups were comparable with respect to baseline characteristics.

Methods: We retrospectively analyzed the patients who underwent coronary artery bypass surgery (CABG, n=979), valve replacement (n=95) or CABG plus valve replacement (n=126) between January and August 2000. We compared the early clinical outcome between two groups: group A who received preoperative clopidogrel (75 mg, once per day, orally) and aspirin (325 mg, once per day), (n=121) and Group B who received aspirin alone (325 mg, once per day), (n=1079). Early thromboembolic and hemorrhagic complications were recorded in patients from both groups. Patients from the two groups were comparable with respect to baseline characteristics.

Results: Comparative analysis is summarized in Table.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Group A (n=121)</th>
<th>Group B (n=1079)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemorrhagic</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postoperative transfusions</td>
<td>61%</td>
<td>48%</td>
<td>0.001</td>
</tr>
<tr>
<td>Resorption for bleeding</td>
<td>3%</td>
<td>2%</td>
<td>0.32</td>
</tr>
<tr>
<td>Caesarean section (delivery)</td>
<td>7%</td>
<td>1%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thrombotorric</td>
<td>1%</td>
<td>1%</td>
<td>0.38</td>
</tr>
<tr>
<td>Pulmonary embolism</td>
<td>2%</td>
<td>1%</td>
<td></td>
</tr>
<tr>
<td>Deep venous thrombosis</td>
<td>0%</td>
<td>0.2%</td>
<td>1</td>
</tr>
<tr>
<td>Stroke</td>
<td>2%</td>
<td>3%</td>
<td>0.57</td>
</tr>
</tbody>
</table>

Conclusions: Clopidogrel plus aspirin preoperative has a significantly higher rate of postoperative hemorrhagic complications than aspirin alone.

POSTER SESSION

1251 Myocardial Infarction and Ischemia: Focus on Nitric Oxide and Coronary Flow Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

1251-84 Basal Nitric Oxide Synthesis in Coronary Stenoses: Relation to Morphology, Length, Severity

Dimiris Tousoulis, Costas Tantikos, George S. Goumen, Costas Kanakis, Tom Crake, Cufick Tobias, John Anagnostis, Chandrika Suchak, Symans Poulou, Panos Toukouzis, Hoptontown Hospital, Athens, Greece, Hammersmith Hospital, London, United Kingdom

Background: Nitric oxide (NO), a major component of endothelium-derived relaxing factor, is synthesized from the amino acid-L-arginine by a family of enzymes. The synthesis of NO is competitively inhibited by NO-nonspecific methyl-L-arginine (LNMMA). The effect of inhibition of NO synthesis on coronary stenoses in relation to their geometric characteristics is unknown. Methods: In 28 patients (24 male, 4 female) with coronary artery disease (CAD) and chronic stable angina, normal saline (NS) and 4 imol/min LNMMA were infused intracoronary, each for 4 minutes, followed by an intracoronary bolus of 10 mg nitroglycerin(GT2). Coronary stenoses were classified as smooth (smooth concentric or eccentric with regular borders) or irregular. The diameter of 26 smooth and 12 irregular coronary stenoses and their adjacent reference (r) segment was measured by computed-quantitative angiography. Results: The mean (+SEM) change from baseline was:

<table>
<thead>
<tr>
<th></th>
<th>NS</th>
<th>LNMMA</th>
<th>GTN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth stenoses</td>
<td>0.3±0.5</td>
<td>-1.9±0.8</td>
<td>11.2±2.1</td>
</tr>
<tr>
<td>R segments</td>
<td>1.0±0.3</td>
<td>-7.4±1.8</td>
<td>8.3±1.9</td>
</tr>
<tr>
<td>Smooth stenoses</td>
<td>0.5±0.4</td>
<td>-1.2±2.1</td>
<td>10.6±2.1</td>
</tr>
</tbody>
</table>

p<0.05 vs smooth stenoses, =p<0.05 vs R segments. The severity of stenoses at baseline correlated with the magnitude of LNMMA response irrespective of the type of morphology (p<0.01), whereas there was a weak correlation (r=0.03) between length of stenoses and the level of constriction to LNMMA. No correlation was found between eccentricity ratio and the response to LNMMA (p=NS). Conclusion: In patients with CAD, irregular coronary stenoses constrict significantly more than smooth stenoses, following inhibition of nitric oxide synthesis with LNMMA. This enhanced constriction is focal to the stenoses present at the reference-segment. The degree of response to LNMMA is related to stenoses length and stenoses severity and is unrelated to eccentricity ratio.

1251-85 Amelioration of Ischemia- and Reperfusion-Induced Myocardial Injury by Raloxifene: Roles of Nitric Oxide and the Opening of Calcium-Activated Potassium Channels

Hisakazu Ogita, Masatoshi Kitakaze, Koichi Node, Hisato Asamura, Shoji Sanada, Seiji Takahashi, Masanori Asakura, Yuliu Liao, Yoshio Shinozaki, Hideko Mori, Taun Hundred Kuzuya, Masatoshi Horii, Osaka University Graduate School of Medicine, Suta, Japan

Background: 1251 Estradiol reduces myocardial infarct size via nitric oxide (NO) and the opening of calcium-activated potassium channels (KCa) channels. Raloxifene, a selective agonist of estrogen receptors, is reported to causes antihypertensive coronary artery vasodilating effects. We investigated whether raloxifene reduces infarct size, and what mechanisms are involved in the effects. Methods: In the unanesthetized open chest beagle dogs, the left anterior descending coronary artery (LAD) was occluded and perfused with blood from the left internal artery through an extracoronary bypass tube. We occluded the LAD for 90 minutes followed by 6 hours of reperfusion. Infarct size was measured by TTC staining, infusion of raloxifene (10 mg/kg/min) into the LAD through an extracoronary bypass tube was initiated 10 minutes before coronary occlusion and continued up to 1 hour of reperfusion except the coronary occlusion period. Results: Heart rate (134±4 beats/minute) and mean arterial blood pressure (100±2 mmHg) remained stable throughout the study and were not significantly different among groups. Infarct size was significantly
Background: Nitric oxide (NO) exerts various pathophysiological effects on the cardiovascular system and there was a reduction of NO activities in both coronary and brachial arteries of the patients with coronary vasospasm. Recently, it has been reported that endothelial nitric oxide synthase (eNOS) gene intron 4 polymorphism is one of the genetic factors to control coronary vasospasm. However, the correlation between eNOS gene polymorphism and coronary vasospasm has not been thoroughly investigated.

Methods: In this study, 60 admitted patients with chest pain were investigated. On admission, all patients and the lumen diameters of large epicardial coronary arteries were assessed by quantitative coronary arteriography. According to the presence or absence of coronary vasospasm, the patients were divided into two groups, coronary vasospasm group (n=27) and control group (n=33). There was a significantly higher incidence of coronary vasospasm in the control group than in the NO group (p=0.025) with no presence of a/a genotype. The ratio of smokers was higher in the control group than in the control (0.0001 < p < 0.01) and other conventional coronary risk factors such as hypertension, diabetes mellitus, hyperlipidemia, BMI and serum level of lipids showed no significant difference between the groups. Furthermore, there were 17 cases with a/a genotype and 25 cases with b/b genotype in CVS. The incidence of multi-vessel disease and diffuse spasm was significantly higher in b/b genotype than in b/b genotype (p=0.007). Stepwise multivariate regression analysis on gene polymorphism and the conventional coronary risk factors showed that smoking and a/b genotype were the independent factors to predict coronary vasospasm (F=5.364 and 5.297 respectively, p<0.02). Conclusion: It suggested that eNOS gene a/b genotype as well as smoking habit might be the key factors to coronary vasospasm.

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1252 Stable Ischemic Syndrome: Pathophysiology, Diagnosis, and Prognosis II

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4

Presentation Hour: 4:00 p.m.-5:00 p.m.

Poster Session 1252A

1252-91 Silent Ischemia During Daily Life Is Related to Increased Thrombin Generation in Patients With Chronic Stable Angina

Ifigenos Iliomaris, Felicita Andronati, Christodoulos Stefanakis, Christos Pitsavos, Emmanouil Economou, Pavlos Toutouzas, Petros Nihoyannopoulos, Hammersmith Hospital, London, Greece, Ippokration Hospital, Athens, Greece

Background: Patients with chronic stable angina (SA) and silent ischemia during daily life usually present complex and thus potentially thrombogenic atherosclerotic plaques at coronary angiography. We investigated whether thrombin generation, platelet activation, or high plasma levels of procoagulant cytokines are related to silent ischemia in SA and whether reduction of the above factors by aspirin (ASA) is associated with a reduction of silent ischemia.

Methods: We measured thrombin fragments (PF-1, 2, and 3), monocyte colony stimulating factor (MCSF), interleukins 1b (IL-1b) and 6 (IL-6) (pg/ml plasma levels and 24-h urine excretion of 11-dehydrothromboxane B2 (DTXB2, ng/ml) in patients with SA and in 24 Mediterranean controls. Samples were collected before the end of a 48-h Holter monitoring. Patients with chronic stable angina who had angiographically documented disease. Forty had ischemia at HM and were randomly treated with ASA 300 mg/d for 3 weeks in a double-blind, cross-over trial. Results: PF-1, 2, and 3 were increased in patients compared to controls (p < 0.05). Patients with ischemia at HM had higher MCSF and DTXB2 compared to those without (MCSF: 1174+1417 vs 598+417, P < 0.001; DTXB2: 4.5+1.5 vs 2.7+1.4, P < 0.01). Patients with silent ischemia (20/60) had higher PF-1+2 than patients with both silent and symptomatic episodes (20/60) or patients with no ischemia (20/60) (PF-1+2: 2.26+1.8 vs 1.73+1.2 vs 0.93+0.9, P < 0.01). MCSF was related to DTXB2 before and after ASA treatment (r = 0.47, P < 0.01). Patients with SA is related to increased platelet activation induced by high cytokine levels. Whether reduction of the above factors by aspirin (ASA) is associated with reduction of silent ischemia is clinically asymptomatic. Of the OCG recorded ischemic events, only 5% had silent ischemia symptoms. Important inactivation of platelets is observed (0.7%). The frequency of these ischemic events increases suddenly from 7 AM culminating at 10 AM and then decreases quickly until after 11 PM. The pattern then remains constant from 9 PM to 5 AM and decreases gradually during the evening to reach a threshold of low activity before the early morning. Conclusion: The circadian variations of silent ischemic events and in particular the increase in the frequency if ischemic events early in the morning chronologically correspond with the variations of the symptomatic ischemia observed in the study. They are also related with the sudden rise of the blood pressure and the peak of frequency of myocardial infarction described in the literature during this period.

1252-92 Minimal Coronary Artery Disease Is Associated With Persistent Chest Pain in Women: Results From the NHLBI-Sponsored Wise Study Coronary Angiographic Core Laboratory

Barry L. Sharat, B. Desa Johnson, Marion B. Gazon, Carin J. Napier, Steven E. Hess, William J. Rogers, Nathaniel Reichek, C. Noel Bairley Menz. Rhode Island Hospital and Brown University School of Medicine, Providence, RI

Background: Although the patients (pts) with vasospastic angina treated with calcium channel antagonists have good outcome, few data exist regarding ultra long term prognosis particularly in pts with normal coronary angiography. Therefore, we studied the relationship between the ultra long term outcome of vasospastic angina prospectively followed up to 20 years and the factors influencing the prognosis.

Methods: Total 165 pts (110 men and 55 women) with mean age of 44±11 who had angiographic evidence of intense coronary vasospasm without presenting disease at the sites of vasospasm were enrolled and prospectively followed to 20 (mean 12.5±2) years. Cardiac events occurring at the cardiac and the ischemic events which involved acute myocardial infarction and unstable angina. Cox analysis, that was used to identify potentially important prognostic variables, selected coronary risk factors such as hypertension, diabetes mellitus, hyperlipidemia and history of smoking. Results: Cardiac events occurred in 10 pts (5.2%) and the ischemic events in 31 pts (16%) during the follow up period. Under these conditions, hyperlipidemia (OR=3.6, 95% CI=1.4-9.6, P=0.03) was the only independent predictor of event-free survival by the Cox analysis. Kaplan-Meier survival analysis revealed an event-free survival curve in vasospastic angina with normal coronary (survival rate: 5y, 10y, 15y, and 20 yrs: 90.5%, 79.0%, 76.5%, and 73.9% respectively).

Conclusions: These results demonstrate that vasospastic angina with normal coronary angiography treated with calcium channel antagonists has good outcome. Under these conditions, the most important factor affecting the prognosis is revealed to be hyperlipidemia, thus this entity needs to be considered under coronary syndrome.
Evolving Antithrombotic Approaches in Acute Coronary Syndromes

Tuesday, March 20, 2001, 3:00 p.m.-5:00 p.m.
Orange County Convention Center, Hall A4
Presentation Hour: 4:00 p.m.-5:00 p.m.

Enoxaparin Versus Tinzaparin in the Management of Unstable Coronary Artery Disease (EVET Study)


Background: There is no published data evaluating low-molecular-weight heparins in obese patients and patients with renal impairment. Methods: In a prospective study 438 patients with unstable angina or non-Q wave myocardial infarction were enrolled. Enoxaparin (E) 1 mg/kg was given subcutaneously ever 12 hours while Tinzaparin (T) 2500 IU once daily was given subcutaneously. The primary end-points were death, myocardial infarction, refractory angina and recurrence of unstable angina. Secondary end points were rehospitalisation due to unstable angina or myocardial infarction, death and need for revascularisation at 30 days. Results: At 7 days recurrence of unstable angina occurred less frequently in the enoxaparin than in the tinzaparin group (N=192 vs 41/218, p=0.029). No statistical significant differences were observed between these 2 groups with respect to death, myocardial infarction or refractory angina at 7 days. At 30 days there were no differences between the 2 groups regarding rehospitalisation and death. The need for revascularisation at 30 days was significantly less frequent in the patients assigned to enoxaparin (9/220 vs 17/218, p=0.018). Bleeding complication rates were similar in the two groups. Conclusions: Antithrombotic treatment with enoxaparin for 7 days was more effective than tinzaparin in reducing the incidence of recurrent angina in patients with unstable angina or non-Q wave myocardial infarction in the early phase. Enoxaparin recipients had also significantly reduced need for revascularisation at 30 days. This benefit was achieved without an increase of bleeding complications.

Safety and Efficacy of Unfractionated Heparin (UH) Versus Enoxaparin (E) in Obese Patients and Patients With Renal Impairment: Analysis From ESSENCE and TIMI 11B Studies

Stephanie M. Inverno, Marc Cohen, Elliott M. Antman, Sarah A. Spitzer, for the ESSENCE and TIMI 11B Investigators. Philadelphia College of Pharmacy at the University of the Sciences in Philadelphia, Philadelphia, PA

Background: There has been no published data evaluating low-molecular-weight heparins in obese and renally-impaired patients with acute coronary syndromes. Methods: The composite endpoint of death, myocardial infarction or urgent revascularisation (DM/UIR) at 7 days, a major bleeding event or any bleeding (measured during the weight-adjusted treatment phase of the initial hospitalization) were compared between subgroups of patients: obese (N=3439) versus non-obese (N=3558) and renal impairment (N=1343) versus no renal impairment (N=3558) from ESSENCE and TIMI 11B. Results: In obese and non-obese patients, E significantly decreased the risk of DM/UIR when compared to UH (RR 0.68, p=0.0008 and RR 0.95, p=0.002). Similar major bleeding rates were observed between UH and E in obese patients (0.6% vs 0.7%) and non-obese patients (1.0% vs 1.8%), there was less major bleeding in the obese treated with E compared to the non-obese (RR 0.55, p=0.056). E significantly decreased the rate of DM/UIR in patients without renal impairment (RR 0.91, p=0.003). An increased risk of DM/UIR was seen in patients with renal impairment receiving UH when compared to those with no renal impairment (RR 2.1, p=0.004). There was no difference in the rate of DM/UIR in those with and without renal impairment receiving E (18.8% vs 15.7%). Increased rates of major bleeding were seen in patients with impaired renal function compared to those with no renal impairment receiving both E (7.5% vs 1.2%, p=0.002) and UH (5.8% vs 1.2%, p=0.001). Similarly, there was an increase in any bleeding in patients with renal impairment compared to those with no renal impairment receiving both E (11.9% vs 5.9%, p=0.001) and UH (18.8% vs 3.9%, p=0.001). Conclusion: E significantly reduced the risk of DM/UIR at 7 days in obese, non-obese and patients without renal impairment. A reduction in DM/UIR was not demonstrated with E in patients with renal impairment perhaps due to small sample size. Similar to other trials, obesity did not increase the risk of DM/UIR and less major bleeding occurred in obese patients. Renal impairment is a risk factor for bleeding with both E and UH. Large clinical trials focusing on patients with renal impairment are needed.

Glycoprotein IIb/IIIa Inhibitors in the Medical Management of Unstable Ischemic Syndrome Without Percutent ST Segment Elevation: A Meta-Analysis of the Randomized Trials

Marcio Roã§, Derek P. Chew, Debabrata Mukherjee, Deepak L. BHATT, Mark A. Robbins, Eric J. TOPOLO. Cleveland Clinic Foundation, Cleveland, OH

Background: The role of intravenous glycoprotein IIb/IIIa inhibitors in revascularisation of unstable ischemic syndromes without persistent ST-segment elevation treated medically has recently become controversial. So far six placebo-controlled trials have been performed in this setting. Methods: PRISM, PRISM PLUS, PAPAGOON A, PURSUIT, PAPAGOON B, and GUSTO IV ACS enrolled a total of 29,855 patients. We performed a meta-analysis of these trials and assessed the incidence of major bleeding interaction (MI) at 30 days. The analysis included all patients enrolled in the trials. Results: The results are reported in the figure. The pooled incidence of death or MI at 30 days was significantly reduced by the use of GP IIb/IIIa inhibitors (10.7% of the GP IIb/IIIa inhibitor's treated patients and 11.5% of the placebo treated patients had an event [OR 0.89; 95% CI 0.85-0.95; p=0.037]. The p-value of the Breslow-Day test was 0.039, excluding heterogeneity of the trials.

Trial

<table>
<thead>
<tr>
<th>N</th>
<th>Odds Ratio 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>PRISM</td>
<td>1.32</td>
</tr>
<tr>
<td>PRISM Plus</td>
<td>1.13</td>
</tr>
<tr>
<td>PAPAGOON A</td>
<td>1.30</td>
</tr>
<tr>
<td>PURSUIT</td>
<td>0.94</td>
</tr>
<tr>
<td>PAPAGOON B</td>
<td>1.17</td>
</tr>
<tr>
<td>GUSTO IV ACS</td>
<td>1.34</td>
</tr>
<tr>
<td>Model</td>
<td>1.05</td>
</tr>
</tbody>
</table>

Conclusions: The meta-analysis of the six so far performed placebo-controlled trials demonstrate that the use of GP IIb/IIIa inhibitors was associated with a modest (9%) but significant reduction in death or MI at 30 days improving in unstable ischemic syndromes without persistent ST-segment elevation treated medically.
Background: Intraoperative hemorrhage is a common occurrence in cardiac surgery. Many factors are involved in this process and their interactions are poorly characterized. In this study we examined the relationship between perioperative blood transfusion and postoperative outcomes in the setting of cardiac surgery.

Methods: We performed a prospective study of consecutive patients from a single institution who underwent cardiac surgery. Postoperative complications were defined as either major or minor morbidity. Major complications were defined as mortality, myocardial infarction, cerebrovascular accident, and ventilator support >24h. Minor complications included any additional blood transfusion, reexploration for wound bleeding, and intra-thoracic bleeding requiring chest tube placement. We performed logistic regression analysis to determine the independent effect of perioperative blood transfusion on the incidence of complications.

Results: A total of 180 patients were analyzed. The mean age of the study population was 66.5 years. The mean body mass index was 27.2 kg/m². The mean duration of surgery was 3.5 hours. Postoperative complications occurred in 40 patients (22.2%). The mean volume of blood transfused was 2.6 units (median 2.0 units). On univariate analysis, the volume of transfused blood was significantly associated with the occurrence of complications (p=0.003). In the multivariate analysis, the volume of transfused blood was independently associated with the occurrence of complications (odds ratio 1.38 per unit transfused, 95% confidence interval 1.03-1.85, p=0.028).

Conclusions: In this study, we observed a statistically significant association between perioperative blood transfusion and postoperative complications after cardiac surgery. These findings suggest that efforts to reduce perioperative blood transfusion may have a beneficial effect on postoperative outcomes in cardiac surgery.
**ABSTRACTS - Myocardial Ischemia and Infarction 367A**

### Background:
Angiopoietin-1 (Ang-1) is a newly described angiogenic factor that promotes vessel maturation and stabilization. In contrast, Ang-2 is thought to act as an endogenous antagonist of the endothelial cell receptor Tie-2. We examined the expression of Ang-1 and Ang-2 in a rat myocardial infarction (MI) model.

### Methods:
Hearts were explanted from male SD rats at 24 h, 1 and 6 weeks after ligation of the left coronary artery (n=5-7 animals/group). Sham operated (n=6) and untreated rats served as controls. Immunohistochemistry.

### Results:
At 24h, Ang-1 levels were decreased in both the I (56±7%, p<0.05) and PI zones (98±8%, p=0.05) compared with the NI zone, while Ang-2 levels were increased in the I (24±6%, p=0.03) and PI zones (22±6%, p=0.03). At 1 week, the I zone showed persistent decreases in Ang-1 (84±3%, p=0.02) and increases in Ang-2 expression (144±9%, p<0.008), whereas Ang-1 and Ang-2 expression had returned to baseline in the PI zone (81±3% and 48±3%, respectively). At 6 weeks, levels of Ang-1 and Ang-2 were not significantly different from controls in both territories. Tie-2 receptor levels were reduced at all time points up to 7 days.

### Conclusions:
Ang-1 and Ang-2 expression are opposed in MI. Ang-1 expression is reduced in the I zone, whereas Ang-2 expression is increased. These findings suggest that the TI and PI regions may support revascularization and neovascularization, respectively.

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**412 Aortic Valve Calcification (AVC) and Prognosis: A Necropsy Study**

**Background:** Aortic valve calcification (AVC) is a common degenerative process that can affect valve function and cause cardiac dysfunction. The purpose of this study was to determine the prevalence of AVC and its association with cardiovascular outcomes in a necropsy population.

**Methods:** Necropsies were performed on 100 patients who underwent cardiac surgery at our institution. The presence and extent of AVC were evaluated and correlated with various clinical and histological parameters.

**Results:** AVC was present in 75% of the patients, with varying degrees of severity. Patients with AVC had a higher incidence of cardiovascular events, including coronary artery disease, congestive heart failure, and atrial fibrillation. Additionally, AVC was associated with increased cardiovascular mortality.

**Conclusion:** Our findings suggest that AVC is a significant predictor of cardiac morbidity and mortality. Early identification and interventions may be necessary to improve patient outcomes.

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**878 Stable Ischemic Syndrome: Mechanistic Insights**

**Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.**

**Large Brachial Artery Diameter Is Associated With Angiographic CAD in Women: A Report From the NHLBI Women's Ischemia Syndrome Evaluation (WISE)**

**Background:** The prevalence of coronary artery disease (CAD) is increasing in women, and understanding the factors associated with CAD in this population is crucial.

**Methods:** The WISE study is a large, multicenter trial that examines the prevalence and mechanisms of ischemia in women with stable CAD. The study includes data from more than 2,500 women who underwent coronary angiography.

**Results:** In this subset of women, the large brachial artery diameter was strongly associated with the presence of angiographic CAD (OR 2.8, 95% CI 1.2-6.6). Furthermore, the association was independent of traditional risk factors such as age, hypertension, and diabetes.

**Conclusion:** Large brachial artery diameter is an important predictor of angiographic CAD in women, highlighting the need for further research into mechanisms underlying this association.

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**ORAL CONTRIBUTIONS**

**878 Morbidly Obese Patients Undergoing Cardiac Catheterization: Less Disease, Less Aggressive Revascularization, and Similar Outcomes**

**Background:** Morbid obesity is a significant risk factor for cardiac disease. The purpose of this study was to evaluate the characteristics and outcomes of morbidly obese patients undergoing cardiac catheterization.

**Methods:** A retrospective review of patient records from a single institution was conducted. Morbid obesity was defined as a body mass index (BMI) greater than 40 kg/m².

**Results:** Of 2,716 patients who underwent cardiac catheterization, 136 (5%) were morbidly obese. Morbidly obese patients had a lower prevalence of significant CAD compared to non-obese patients (39% vs. 67%, p<0.001). Despite this, revascularization rates were similar between the two groups (42% vs. 45%, p=0.45).

**Conclusion:** Morbid obesity is associated with less disease and less aggressive revascularization, but similar outcomes to non-obese patients undergoing cardiac catheterization.

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**879 Large Brachial Artery Diameter Is Associated With Angiographic CAD in Women: A Report From the NHLBI Women's Ischemia Syndrome Evaluation (WISE)**

**Background:** The WISE study is a large, multicenter trial that examines the prevalence and mechanisms of ischemia in women with stable CAD. The study includes data from more than 2,500 women who underwent coronary angiography.

**Methods:** The study used a combination of clinical and angiographic data to assess the association between large brachial artery diameter and the presence of angiographic CAD.

**Results:** In this subset of women, the large brachial artery diameter was strongly associated with the presence of angiographic CAD (OR 2.8, 95% CI 1.2-6.6). Furthermore, the association was independent of traditional risk factors such as age, hypertension, and diabetes.

**Conclusion:** Large brachial artery diameter is an important predictor of angiographic CAD in women, highlighting the need for further research into mechanisms underlying this association.

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**881 Stable Angina Pectoris: Clinical and Hemodynamic Correlates**

**Background:** The mechanisms underlying stable angina pectoris (SAP) are complex and not fully understood. This study aimed to identify clinical and hemodynamic correlates of SAP.

**Methods:** A retrospective analysis of patient records from a single institution was conducted. SAP patients were compared based on clinical characteristics and hemodynamic parameters.

**Results:** SAP patients with lower cardiac output and higher resting heart rate had a higher prevalence of CAD. Additionally, patients with SAP and lower cardiac output had a higher risk of hospitalization for heart failure.

**Conclusion:** Clinical and hemodynamic correlates of SAP are important for understanding the pathophysiology of this condition and guiding patient management.
368A ABSTRACTS - Myocardial Ischemia and Infarction

American Race, and to Have Diabetes, Hypertension, and Hyperlipidemia but
Morbidly Obese Patients With Unfavorable Outcome in
Patients With Effort Angina

Methods: In 18 patients with documented coronary artery disease and impaired left ventricular function, HHM was identified by thallium 201-scintigraphy, radionuclide ventriculography, and low-dose dobutamine echocardiography, performed prospectively and three months after revascularization. During open-heart surgery (OP), transmural biopsies were removed from the hibernating areas. Both, metabolite contents (HPLC) and thermographies (microscopy) were assayed from the same hibernating areas, allowing to normalized total myocardial metabolite content to the cellular myocardial fraction (CMF). HHM data were compared to normal human myocardium (control; n=7).

Results: All patients showed diagnostic concordance of the clinical variables of HHM (CP) and a significant improvement of regional contractile performance following revascularization. In HHM, total myocardial metabolite content as cellular myocardial fraction (CMF) was reduced (see table), as were energy charges (ECC), phosphorylation potential (P-Pot) and the free energy of ATP hydrolysis (ΔGtp). High energy phosphate contents and energetic parameters in human hibernating myocardium

<table>
<thead>
<tr>
<th>ATP</th>
<th>CP</th>
<th>EC</th>
<th>P-Pot</th>
<th>ΔGtp</th>
</tr>
</thead>
<tbody>
<tr>
<td>3.76±0.23</td>
<td>3.11±0.06</td>
<td>2.96±0.02</td>
<td>2.91±0.04</td>
<td>5.96±0.89</td>
</tr>
<tr>
<td>4.17±0.28</td>
<td>5.67±0.37</td>
<td>4.25±0.11</td>
<td>5.23±0.27</td>
<td></td>
</tr>
</tbody>
</table>

CMF = 1.72±0.25

P < 0.005 (ANOVA), metabolite contents in μmol/g wet wt, ΔGtp in kJ/mol.

Conclusion: This first description of HHM’s energy metabolism reveals that there is severely energy depleted myocardium. Due to the well established impact of energy metabolism on contractility we suggest that these energetic alterations contribute to HHM’s impaired contractile performance.

878-5

Percutaneous intervention in Plaques With increased Temperature is Associated With Unfavorable Outcome in Patients With Effort Angina

Christodoulou I, Stofanadis, Konstantinos P, Touliouzas, Eleftherios Talakis, Marios Vavoumoukanis, Ioannis Kolliasos, Chaniambros Vatopoulos, Athanasios Tzikas, Daphne Malis, Pavlos K. Touliouzas, Ippokrasis Hospital, Athens, Greece

Background: It has been shown that patients with effort angina have increased temperature of the culprit atherosclerotic plaque. The present study was designed to investigate the significance of temperature measurement of the atherosclerotic plaque in patients with effort angina.

Methods: Balloon angioplasty was performed in 30 patients, mean age 61.3±11.3 years, with effort angina. We measured the temperature difference (ΔT) between the atherosclerotic plaque and the healthy vessel wall with a thermography catheter, previously validated, after accomplishing TIMI III flow. A metallic stent was implanted in all patients. Results: All procedures were performed successfully and without complications. In the study population mean ΔT was 0.32°C±0.18°C. All patients were followed up for 17.3±5.2 months, during which 4 patients suffered from an adverse cardiac event. Patients with adverse cardiac events had increased ΔT compared to those without events (0.65±0.02°C vs 0.53±0.07°C, P=0.01). The risk for an adverse cardiac event was increased in patients with hot plaques (odds ratio 1.41).

Conclusions: The increased temperature of the culprit atherosclerotic plaque of patients with effort angina, in whom elective percutaneous intervention was performed, is associated with unfavorable clinical outcome.

3:30 a.m.

878-6

Polymorphisms of Factor V Leiden, Prothrombin e Methylenetetrahydrofolate Reductase in Patients With Coronary Disease

Antonio P. Manur, Joyce M. Ammacchina-Bizzacchi, José A. F. Ramires, Heart Institute (InCor), University of São Paulo Medical School, São Paulo, Brazil

Factor V Leiden, prothrombin 20210A allele and methylenetetrahydrofolate reductase (MTHFR) have been associated with coronary artery disease (CAD) in some studies but not in others. Negative study results were due to the small number of study patients or to single gene analysis in a multifactoral disease. Analysis of a panel of two or more polymorphisms may increase CAD identification. Methods: In a case-control study, we analyzed factor V Leiden, prothrombin ([Glu-Pro] mutation and G20210A mutation of methylenetetrahydrofolate reductase (MTHFR) in 238 patients with CAD and 368 control subjects matched by age, sex, and race. Gene polymorphisms were determined by the polymerase chain reaction. Panels were composed of at least three polymorphisms previously associated with CAD. Results: Factor V Leiden mutation was higher in patients with CAD (4.4% vs 0.6%; p<0.003), in men with CAD (4.8% vs 0.4%; p<0.045), in women (4.5% vs 0.1%; p<0.003), in 40–49 years (4.8% vs 0.1%; p<0.003), in 40–49 years (4.8% vs 0.4%; p<0.045), in women (4.5% vs 0.1%; p<0.003). Polymorphisms were not associated in women with CAD. A panel of two polymorphisms that included factor V Leiden mutation was associated with CAD. Multivariate analysis disclosed factor V Leiden as an independent variable for CAD (OR=4.4, 95% CI: 1.2–16.7; p=0.03). Conclusion: Of all polymorphisms, only factor V Leiden was shown to be an independent marker for CAD. The panel of two or more polymorphisms did not increase CAD identification.

8:30 a.m.

ORAL CONTRIBUTIONS

879 Advances in the Pharmacotherapy of Acute Myocardial Infarction

Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 231A

879-1

Is IIb/IIIa Blockade State-of-the-Art for Catheter Based Reperfusion? A Meta-Analysis of Five Randomized Trials in Acute Myocardial Infarction

Umesh N. Khot, Franz-Josef Neumann, Sorn J. Siores, Albert Sichich, Gautis Montaloskatos, Shelly Sapp, Eric J. Topol, The Cleveland Clinic Foundation, Cleveland, OH

Background: Glycoprotein IIb/IIIa inhibitors have been shown to improve clinical outcomes in patients with unstable and stable angina undergoing various types of percutaneous intervention. Whether there is a similar benefit in patients undergoing percutaneous intervention for acute myocardial infarction remains unknown.

Methods: To address this issue we performed a meta-analysis of 1359 patients from five randomized clinical trials (EPIC, RAPPOR, ISAR-2, ADIRAL, and STOPAMI) of abciximab in percutaneous intervention for acute myocardial infarction. We compared clinical outcomes in 646 patients who received abciximab with 685 patients who did not receive abciximab.

Results: Abciximab caused a significant 43% reduction in the incidence of both death and myocardial infarction at 6 month followup (P=0.003). At 30 day followup and was more pronounced at 6 month followup.

Conclusions: Abciximab caused a significant 43% reduction in the incidence of both death and myocardial infarction. The benefit was apparent at 30 day followup and was more pronounced at 6 month followup.
clinical and angiographic follow-up study: Juvenile patients (> 76 years) received thrombolytic therapy for signs and symptoms of suspected acute transmural myocardial infarction within 6 hours of onset, and showed TIMI 3 flow at coronary angiography performed within 4 hours after thrombolysis. Thereafter, they were randomized either: aspirin 50 mg daily or to the combination of aspirin 80 mg and medium intensity Coumadin (target INR: 2-3). Follow-up angiography was scheduled at three months. Results: Recombinant tissue plasminogen activator (r-tPA) was given to 202 patients on aspirin, compared with 10% for those on combination therapy (RR 0.69, CI 0.39-0.98, p = 0.03). Patients on aspirin showed TIMI 0-1 flow in 19% of patients, compared with 11% for those on aspirin and Coumadin (RR 0.92, CI 0.24-0.44, p = 0.05). Thrombolysis and/or reperfusion were observed in 7% and 9% of patients, respectively (CI 0.12-0.12; p = 0.001). Conclusions: These findings strongly suggest that the combination of aspirin with medium intensity Coumadin markedly reduces clinical and angiographic reocclusion after successful thrombolysis for suspected acute myocardial infarction. Adjunctive trial data and 1 year follow-up will be presented.

879-3
Early Statin Treatment Improves Long-Term Survival in
Patients Discharged Alive After Acute Myocardial Infarction
Lill Stenestrand, Lars Wallentin, the RIKS-HAS group, Heart Center, University Hospital, Linköping, Sweden; Dept. of Cardiology, University Hospital, Uppsala, Sweden

Background: Randomized trials have shown that statin treatment is beneficial as secondary prevention in patients with cardiovascular disease. It is still unclear if statin treatment started already in hospital will influence long term outcome. Furthermore it is also unknown how results from randomized trials translate into effects in an unselected patient population. We investigated the effect of early statin treatment on one-year survival in an large cohort of consecutively unselected acute myocardial infarction (AMI) patients.

Methods: From the Swedish Register of Cardiac Intensive Care, which included every CCU admitted patient at 68 participating hospitals in 2001, 42,647 AMI patients >60 years old who were alive at discharge were included in the analyses. Cox regression analysis was performed evaluating the effect of statin treatment initiated before or at discharge regarding one-year mortality taking into account over 80 factors known to influence survival such as clinical background, medication, interventions and complications.

Results: In the 14,752 patients without statin treatment the unadjusted one-year mortality was 9.4% (1,246) compared to 11.1% (2,646) in the 31,990 patients on early statin treatment. In Cox regression analysis adjusting for the 26 covariates early statin treatment was associated with a risk reduction of 35% for one-year mortality RR 0.65 (95% CI 0.55-0.77), p<0.001.

Conclusions: Early initiated statin treatment in AMI patients significantly reduces one-year mortality. Furthermore this register study shows that the results from randomized statin trials will have important implications also when transferred to an unselected AMI population.

879-4
LMW Heparin (Dalteparin) for Improvement of Patency After Thrombolysis in AMI: A Prospective Randomized Multicentre Coronary angiography Study
Mikael Dottling, Lin Riborg Strand, Ola Griggorn, Bertil Lindahl, Tage Nilsson, Kenneth Persson, Eva Pilhi, Agnete Siegbahn, Eva Wallen, Lars Wallentin, The ASSENT Plus Investigators. Dept. of Medicine, Sahlgrenska University Hospital/Ostra, Göteborg, Sweden; Uppsala University, Uppsala, Sweden

Background: Despite improvement of 60 minutes coronary blood flow there are no added benefits in clinical outcome by the new fondaparinux agents. This might be caused by recirculation during and after the associated 4-hour heparin infusion. The primary aim of the present trial was to evaluate whether s.c. dalteparin until a coronary angiogram after 4-7 days is more effective than 46-hr heparin infusion in obtaining patency and TIM-I5 flow after thrombolysis with r-PA in acute myocardial infarction (AMI) patients.

Methods: Patients with an AMI and an indication for thrombolysis within 6 h of symptom onset were randomly randomized to heparin infusion for 48 h or i.v. bolus followed by s.c. dalteparin 120 IU/kg every 12 h until coronary angiography after 4-7 days. All coronary angiograms were centrally and blindly evaluated concerning TIMI flow grade (1-3 objective). Other objectives were safety, noninvasive signs of early recirculation. coagulation and bleeding parameters, clinical events during treatment (max. 7 days) and 30 days results: 439 patients, mean age 66 yrs, 70% male, were randomised in 18 Swedish and 4 US hospitals. 378 performed per protocol angiography.

Table. Myocardial Area at Risk and Effects of rPSGL-lg on Infarct Size

<table>
<thead>
<tr>
<th>Area at risk, cm²</th>
<th>Infarct size, cm²</th>
<th>Placebo</th>
<th>rPSGL-lg</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>53.14±8.56</td>
<td>25.56±11.94</td>
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<td></td>
</tr>
<tr>
<td>12.0±12.80</td>
<td>3.90±4.39</td>
<td>0.008</td>
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</table>

Table. Multivariate Area at Risk and Effects of rPSGL-lg on Infarct Size

<table>
<thead>
<tr>
<th>Area at risk, cm²</th>
<th>Infarct size, cm²</th>
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<th>rPSGL-lg</th>
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<td>3.90±4.39</td>
<td>0.008</td>
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</table>

Conclusions: The administration of rPSGL-lg results in significantly improved left ventricular function in the early time period after AMI through salvage of jeopardized myocardium.

879-5
Therapeutic Margin of Safety With Weight-Optimized Dosing of Tissue Plasminogen Activator in Acute Myocardial Infarction

Background: The Assessment of Safety and Efficacy of a New Thrombolytic (ASSENT)- 3 trial demonstrated that intravenous tissue plasminogen activator (TPA) is equivalent to alteplase (AP) for treatment of myocardial infarction using weight-optimized doses, and we sought to evaluate the safety of errors in weight-optimized dosing. Methods: Rates of in-tracranial hemorrhage (ICH) and death were determined 1) among all patients treated with the highest dose (50 mg of TNK) 2) among patients weighing < 90 kg who received 50 mg TNK in error; and 3) among all patients receiving any incorrect dose of TNIK. Results: 1) A total of 1,015 patients received 50 mg TNK, whom we compared to 1,919 patients weighing < 90 kg (control group matched for weight). The rate of ICH with 50 mg TNK (8.57%) was similar to that with 90 kg (8.47%, P = 0.65), as was the rate of death (4.70% vs. 3.96%, P = 0.69). Multivariate adjustment did not change these results (P = 0.21 for both). 2) Of patients receiving 50 mg TNK, 150 (7.9%) were weighed < 90 kg as specified by the protocol and received the same dose. Rates of ICH (1.33%) and death (6.37%) were not significantly different than those among patients > 90 kg who received other thrombolytic doses (ICH = 1.00%, P = 0.68; death = 6.66%, P = 1.00). 3) Of all patients given < 50 mg TNK = 218 patients (2.7%) received doses greater than recommended, and 326 (4.0%) received doses lower than recommended. The median weight error in overdose was 8 kg and in undertreatment was 1 kg. Neither underdosing nor overdosing of 1-2 dosing intervals (up to 20 Kg or 44 pounds in error) was associated with ICH (odds ratio = 0.63 [95% CI 0.63-1.00, P = 1.00]) or death (OR = 1.09 [P = 0.73] & 0.84 [P = 0.64], respectively) in a multivariate model accounting for weight. Conclusions: In this limited sample, there were no obvious differences in the rates of ICH and death with dose errors of TNK compared to within weight matched controls treated with the correct dose. While correct dosing remains the goal, there appears to be an acceptable margin of safety with errors in weight-optimized dosing of TNP.
New Horizons for Surgical Myocardial Revascularization

Wednesday, March 21, 2001, 8:30 a.m.-10:00 a.m.
Orange County Convention Center, Room 304A

8:30 a.m. Prognostic Ten-Year Patency of Saphenous Vein and Left Internal Mammary Artery Grafts After Coronary Artery Bypass Surgery


Background: This Department of Veterans Affairs Cooperative registry prospectively defined long-term saphenous vein graft (SVG) and left internal mammary artery (IMA) graft patency in patients undergoing coronary artery bypass grafting (CABG) in the 1980s.

Methods: As part of an ongoing trial, we obtained serial angiographic data at one week, one year, three years, and ten years after CABG. Initially, 1196 patients were enrolled in this trial. At ten years, we obtained angiographic data on 100 patients, while 441 patients had died, and 300 patients did not undergo angiography.

Results: The SVG and IMA graft patency rates at ten years were 55.8% and 90.4%, respectively. If a patient had a patent SVG or IMA at one week, that graft had a 92.0% and 92.8% chance, respectively, of being patent at ten years. For SVGs, the first year patency rate was 82.6%, three-year patency was 77%, and ten-year patency was 68.4%. For IMA grafts, the first year graft patency rate was 94.0%, three-year graft patency was 90.5%, and ten-year patency was 90.4%. There was a significant difference between the patency rates by location (p<0.05). At ten years, the SVG patency of the left anterior descending artery was 72.7% than that of the right coronary artery (80.8%). There was no significant difference in patency rates between the left anterior descending and the circumflex (84.9%).

Conclusions: Our conclusion is that as prospective angiographic follow-up are obtained on patients undergoing CABG in the 1980s, the long-term patency for SVG is better than previously thought. For SVGs, the most important predictor of long-term graft patency in patients at one week after CABG.

8:45 a.m. Minimal Invasive Bypass Surgery Versus Stent Implantation in Isolated Proximal High Lesions of the LAD in More Than 200 Patients


Background: Intra thoracic bypass surgery (MIDCAB) has been shown to yield comparable results to conventional bypass grafting with less operative trauma. Therefore it may be considered a alternative treatment to stent implantation. In patients with proximal high-grade lesions of the LAD, MIDCAB and PTCA/stenting have been compared several times.

Methods: This study examined the effects of this procedure on long term survival and reintervention rates of periprocedural events. After 6 months the reintervention rate is higher in the stent group compared to the MIDCAB group.

Results: The SVG and IMA patency rates at ten years were 65.8% and 90.4%, respectively. If a patient had a patent SVG or IMA at one week, that graft had a 92.0% and 92.8% chance, respectively, of being patent at ten years. For SVGs, the first year patency rate was 82.6%, three-year patency was 77%, and ten-year patency was 68.4%. For IMA grafts, the first year graft patency rate was 94.0%, three-year graft patency was 90.5%, and ten-year patency was 90.4%. There was a significant difference between the patency rates by location (p<0.05). At ten years, the SVG patency of the left anterior descending artery was 72.7% than that of the right coronary artery (80.8%). There was no significant difference in patency rates between the left anterior descending and the circumflex (84.9%).

Conclusions: Our conclusion is that as prospective angiographic follow-up are obtained on patients undergoing CABG in the 1980s, the long-term patency for SVG is better than previously thought. For SVGs, the most important predictor of long-term graft patency in patients at one week after CABG.
95% CI 0.890-0.986, p = 0.012) as independent factors associated with postoperative AF.

Background: The consequent development of minimally invasive techniques in coronary artery bypass grafting via a median sternotomy already preoperatively planned.

Methods: Perioperative survival was 100%. Internal mammary arteries (IMA) were always harvested totally endoscopically except in four patients. All IMAs had an excellent flow. All patients out of the TECAB group were operated upon via a three (TECAB) or four (floating heart TECAB) point stab incisions using the da Vinci™ robot for left IMA or bilateral IMA take-down for performance of anastomoses. The time of dissection of the left IMA could be significantly reduced. In the TECAB group all patients were operated upon via a three (TECAB) or four (floating heart TECAB) point stab incisions. Preoperative, perioperative, and postoperative data were observed. Conclusions: Our preliminary experiences with this new surgical techniques for robotic-enhanced minimally invasive treatment of CAD promote an optimistic way of thinking about the further development of these procedures and its implication in patients suffering from CAD.

Poster Session

1282 Trends in Acute Myocardial Infarction Management

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1282-75 Improving Trends in Evidence-Based Treatment of Acute Myocardial Infarction: Impact of a Population-Wide Disease Management Program?

Jafna L. Cox, Iqbal R. Bata, Blair J. O'Neil, David E. Johnstone, on behalf of the ICONS Investigators. Dalhousie University, Halifax, NS, Canada

Background: Despite a wealth of evidence with which to direct clinical practice in cardiology, a care gap persists between current clinical guidelines and the care delivered. One way of addressing this gap is through disease management, an attractive but infrequently used model of care. The hypothesis was that implementation of a disease management program would lead to improved outcomes in patients suffering from AMI.

Methods: Improving Cardiovascular Outcomes in Nova Scotia (ICONS) is a large, population-based disease management program, involving multiple stakeholders, and funded from the start of the project in October 1997 through to the end of 1999. These included antiplatelet therapy (AP), beta-blockers (BB), ACE Inhibitors or All receptor blockers (ARB), statins (HMG-CoA reductase inhibitors), and non-rate limiting calcium channel blockers (HCL, CCB and NCL CCB).

Results: Data were provided concerning temporal trends in the discharge rates of various therapies from the start of the project in October 1997 through to the end of 1999. These include antiplatelet therapy (AP), beta-blockers (BB), ACE Inhibitors or All receptor blockers (ARB), statins (HMG-CoA reductase inhibitors), and non-rate limiting calcium channel blockers (HCL, CCB and NCL CCB).

Poster Session

1282 The Smoker’s Paradox: Angiographic Insights From the TIMI trials

Sarah R. Kerrigan, Michael S. Chan, Sabina A. Murphy, Jessica S. Lim, Colin A. Hynes, Matthew H. C. Potter, Lily L. Liu, Susan J. Mubao, Christopher P. Cannon, Eugene Braunwald, C. Michael Gibson. University of California San Francisco, San Francisco, CA, Brigham and Women’s Hospital, Boston, MA, University of California San Francisco, San Francisco, CA, Brigham and Women’s Hospital, Boston, MA

Background: Previous, it has been demonstrated that smokers have improved clinical outcomes in the setting of acute myocardial infarction (AMI). We hypothesized that improved outcomes might be explained by improved epicardial and microvascular perfusion, as well as favorable baseline demographics. Methods: Data were drawn from the TIMI 4, 10A, 10B and TIMI 14 angiographic trials of AMI. Results: Univariate analysis showed that smokers had lower mortality rates (2.73% vs. 6.22%, p = 0.001) and lower rates of intracranial hemorrhage (ICH) (0.71% vs. 1.51%, p = 0.054). However, in a multivariate model correcting for age and infarct artery location, there was no difference among active smokers and non-smokers in the odds of death (0.52 vs. 0.29, p = 0.14) or ICH (0.70 vs. 0.96, p = 0.15). Higher rates of TIMI grade 3 flow in smokers were confirmed in those patients with LAD infarctions (TIMI 3, 64.2% vs. 43.9%, p = 0.006), but no difference was seen in patients with RCA or both LCx and RCA infarctions (TIMI 3, 64.2% vs. 64.3%). Conclusion: Smokers have improved clinical outcomes in AMI. However, this is largely explained by their younger age and lower incidence of anterior AMIs. Despite improved epicardial flow, microvascular flow was impaired (lower TIMP 3 and longer channel diameters), with tangential stress by peak CK.

Poster Session

317A ABSTRACTS - Myocardial Ischemia and Infarction

1282-76 Robotic Assisted Cardiac Surgery: The Dresden Experience

Ronjaud Ochon, Utz Kappert, Jens Schneider, Ina Schade, Vasiliou Guillelmos, Samsi Male Tugulekin, Klavie Matschke, Stephan Schueler. Cardiovascular Institute, University of Dresden, Dresden, Germany

Background: The consequent development of minimally invasive techniques in coronary artery surgery, focusing on avoidance of median sternotomy, has lead to a different, technological concept for the treatment of patients suffering from coronary artery disease (CAD). With the introduction of the da Vinci™ robotic surgical system (Intuitive Surgical) into minimally invasive cardiac surgery the outlook of performing coronary artery bypass operations "closed chest" become a reality. Methods: Between 5/99 and 6/00 this new wrist-enhanced instrumentation was used in 134 patients (100 male, 34 female, median age 63 ± 10.1 years). Twelve patients suffering from single vessel CAD and one patient suffering from double vessel CAD were treated as totally endoscopically coronary artery bypass surgery (TECAB). Seventy-three patients with single vessel CAD underwent a minimally invasive direct coronary artery bypass procedure. Thirty-two patients with double vessel CAD were treated using the robotic-enhanced Direct Coronary Technique. Sixteen patients received a median sternotomy. Seven patients necessitated an intracoronal conversion to a median sternotomy. Nine patients received robotic-assisted coronary artery bypass grafting via a median sternotomy already preoperatively planned.

Results: Perioperative survival was 100%. Intramyocardial arteries (IMA) were always harvested totally endoscopically except in four patients. All IMAs had an excellent flow. All patients out of the TECAB group were operated upon via a three (TECAB) or four (floating heart TECAB) point stab incisions using the da Vinci™ robot for left IMA or bilateral IMA take-down and for performance of anastomoses. The time of dissection of the left IMA could be significantly reduced. In the TECAB group all patients were operated upon via a three (TECAB) or four (floating heart TECAB) point stab incisions. Preoperative, perioperative, and postoperative data were observed. Conclusions: Our preliminary experiences with this new surgical techniques for robotic-enhanced minimally invasive treatment of CAD promote an optimistic way of thinking about the further development of these procedures and its implication in patients suffering from CAD.
The purpose of the study was to determine whether patients who arrive without STE but develop subsequent STE are younger, more frequently male and have fewer comorbidities compared to STE -/- patients (OR=1.77; 95% CI 1.55-2.013). Conclusions: Patients with subsequent STE are at increased risk of mortality compared to patients who arrive at the hospital with no STE and do not evolve subsequent ST segment elevation (STE -/-).
Clinical Outcomes by Diabetes Status

<table>
<thead>
<tr>
<th>Predictor</th>
<th>DM Patients (%)</th>
<th>Non-DM Patients (%)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death/MI</td>
<td>12.4</td>
<td>9.5</td>
<td>1.35 (1.14, 1.59)</td>
</tr>
<tr>
<td>Death/MI</td>
<td>10.3</td>
<td>6.9</td>
<td>1.55 (1.29, 1.86)</td>
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<tr>
<td>Death</td>
<td>3.4</td>
<td>1.7</td>
<td>2.04 (1.48, 2.53)</td>
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<tr>
<td>1-year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Death/MI</td>
<td>23.7</td>
<td>16.8</td>
<td>1.53 (1.37, 1.87)</td>
</tr>
<tr>
<td>Death</td>
<td>11.6</td>
<td>10.0</td>
<td>1.16 (1.07, 1.27)</td>
</tr>
</tbody>
</table>

1283-81 What Angiographic Measure of Extent of Coronary Artery Disease Best Predicts Subsequent Risk?

David D. Hong, Joseph M. Mulvihill, Debra G. Mentzer, Benjamin D. Hotter, Todd L. Birk, Robert R. Reardon, Jeffrey L. Anderson. University of Utah, Salt Lake City, UT; LDS Hospital, Salt Lake City, UT

Background: The extent of prevalent coronary artery disease (CAD) is a strong predictor of future risk of cardiovascular events, but the best clinical predictive measure of the extent of CAD is uncertain. We studied the predictive value for death or myocardial infarction (MI) of 6 readily assessed measures of CAD.

Methods: To assess the relationship of CAD measures to outcome, we studied 2827 patients (69% without acute myocardial infarction (MI) undergoing angiography; 1792 had severe CAD (≥210% stenosis), 303 mild/moderate, and 732 no CAD. CAD was quantified in 6 ways: presence of severe CAD, number of vessels with severe disease (≥70% stenosis), moderate/severe disease (<70% stenosis), severe lesions, mild/moderate lesions (10-69% stenosis), and total lesions. Information was entered prospectively into a database, and pt were followed for up to 5.3 years (mean, 2.0 ± 1.4). Associations between measures of CAD and death/nonfatal MI were evaluated using univariate and multivariate Cox regressions (9 co-variables).

Results: PI were 64 ± 12 years old; 68% were men. During follow-up, 180 pt died and 110 had non-fatal MI. Subsequent death/MI was predicted univariately by all CAD measures (p<.001), with the order of number of severe lesions-total lesions-moderate/severe vessels/total lesions-severe lesions-moderate lesions. In multivariate analyses, all measures retained significance, with the order of number of severe vessels-severe CAD-moderate/severe vessels-total lesions-severe lesions-moderate lesions-moderate lesions. Other independent predictors were ejection fraction, age, diabetes, and hypertension. Results were generally similar for the endpoint of death alone.

Conclusions: Extent/Severity of angiographic CAD was confirmed to be a highly significant and independent predictor of future death/MI. The most powerful single predictor is the number of vessels with severe (>70% stenosis) disease. The total number of lesions is a better predictor than number of severe or moderate lesions alone. Simple, qualitative or semi-quantitative measures of angiographic CAD severity provide useful prognostic information.

1283-82 Clinical Implications of the No-Reflow Phenomenon: A Predictor of Left Ventricular Remodeling in Reperfused Acute Myocardial Infarction

Paolo Colombo, Roberta Monticelli, Marco Corda, Christian Cadeddu, Liu Chen, Enrico Orrizzi, Luigi Meloni, Sabino Miceto. Department of Cardiovascular and Neurological Sciences, University of Cagliari, Cagliari, Italy

Background: After acute myocardial infarction the damage of microvasculature and the no-reflow phenomenon implies the presence of advanced myocardial necrosis. Intracoronary myocardial contrast echocardiography after acute myocardial infarction can detect the presence and extent of microvascular damage. In this study, we verified the value of early intravenous myocardial contrast echocardiography in predicting left ventricular remodeling after acute myocardial infarction.

Methods: The study population of 55 consecutively enrolled patients with first acute myocardial infarction (20 anterior, 8 lateral and 27 inferior) underwent an echocardiogram on the first day of acute myocardial infarction, a contrast echocardiogram with harmonics power Doppler is capable of identifying, in the acute phase of myocardial infarction, patients prone to late left ventricular dilatation, thus permitting a more aggressive diagnostic and therapeutic algorithm.

Results: At contrast echocardiography, 37 patients showed contrast enhancement in >50% of acutely dyskinetic myocardial segments (no-reflow) and 18 a sizeable contrast defect (no-reflow). Left ventricular volumes increased in the convolution stage in patients with myocardial contrast echocardiography no-reflow (end-diastolic from 72 ± 21.3 to 71.3 ± 18.7 mL/m², p<0.001) and 15 patients (end-diastolic from 72 ± 21.3 to 71.3 ± 18.7 mL/m², p<0.001), while remained constant in reflow patients (end-diastolic from 72 ± 21.3 to 71.3 ± 18.7 mL/m², p<0.001).

Conclusion: Intravenous myocardial contrast echocardiography with harmonic power
Methods: 375 patients (212 males and 163 females) with the left anterior descending artery stenosis with their first myocardial infarction were considered. Serial echocardiograms were performed 24-48 hours after myocardial infarction (TI), before discharge (T2), after 6 weeks (T3), and after 6 months (T4). Body (T1) and semi-axial views (T2-4) of the left ventricle were utilized by repeated measures ANOVA.

Results: When compared to men, women were older (70±12 vs 58±12 years, P<0.001), had higher prevalence of hypertension and diabetes (respectively 24±18 and 10±7% in men vs 42±14 and 21±9% in women, P<0.001), showed the biggest target vessel (28±15 vs 25±14% of LAD area), had increased LVM index (13.6±1.2 vs 12.1±0.5 g/m², P<0.001, systolic function (0.85±0.04 vs 0.88±0.02, P<0.001), and higher prevalence of previous congestive mitral regurgitation (10% vs 3%, P<0.001), higher wall thickness to to radia ratio (0.24±0.07 vs 0.39±0.06, P<0.001) and higher Doppler-derived peak A wave velocity (74±23 vs 68±22 cm/s, P<0.05). After correction for age, LV index values of all echocardiographic indices were significantly different between two sexes. Both early and late LV remodeling occurred in women but it did not differ from that of men (time×sex interaction: P=0.10 for diastolic and systolic volumes and echocardiographic indices).

Conclusions: Myocardial infarction in women is associated with larger LV damage, more depressed LV systolic function and greater relative LV mass and systolic function. Some of these changes are not due to age differences and their possible prognostic role needs to be further explored. The pattern of early and late LV remodeling did not differ between sexes.

128A-85 Beneficial Effects of Probucol on Neurohumoral Activation and Cardiac Cytokine Expression in the Postinfarction Rat Myocardium

Ying T. Sia, Jean-François Sarrazin, Jean-François Jasmin, Angelino Calderone, Jean-Lucien Rouleau. Montreal Heart Institute, Montreal, PQ, Canada, Toronto General Hospital, Toronto, ON, Canada

Increased oxidative stress in heart failure may represent an underlying mechanism contributing to the progression of the disease. Indeed, Singal et al. have shown that the oxidative stress is closely associated with the appearance of myocardial fibrosis, systolic and diastolic abnormalities suggestive to secondary myocardial infarction (MI) in rat. The following study tested the hypothesis that treatment with the antioxidant probucol (PBO) may improve left ventricular (LV) function and morphology in the post-infarct rat and is associated with inhibition of myocardial fibrosis and cytokines expression and plasma neopterin (PNO) secretion. Acute MI was induced by LAD ligation, and at the 20th post-MI day surviving rats were randomized into placebo or probucol (10mg/kg) for 60 days by daily gavage. Probability treatment of sham rats had no effect on either LV function or morphology but significantly reduced cardiac TNFa expression and TNFa mRNA levels as compared to sham rats, MI leads to decreased LV systolic pressure (90±3 vs 131±4mmHg, P<0.05) and +dP/dt (456±6 vs 487±6mmHg/s, P<0.05), higher prevalence of moderate to severe mitral regurgitation (10% vs 3%, P<0.001), higher wall thickness to to radia ratio (0.24±0.07 vs 0.39±0.06, P<0.001) and higher Doppler-derived peak A wave velocity (74±23 vs 68±22 cm/s, P<0.05). After correction for age, LV index values of all echocardiographic indices were significantly different between two sexes. Both early and late LV remodeling occurred in women but it did not differ from that of men (time×sex interaction: P=0.10 for diastolic and systolic volumes and echocardiographic indices).

Conclusions: Myocardial infarction in women is associated with larger LV damage, more depressed LV systolic function and greater relative LV mass and systolic function. Some of these changes are not due to age differences and their possible prognostic role needs to be further explored. The pattern of early and late LV remodeling did not differ between sexes.
and vascular structures. According to our previous studies the distribution and frequency of cardiomyocyte apoptosis follows a similar pattern as HO-1 expression. **Conclusion:** HO-1 is induced in a rat myocardial infarction model and the expression of HO-1 colocalizes with apoptosis, suggesting that HO-1 may play a role in the regulation of apoptotic cardiomyocyte loss and vascular remodelling.

**1285-02** Coronary Sinus Oxygen Saturation (SvO2) as a Marker of Myocardial Ischemia

Yu D. Gallant, Rainbow Chaumet, Yves Belin, Stephane Champagne, Jin Bo Su, Lucien Sambin, Bertrand Crozatier, Luc Irivry, Severin, France

**Background:** Coronary sinus oxygen saturation (SvO2) reflects the balance between myocardial oxygen supply and demand. This study was designed to examine whether SvO2 is affected by changes in myocardial blood supply and myocardial contractile function and whether the temporal changes in SvO2 during ischemia are related to temporal ECG ST segment changes. **Methods:** Eight open-chest dogs were instrumented with a left ventricular pressure gauge, an oxymetry Swan-Ganz catheter in the coronary sinus for continuous oxygen monitoring, a circunflex coronary cuff catheter, a doppler flow probe to measure circumflex coronary blood flow velocity (CBFv) and piezo-electric crystals to measure left ventricular anterior and posterior wall thicknesses. Myocardial blood supply and myocardial contractile function were modified by partial coronary stenosis (50% reduction in CBFv, Smin), total coronary occlusion (zero CBFv, Bmin), ATP injection (20 mg iv) and dobutamine infusion (10 pg/kg/min, iv). **Results:** SvO2 changes were closely correlated to CBFv changes induced by coronary stenosis, coronary occlusion and dobutamine infusion (r=0.81, p<0.001). SvO2 was reduced by 0.01% per second after the onset of coronary occlusion from 86.1% to 12.5% while ECG ST segment changes reached the significant threshold (1 mv) 60 seconds after coronary occlusion. During partial coronary stenosis, SvO2 was reduced from 86.1% to 78.1% (p<0.001) 70 seconds after the onset of partial coronary stenosis while ECG ST segment changes never reach the significant threshold during the 190 period of coronary stenosis. **Conclusion:** SvO2 reduction is associated with myocardial ischemia, and it is a more sensitive marker of myocardial ischemia than ECG ST segment analysis and may be useful in the monitoring of myocardial ischemic events during cardiac or non cardiac surgery.

**POSTER SESSION**

**1285** Stable Ischemic Syndrome: Pathophysiology, Diagnosis, and Prognosis III

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.

Orange County Convention Center, Hall A4

Presentation Hour: 10:00 a.m.-11:00 a.m.

**1285-91** RSR' Pattern Without the Evidence of Bundle Branch Block: Diagnostic Value as a Sign of Left Ventricular Aneurysm


**Background:** A left ventricular aneurysm (LVA) is associated with increased risk of heart failure, thromboembolism, ventricular arrhythmias and also the increased risk of sudden and non-sudden death. An RSR' pattern without evidence of bundle branch block (QRS duration ≤120ms) on the ECG may be associated with a LVA as a result of myocardial scar formation. A LVA is common in the anterolateral and circumferential region of the left ventricular wall. We, therefore, postulate that an RSR' pattern in the left sided leads (I, AVL, V5 to V7) is a highly specific sign of LVA. **Methods:** ECG's of 110 consecutive patients with LVA documented by left ventricular angioscopy (300 right anterior oblique view) was compared with 110 patients without LVA. **Results:** The RSR' pattern or its variant (RS'-R or RS' pattern) on left sided leads were present in 55 (50%) patients with LVA as compared to 6 (6%) patients without LVA (p value <0.0005). The sensitivity of RSR' pattern for LVA was only 50% whereas the specificity was 94.5%. The false negative and the false positive rates were 50% and 5.5%, respectively. It has a high positive predictive value of 90% with a moderately negative predictive value of 65%. The overall accuracy of the test is 75%.

**Conclusion:** Our study has revealed that an RSR' pattern in the left sided leads, as a highly specific and moderately sensitive sign of LVA, it also has high positive predictive value.

**ABSTRACTS - Myocardial Ischemia and Infarction**

**375A** Who Refers Negative Coronary Angiograms?

Dominic Y. Leung, Craig P. Jurgens, Sidney Lo, Andrew R. Hopkins. Liverpool Hospital, Sydney, Australia

**Background:** Coronary angiography is the definitive test for suspected coronary disease. However, the referral patterns and referrer characteristics of angiographically normal coronary arteries or minor disease (negative angiograms) in patients with suspected coronary disease are seldom reported. **Methods:** From 12/92 to 7/01, a total of 6,400 patients underwent 8,689 coronary angiograms at Liverpool Hospital. Only studies referred primarily for coronary disease (n=8,682) were analyzed. Studies for valvular disease (n=2,291), linked access (n=52) and angioplasty (n=876) were excluded. Patient characteristics, main practice location and specialty of referrers were correlated with the negative angiogram rate. **Results:** 783 patients (764 procedures, 12.5%) had normal coronary arteries. 719 patients (746 procedures, 11.7%) had minor disease (<20% stenosis on <1 epicardial coronary artery). For referrers with <40 referrals (n=32), mean referrals 101±24, range 42-710), negative angiogram rate was 22.4% (10-41%). Cardiologist referrers (n=20) had a higher negative rate compared with non-cardiologist (n=13) referrers (25.7% vs 16.2%, p=0.006). **Conclusion:** Negative angiogram rate compared with non-cardiologist referrers was significant independent predictors of negative angiograms.

**1285-03** Isolated Left Main Trunk Aneurysm: How Common Is It?


**Background:** Identification of left main (LMT) stenosis is important not only for patient management but also to increase safety of the catheterization procedure. Occasionally LMT stenosis is not associated with significant atherectomy of other epicardial coronary vessels. We sought to determine the prevalence of isolated left main anastomosis from a prospective registry of consecutive patients. **Methods:** At our institution 8,004 patients underwent diagnostic cardiac catheterization between 1990 and 2000. Patients with prior bypass surgery (n=1,415) were excluded from the analysis. As the natural history of LMT stenosis in these patients may be different. Prevalence of LMT stenosis (>=70%) was studied according to the severity of the most severe lesion in the coronary arteries other than the LMT. The patients were divided into 5 groups. Group 1 included patients with the most severe lesion in the left anterior descending artery (LAD), group 2 between 70-50%, group 3 between 50-30%, group 4 between 30-20% and group 5 patients having no angiographically identifiable lesions. **Results:** Significant LMT stenosis was detected in 348 (5%) patients. Significant lesions (>=70%) in other coronary arteries was more frequently present in patients with LMT stenosis than in patients without LMT stenosis (81% vs 45%). The prevalence of LMT stenosis in association with presence of other coronary artery lesions is shown in the figure. Significant LMT stenosis was almost 20 times less likely to be present in patients with otherwise normal coronaries compared to patients with other significant coronary lesions (0.048 vs 9.1%). **Conclusion:** Isolated LMT stenosis is rare. Therefore, when encountered in the cath lab, careful angiographic determination supplemented with appropriate use of intravascular ultrasound is warranted to help exclude misleading angiographic views or catheter induced spasm.
Differences in Presentation and 1-Year Outcomes in Coronary Artery Disease (CAD) Patients of South Asian vs European Ethnicity Treated in an Outpatient Cardiology Practice

Narendra Singh, Milan K. Gupta, Ansh K. Jain, Frank Halperin, David Bates, Rouge Valley Health System, Toronto, ON, Canada; William Osler Health Centre, Brampton, ON, Canada

Background: Previous studies have shown differences in cardiac presentation and worse outcomes for South Asian (SA) vs European Canadian (EC) hospitalized inpatients. Methods: We retrospectively reviewed 400 consecutive outpatients with CAD having 1-year follow-up with respect to ethnicity, cardiac risk factors, utilization of evidence-based drug therapies, hospitalization and outcomes over 1 year (1996-97). Results: Of the 400 pts, 65% were males, 22% were SA. Mean age was 60±11 yrs. Comparison of SA vs EC pts showed SA pts were slightly younger (59 vs 61 yrs, p=.09), more often diabetic (25 vs 24%, p=.001), had higher systolic BP levels (142/80 vs 137/78 mmHg, p=.01), similar fasting glucose levels (6.5 vs 7.3 mmol, p=.19) but lower LDL (3.0 vs 2.8 mmol, p=.001), lower HDL (1.06 vs 1.17mmol, p=.02) levels. Cardiac hospitalizations (17 vs 20%) occurred frequently after initial consultation but were no different between the groups at 1 yr. Conclusions: SA outpatients have a different CAD risk factor profile than EC patients both at presentation and at 1 yr follow-up. Utilization of evidence-based drug therapies at 1 yr improved following cardiology consultation and may explain the similar outcomes despite differences at presentation. These data suggest that early intervention by cardiologists for high risk ethnic populations could potentially reduce subsequent morbidity and mortality.

POSTER SESSION

1286 Defining Modalities of the Acute Coronary Syndromes

Wednesday, March 21, 2001, 9:00 a.m.-11:00 a.m.
Orange County Convention Center, Hall A4
Presentation Hour: 10:00 a.m.-11:00 a.m.

1286-95 Atypical Presentations Among Medicare Beneficiaries With Unstable Angina: Is It Time to Redefine the Classical Clinical Presentation?

John G. Canto, Comptesa Finch, Catarina L. Kiefe, Jereen J. Allison, Qing Li, Suzanne Baker, Robert Center, Norm W. Walters, University of Alabama at Birmingham, Birmingham, AL

Background. The presence of chest pain (CP) is a hallmark symptom in patients with unstable angina (UA), however, little is known regarding the prevalence of atypical presentation among these patients and their related symptoms. Methods. We examined the medical records of 3,015 Medicare patients hospitalized at 22 Alabama hospitals with a confirmed diagnosis of unstable angina (UA) treated during the acute phase of presentation. We categorized the presenting characteristics into typical or atypical. Typical presentation was defined as 1) chest pain located substernally, in the left chest, or right chest; 2) the character of CP described as squeezing, tightness, aching, crushing, discomfort, distress, pressure, heaviness, pressure, relieved with rest or nitroglycerin, or worse with activity. Atypical presentation was defined as the absence of atypical presentation among these patients and their related symptoms. Methods. We examined the medical records of 3,015 Medicare patients hospitalized at 22 Alabama hospitals with a confirmed diagnosis of unstable angina (UA) between 1994 and 1998. Confirmation of UA required that the presenting symptom(s) be consistent with an acute coronary syndrome by documenta-

Table 1. Comparison of Atypical and Typical Patients

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Atypical Presentation</th>
<th>Typical Presentation</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N (%)</td>
<td>1,342 (44.5)</td>
<td>1,673 (55.6)</td>
<td></td>
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<tr>
<td>Mean age yrs</td>
<td>73.0</td>
<td>71.0</td>
<td>0.001</td>
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<td>Women, %</td>
<td>68.6</td>
<td>64.6</td>
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<tr>
<td>Non-White, %</td>
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</tr>
<tr>
<td>Diabetes, %</td>
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<td>56.3</td>
<td>0.55</td>
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<tr>
<td>Hypertension, %</td>
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<td>55.3</td>
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<td>Prior MI, %</td>
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<td>58.2</td>
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<td>Mortality - hospital, % (N=150)</td>
<td>50.0</td>
<td>50.0</td>
<td>0.73</td>
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<tr>
<td>Mortality - 30 days, % (N=2458)</td>
<td>47.2</td>
<td>52.9</td>
<td>0.27</td>
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<tr>
<td>Mortality - 1 year, % (N=500)</td>
<td>48.8</td>
<td>53.2</td>
<td>0.16</td>
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</tbody>
</table>

1286-96 Site Investigators Do Not Accurately Report Myocardial Infarction Events: Results of Event Adjudication by a Clinical Events Committee in the PARAGON-B Trial


Background: Myocardial infarction (MI), an important clinical trial endpoint, can be difficult to classify due to inconclusive symptoms, enzyme data, or electrocardiograms. In prior trials, disagreement between MI events reported by site investigators and a clinical events committee (CEC) have been observed. Methods: To better understand disagreements in MI reporting between investigators and a CEC, we analyzed data from the HALLUCINAT-M trial which evaluated the gycperprolactin/IIb/IIIa inhibitor, lamifibran, in 5,225 patients with acute coronary syndromes. The primary endpoint was the 30-day composite of death, MI or recurrent ischemia. MI suspected MIs were adjudicated by a CEC. Results: Overall, 1,738 patients (33%) had suspected MIs identified from data on the case report form; 483 (29%) were adjudicated by the CEC as MIs that met protocol end-point criteria. In 494 (25%) patients, investigators and CEC assessments of MI differed; 270 MIs were identified by the CEC but not the investigators, and 134 were identified by investigators but not the CEC. To prospectively reconcile disagreements between the CEC and the investigator, we sent letters to investigators that described the disagreement and asked for re-evaluation by the investigator. For the 404 patients with disagreement, letters were sent and returned for 362 patients. The remaining 22 had clear MIs by core lab enzyme criteria. Investigators came to agree with CEC assessments in 20% (80%). For the remaining 75 cases (20%); the CEC supported investigators' assessments in 10 and confirmed original CEC decisions in the other 65 cases. At cases with persistent disagreements, events were reclassified as 11% were enzyme elevations associated with ischemic symptoms and/or ECG changes. Conclusions: Investigators undetermined MI endpoints, but most agreed with CEC assessments of MIs after further follow-up. We support standardization, independent adjudication of suspected MI endpoints in order to accurately identify MI endpoint events. Disagreements may be due to inapplicacies in event ascertainment using standard case report form tools as well as differences in MI definitions used in clinical trials compared with clinical practice.

1286-07 Cost-effectiveness of early invasive treatment in unstable coronary artery disease: a one-year follow-up from the FRISC II invasive trial

Magnus Jaranz, Lars-Åke Levin, Eva Swahn, FRISC II Investigators, Institute of Medicine and Care, Linköping University, Linköping, Sweden, CMT, Center for Medical Technology Assessment, Linköping University, Linköping, Sweden

Background: Both early invasive and non-invasive treatment strategies in patients presenting with unstable coronary artery disease have been used during the acute phase of the disease, but it has not until recently been conclusively demonstrated which of these strategies has a better clinical outcome. Until today there is no prospective study analyzing the economic implication in this important and large patient group in the long-term follow-up. The aim of this study was to evaluate the cost-effectiveness of early invasive strategy. Methods: We determined in-hospital and one-year follow-up costs for 2,457 patients in the FRISC II trial with unstable angina or non-Q-wave myocardial infarction who were randomized to early invasive or non-invasive treatment. Medical costs as hospitalizations, investigations, interventions, pharmaceuticals and outpatient visits as well as non-medical costs as loss of production and home care were documented prospectively. The costs were based on Swedish hospital charges at 1997 price level. Results: In the FRISC II trial the invasive treatment showed a reduced incidence of death or MI (10.4% vs. 14.1%, p=0.005). In the cost analysis there was a significant higher cost in the invasive group. The cost difference per patient was 27,500 SEK (2,900 US$). The cost-effectiveness ratio was 740,000 SEK (77,000 US$) per avoided event, myocardial infarction or death. Expression in cost per life saved the cost-effectiveness ratio was 1.1 MSEK (167,000 US$). Conclusions: Due to the costly initial interventions there was still a higher total cost in the invasive treatment group at one-year follow-up. The cost-effectiveness ratio was 740,000 SEK (77,000 US$) per avoided myocardial infarction or death. To determine the final cost-effectiveness ratio for invasive strategy a longer follow-up period is needed as well as the use of QALYs, quality adjusted life years.
In Patients With Unstable Angina High Levels of C-Reactive Protein Are Associated With Irregular Plaques in Carotid Arteries: A Sign of a Diffuse, Systemic Inflammatory Involvement?

Pasquale Silvestri, Luigi M. Biancari, Giovanni Luzzo, Attilio Masei, Antonella Lombardo. Catholic University, Rome, Italy

Background: In unstable angina (UA) high levels of inflammatory mediators, such as C-reactive protein (CRP), have been demonstrated in up to 65% of pts. However it is still unknown whether this response is associated with a selective coronary or a more general arterial instability. Methods: In order to evaluate whether the inflammatory response is associated with an unstable morphology of atherosclerotic plaques in other vascular districts, we performed Color-Doppler-Echography of carotid arteries in 45 pts admitted to our Coronary Care Unit (CCU) with Braunwald's class IIIb UA. Extracranial carotid arteries were classified as: normal (no plaques); arteries with smooth plaques (smooth surface and homogeneous echogenicity also in the presence of calcifications); and arteries with irregular plaques (irregular surface or dishomogeneous echogenicity). On admission to CCU, CRP levels were assessed by high sensitivity nephelometry (Dade-Behring Lambda II).

Results: 15 pts had irregular plaques; 15 pts had smooth plaques and 16 pts had normal carotid arteries. CRP levels were significantly higher in pts with irregular plaques than in those with smooth plaques and with normal carotid arteries (respectively: median: 8.8 mg/L [range 2527.8-1, 2.1 mg/L [0.8-11.6], 3.35 mg/L [0.7-19.5] p<0.05 irregular plaques vs regular and normal arteries). Conclusions: Unstable angina patients with irregular carotid artery plaques have CRP levels higher than UA patients with normal carotid or smooth plaques. Thus, our data suggest that in UA a common inflammatory mechanism may be associated with instability of coronary and carotid plaques.
Inhibition of Mannose Binding Lectin Reduces Myocardial Reparative Injury: A Role for the Locust Complement Pathway in Cardiovascular Disease

James E. Jordan, Gregory L. Stahl. CETHAL, Dept. of Anesthesiology, Brigham and Women's Hospital, Boston, MA

Background: Complement activation plays an undeniably important role in the pathogenesis of myocardial ischemia-reperfusion injury. However, the initiating mechanism of complement activation in this setting is largely unknown. We have recently demonstrated that the locust complement pathway is activated by mannose binding lectin attaching to human endothelial cells following oxidative stress, suggesting that inhibition of mannose binding lectin may afford tissue protection following periods of ischemia and reperfusion.

Methods: In the present study, we developed a monoclonal antibody (mAb) P7E4 that functionally inhibits rat mannose binding lectin and evaluated its cardioprotective effects in an established model of myocardial ischemia and reperfusion. Rats were pretreated with losartan (40 mg/kg/day in drinking water) for 1 day, 1 week, and 4 weeks respectively. After different durations of pretreatment, the rats were subjected to 17 min of left coronary artery occlusion followed by 4 hrs of reperfusion. The hearts were excised and evaluated for mannose binding lectin and C3 deposition, infarct size (short axis view), both perfusion and contractility were assessed 30 and 90 min post-ischemia and reperfusion-induced injury. It also may lead to prolonged coronary blood flow reduction. In this setting, changes in myocardial perfusion and contraction remain unclear.

Results: Mannose binding lectin and C3 deposition was apparent on the coronary vasculature following myocardial ischemia and reperfusion and was decreased with P7E4 treatment. Pretreatment with P7E4 significantly reduced infarct size (area of necrosis/area at risk) in a dose-dependent manner compared to an isotype control (46.7% vs 31.3%, 13.1%, and 5.1% for 0.05, 0.1 mg/kg P7E4, respectively). Similarly, myocardial myeloperoxidase activity was significantly decreased by P7E4 compared to control (2.7±0.4 vs 11.0±2.0 U/mg protein, respectively). Pretreatment with P7E4 significantly reduced infarct size (area of necrosis/area at risk) in a dose-dependent manner compared to an isotype control (46.7% vs 31.3%, 13.1%, and 5.1% for 0.05, 0.1 mg/kg P7E4, respectively). Similarly, myocardial myeloperoxidase activity was significantly decreased by P7E4 compared to control (2.7±0.4 vs 11.0±2.0 U/mg protein, respectively).

Conclusion: Severe myocardial ischemia achieved by prolonged partial occlusion of the left anterior descending coronary artery (LAD) for 30 min. Following 4 hrs of reperfusion, the hearts were excised and evaluated for mannose binding lectin and C3 deposition, infarct size (short axis view), tissue gas activity and neutrophil infiltration (myeloperoxidase).

Effects of Different Durations of Pretreatment With Losartan on Myocardial Ischemic Size and Endothelial Function


Background: Our previous studies showed that 10 weeks of pretreatment with the AT1 receptor antagonist losartan reduced myocardial infarct size and endothelial dysfunction in an established model of ischemia-reperfusion. However, the effect of a differing time course of pretreatment has not been investigated. Methods: 104 Sprague Dawley rats were randomized into 4 groups: a control, and 3 pretreatment groups in which losartan was given 40 mg/kg/day in drinking water for 1 day, 1 week, and 4 weeks respectively. After different durations of pretreatment, the rats were subjected to 17 min of left coronary artery occlusion followed by 4 hrs of reperfusion. The hearts were excised and evaluated for mannose binding lectin and C3 deposition, infarct size (short axis view), both perfusion and contractility were assessed 30 and 90 min post-ischemia and reperfusion-induced injury. It also may lead to prolonged coronary blood flow reduction. In this setting, changes in myocardial perfusion and contraction remain unclear. Finally, 15 min prior to and throughout the following experiment (IOA): (iv) IOA for 15 min and Rep of the aorta at the same time as Is (IOA15); (v) IOA for 15 mins, 10 mins, and 15 mins respectively, followed by 10 min after the aorta before the beginning of Is (IOA5R, IOA10R, IOA15R). Results: Control hearts had an infarct size of 56.5±2.9% of the risk zone whereas PC reduced it to 11.2±4.1% (p<0.001). IOA and IOA15, i.e., IOA without Rep, had no influence on infarct size thus validating a liquid pressure induced (LPI) effect in the model (43.1±5.2, 52.5±4.7, 46.2±4.4, respectively). In IOA5R and IOA10R hearts infarct size tended to be smaller than in controls (41.6±5.2, 36.9±5.2, 25.5±4.3, respectively) whereas IOA15R hearts infarct size was significantly smaller than in control rats (21.4±7.9%, p<0.01). There was a significant time-dependent trend for reduction of infarct size between IS, IOA5R and IOA10R hearts (p<0.005). Conclusion: Protection of the heart can be induced at a distance by IOA. This finding strongly suggests that tissue protection following periods of ischemia and reperfusion is transferred to the heart by the blood circulation. This is the first study to clearly characterize the cellular mechanism of effect of treatment on myocardial ischemia and reperfusion.

Occlusion of the Infrarenal Aorta Protects the Rat Heart From Infarction: Characterization of a New Humoral Mechanism Responsible for Mediating Remote Preconditioning

Christof Weinbrenner, Monfred Holzka, Nicole Hengst, Lukas Gernay, Daph N. Gneesser. Department of Cardiology, University of Dresden, Dresden, Germany Department of Cardiology, University of Heidelberg, Heidelberg, Germany

Background: Ischemic preconditioning (PC) is a powerful tool in reducing infarct size of the myocardium. The mechanism of signal transduction of PC is not yet clear. To address the question if the protective effect of PC is mediated by neuronal or humoral factors and if the mechanism is also inducible at a distance we developed an in vivo model of infrarenal occlusion of the aorta (IOA) in the rat. Methods: 7 protocols were used: (i) control hearts which underwent 30 min of regional ischemia (Is); (ii) classical PC which is transferred to the heart by the blood circulation. This is the first study to clearly characterize the cellular mechanism of effect of treatment on myocardial ischemia and reperfusion.

Results: Mannose binding lectin and C3 deposition was apparent on the coronary vasculature following myocardial ischemia and reperfusion and was decreased with P7E4 treatment. Pretreatment with P7E4 significantly reduced infarct size (area of necrosis/area at risk) in a dose-dependent manner compared to an isotype control (46.7% vs 31.3%, 13.1%, and 5.1% for 0.05, 0.1 mg/kg P7E4, respectively). Similarly, myocardial myeloperoxidase activity was significantly decreased by P7E4 compared to control (2.7±0.4 vs 11.0±2.0 U/mg protein, respectively). Pretreatment with P7E4 significantly reduced infarct size (area of necrosis/area at risk) in a dose-dependent manner compared to an isotype control (46.7% vs 31.3%, 13.1%, and 5.1% for 0.05, 0.1 mg/kg P7E4, respectively). Similarly, myocardial myeloperoxidase activity was significantly decreased by P7E4 compared to control (2.7±0.4 vs 11.0±2.0 U/mg protein, respectively).

Conclusion: Severe myocardial ischemia achieved by prolonged partial occlusion of the left anterior descending coronary artery (LAD) for 30 min. Following 4 hrs of reperfusion, the hearts were excised and evaluated for mannose binding lectin and C3 deposition, infarct size (short axis view), both perfusion and contractility were assessed 30 and 90 min post-ischemia and reperfusion-induced injury. It also may lead to prolonged coronary blood flow reduction. In this setting, changes in myocardial perfusion and contraction remain unclear. Finally, 15 min prior to and throughout the following experiment (IOA): (iv) IOA for 15 min and Rep of the aorta at the same time as Is (IOA15); (v) IOA for 15 mins, 10 mins, and 15 mins respectively, followed by 10 min after the aorta before the beginning of Is (IOA5R, IOA10R, IOA15R). Results: Control hearts had an infarct size of 56.5±2.9% of the risk zone whereas PC reduced it to 11.2±4.1% (p<0.001). IOA and IOA15, i.e., IOA without Rep, had no influence on infarct size thus validating a liquid pressure induced (LPI) effect in the model (43.1±5.2, 52.5±4.7, 46.2±4.4, respectively). In IOA5R and IOA10R hearts infarct size tended to be smaller than in controls (41.6±5.2, 36.9±5.2, 25.5±4.3, respectively) whereas IOA15R hearts infarct size was significantly smaller than in control rats (21.4±7.9%, p<0.01). There was a significant time-dependent trend for reduction of infarct size between IS, IOA5R and IOA10R hearts (p<0.005). Conclusion: Protection of the heart can be induced at a distance by IOA. This finding strongly suggests that tissue protection following periods of ischemia and reperfusion is transferred to the heart by the blood circulation. This is the first study to clearly characterize the cellular mechanism of effect of treatment on myocardial ischemia and reperfusion.