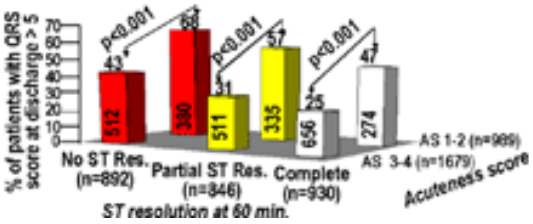
Results: At 60 min, 850/2192 pts with AS ≥3 had an 11% greater absolute frequency of complete STR (>70%) than 344/1239 with low AS (<3) p <0.001. Patients surviving to discharge (fig.), showed that within each subgroup of STR, patients with high AS were statistically more likely to have a small QRS infarct at discharge as compared to those with low AS p<0.001. Moreover in a multivariate logistic regression model including baseline characteristics, Σ ST, STR, time to treatment, the AS ≥3proved the strongest predictor of small infarct size (OR=0.374, CI= 0.315-0.445).
Conclusion: Even after adjusting for time to treatment the AS provides novel insight into the likelihood of STR 60 min after fibrinolysis and the probability of a smaller infarct size regardless of the extent of STR.



1117-90 **Establishing a New Therapeutic Activated Partial Thromboplastin Time Range for Unfractionated Heparin for Acute Coronary Syndromes**

Michael S. Lee, Venu Menon, Joseph Schappert, James R. Wilentz, Varinder Singh, Judith Hochman, St. Luke's-Roosevelt Hospital Center, New York City, NY

Introduction: The therapeutic aPTT range of 50 to 70 sec recommended by the ACC/AHA for patients receiving unfractionated heparin (UFH) for acute coronary syndromes (ACS) is vulnerable to variation in test reagents. Rather than use the standard therapeutic aPTT range, it has been recommended that each institution establish its own therapeutic aPTT range based upon anti-factor Xa levels. We evaluated our institution's therapeutic aPTT range by examining the correlation between aPTTs and anti-factor Xa levels and established a new therapeutic aPTT range with a new thromboplastin reagent based upon the therapeutic anti-factor Xa levels.
Methods: 62 plasma samples were collected from 26 consecutive patients receiving UFH for ACS. APTTs measured with a thromboplastin reagent and a new thromboplastin reagent and anti-factor Xa levels were obtained on each plasma sample. Linear regression analysis was performed to establish a new therapeutic aPTT range from corresponding therapeutic anti-factor Xa levels.
Results: 32% of patients with target range aPTTs had anti-factor Xa levels below the accepted level of 0.35-0.7 U/mL for ACS while 68% had therapeutic anti-factor Xa levels. When the same blood was tested with a new thromboplastin reagent, only 9% of patients with target range aPTTs had anti-factor Xa levels <0.35 U/mL while 91% had therapeutic anti-factor Xa levels. The Pearson correlation coefficient (r) for the new thromboplastin reagent was 0.93. The slope of the regression line was 221.3. The therapeutic aPTT range established with the new thromboplastin reagent was 61-100 sec.
Conclusion: Monitoring aPTTs without standardizing the thromboplastin reagent may not adequately reflect therapeutic heparin levels. Despite apparently therapeutic aPTTs, patients treated with UFH may be under-anticoagulated. Our new anti-Xa-adjusted therapeutic aPTT range shows an increase in the positive predictive value of aPTTs. Large-scale clinical studies are needed to determine the optimal anti-factor Xa range for ACS patients treated with UFH, with further refinements if GP IIb/IIIa antagonists are concomitantly used and to show a clinical benefit for monitoring heparin levels with anti-factor Xa levels.

1117-91 **Invasive Therapy Along With Glycoprotein IIb/IIIa Inhibitors and Intracoronary Stents Improves Survival in Non-ST-Segment Elevation Acute Coronary Syndromes**

Anthony A. Bavry, Dharam J. Kumbhani, Rene Quiroz, Suneil R. Ramchandani, Satish Kenchaiah, Harvard School of Public Health, Boston, MA, Cleveland Clinic Foundation, Cleveland, OH

Background: Although several clinical trials have shown that early invasive therapy in UA/NSTEMI patients reduces the risk of composite endpoints inclusive of death, MI or angina, it is unclear whether such an approach improves survival.
Methods: We conducted a meta-analysis on five studies in a total of 6,766 UA/NSTEMI patients who were randomized to either routine invasive (n=3,371) versus conservative therapy (n=3,395) in the era of GP IIb/IIIa inhibitors and intra-coronary stents.
Results: As compared with conservative therapy, an invasive approach was associated with a reduction in the risk of all-cause mortality at 6-12 months (3.3% vs. 4.2%, relative risk [RR] 0.80, 95% confidence interval [CI] 0.63 to 1.03) and at 24 months (5.0% vs. 6.5%, RR 0.77, 95% CI 0.60 to 0.99) of follow-up. Although invasive therapy reduced the risk of the composite endpoint of death or MI at 6-12 months in men (RR 0.68, 95% CI 0.57 to 0.81) and troponin positive patients (RR 0.74, 95% CI 0.59 to 0.94), the results for women (RR=1.07, 0.82 to 1.41) and troponin negative patients (RR=0.82, 0.59 to 1.14) were equivocal.
Conclusions: Invasive therapy in UA/NSTEMI patients with adjunctive use of GP IIb/IIIa inhibitors and intra-coronary stents improves survival. Enhanced risk stratification is needed in women and troponin negative patients so that invasive therapy may be more effectively recommended in these groups.

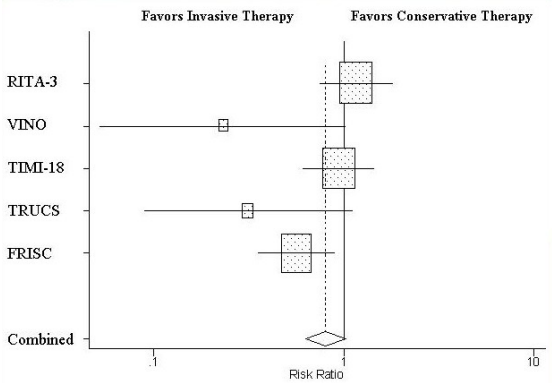


Figure I. Forest plot of death at 6 - 12 months for invasive versus conservative strategies.
Summary estimate RR = 0.80 (95% CI; 0.63, 1.03).

POSTER SESSION

1118

New Observations From Acute Myocardial Intervention Trials III

Tuesday, March 09, 2004, 9:00 a.m.-11:00 a.m.
Morial Convention Center, Hall G
Presentation Hour: 9:00 a.m.-10:00 a.m.

1118-77 **Effects of Carvedilol Compared to Atenolol on Ejection Fraction and Clinical Endpoints After Myocardial Infarction**

Gisli Jonsson, Michael Abdelnoor, Carl Müller, Sverre Erik Kjeldsen, Ingrid Os, Arne Westheim, Ullevaal University Hospital, Oslo, Norway

Background: Beta-blockers have been found to reduce mortality and morbidity in post-myocardial infarction (MI) patients. However, it is not fully understood, whether all beta-blockers have similiar favourable cardiovascular effects. The aim of this study was to compare the effects of carvedilol and atenolol on global and regional ejection fraction (EF), and on predefined cardiovascular endpoints.
Methods: In a randomized, prospective, open and endpoint-blinded single center study, 118 patients received carvedilol (mean dosage 36.2 ± 15.1 mg) and 114 patients atenolol (mean dosage 72.1 ± 30.6 mg). No difference in baseline data, such as age, gender, race, smoking, hypertension, dibetes mellitus or lipid lowering treatment, was observed. There was no difference in baseline characteristics regarding infarct localization, reperfusion therapy and acute treatment between the groups. Treatment with aspirin (96%), statin (98%), and ACE-inhibitors was equal in the 2 groups. The global and regional left ventricular (LV) EF were evaluated with gated blood pool scintigraphy.
Results: In the carvedilol group 90 cardiovascular endpoints were observed compared to 104 endpoints in the atenolol group, with a hazard ratio (RR) 0.84 with 95% confidence interval (0.74-0.94) (p=0.002). This occured despite similar global LVEF was 55 ± 11% at baseline, 57 ± 10% at 3 months and 57 ± 10% at 12 months in the carvedilol group and 53 ± 9%, 56 ± 10% and 56 ± 9% in the atenolol group respectively. No difference in regional EF was observed in the two groups. The main contributor to the difference in cardiovascular endpoints was a composite of cardiovascular deaths, non-fatal MI, and congestive heart failure (worsening and hospitalization).
Conclusion: In patients following an acute MI, carvedilol treatment compared to atenolol was associated with a significant reduction in combined cardiovascular endpoints despite that no difference in global or regional ejection fractions was found. Thus other mechanisms than remodelling might explain this difference in clinical effect between the two drugs.

1118-78 **Primary Angioplasty Versus Facilitated Intervention (Tenecteplase Plus Stenting) in Patients With ST Elevated Acute Myocardial Infarction: Final Results of the GRACIA-2 Trial**

Francisco Fernandez-Aviles, Joaquin J Alonso, Alfonso Castro-Beiras, Javier Goicolea, Jesus Blanco, Juan Alonso, Juan Lopez-Mesa, Luis Diaz-Llera, Nicolas Vazquez, Rosa Hernandez, Armando Perez, Javier Moreu, The GRACIA-2 Investigators, ICICOR, Hospital Clinico Valladolid, Valladolid, Spain

Background: Combined reperfusion therapies widely applicable could benefit the still high proportion of patients (pts) with ST-elevated acute myocardial infarction (STEAMI) for whom primary PCI is not available due to logistic reasons.
Methods: We compared the evolution of 212 pts with STEAMI (<12 hs from onset) randomised to 2 strategies: 1) primary PCI optimally performed (stenting of culprit artery under protection of abcximab within 3 hs from onset); or 2) a combined (facilitated) strategy: immediate thrombolysis (T) with tenecteplase (full bolus dose adjusted by weight)

and intravenous enoxaparin (30 mg) followed by angiography within 3-12 hs of randomisation and adequate revascularisation (culprit artery plus non-culprit severe diseased arteries threatening functionally important areas) with stenting or surgery. When T failed (TIMI flow grade 0 or 1) abciximab was given before stenting. Heparin was stopped in both groups after PCI. The co-primary endpoints were: infarct size (CK-MB mass, cTnT release), left ventricle 6-week angiographic evolution (volume, ejection fraction, wall motion index) and myocardial reperfusion (normalization of ST at 3 and 6 hs). The incidence of cardiac and non-cardiac events was also compared.

Results: There were no differences between primary PCI and facilitated strategies in terms of infarct size (CK-MB mass: 4768±3734 vs 4602±3371 ug/Lxh, p= 0.76; cTnT: 275±211 vs 242±156 ug/Lxh, p=0.55), left ventricular ejection fraction at 6 weeks (56±13 vs 56±12%, p= 0.9); wall motion index at six weeks (-1.1±0.6 vs -1.2±0.4, p= 0.1) and myocardial perfusion (normalization of ST at 3 hs: 47 vs 46%, p= 0.83). However, in facilitated pts the incidence of complete ST resolution at 6 hs was higher (43 vs 61%, p=0.03), and the rate of cardiac events at six month tends to be lower (death, reinfarction or revascularization: 14% vs 9%).

Conclusions: According to the results of the GRACIA-2 trial, the strategy of performing facilitated intervention is as safe as optimal primary PCI for pts with STEAMI. Results also suggest that both strategies have equivalent efficacy in restoring myocardial perfusion, preserving left ventricular size and function and beneficing clinical outcome.

1118-79 Drag Reduction by Polymer Infusion: A New Mechanism to Enhance Microcirculatory Perfusion for the Treatment of Ischemia

John J. Pacella, Erxiong Lu, Joan Gretton, David Fischer, Marina V. Kameneva, Flordeliza S. Villanueva, University of Pittsburgh, Pittsburgh, PA

Background: In the setting of severe, flow-limiting coronary artery stenosis, we have previously shown that drag-reducing polymers (DRPs), which are unique, blood-soluble macromolecules, have therapeutic potential because they further lower microvascular resistance and enhance perfusion, even after autoregulation is exhausted. In bench studies involving rigid tubes, DRPs reduce resistance by altering the hydrodynamic properties of blood flow. Whether changing blood rheology is their mechanism of action *in vivo,* or whether it also involves vasodilation is unclear. To test the hypothesis that DRPs decrease resistance and increase blood flow without causing vasodilation, we examined the microcirculation of the cremaster muscle in rats using intravital microscopy. **Methods:** Catheters were placed in the carotid artery for pressure measurement in 13 anesthetized rats. A flow probe was placed around the abdominal aorta. The cremaster muscle was exposed and mounted on a microscope. Red blood cell (RBC) velocity and vessel diameters were measured in arterioles ***(A),*** venules ***(V),*** and capillaries ***(C)*** pre- and post- intravenous DRP (polyethylene oxide, 1PPM). Vascular resistance was calculated as mean arterial pressure/aortic flow. In 5 controls, topical nipride was applied to the cremaster to confirm measurable vasoactivity in our model. **Results:** Arteriolar diameter increased 18±4% (p<0.03) after topical nipride in controls. DRP increased aortic flow (7.4±1.0 vs. 5.0±0.6 mL/min, p<0.002) and decreased vascular resistance (14.2±1.7 vs. 23.5±2.7 mmHg-min/mL, p<0.01). There was no significant change in diameter at any microvascular level in association with this resistance reduction. DRP increased RBC velocity in the ***A*** (13.0±0.8 vs. 11.4±0.6 mm/sec, p<0.04), ***V*** (10.3±0.4 vs. 8.5±0.6 mm/sec, p<0.003) and ***C*** (149±34 vs. 103±31 μm/sec, p<0.02). **Conclusions:** DRPs lower vascular resistance and increase flow without causing vasodilation. The rise in flow is accompanied by an increase in microvascular RBC velocity. Primary enhancement of microvascular perfusion through modulation of the rheological properties of blood represents a promising, novel therapeutic strategy for ischemic syndromes.

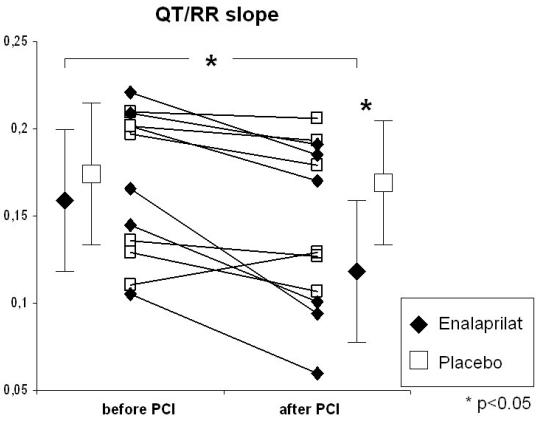
1118-80 Effects of Intracoronary Low-Dose Enalaprilat on QT Dynamicity in Patients Undergoing Direct Percutaneous Coronary Intervention for Acute Myocardial Infarction

Hendrik Bonnemeier, Ulrich Schaefer, Thomas Kurz, Uwe Wiegand, Jasmin Ortak, Hugo A. Katus, Gert Richardt, University Luebeck, Medical Clinic II, Luebeck, Germany

Experimental data suggest that ACE inhibition results in an increased ventricular electrical stability in acute myocardial infarction (AMI). As electrical stability is largely dependent on ventricular repolarization, we sought to determine the impact of low-dose intracoronary application of enalaprilat (EN) as an adjunct to direct PCI on the QT/RR relationship in AMI.

Methods and Results: Twenty-two patients with AMI who underwent direct PCI (TIMI 3 flow) were randomized to EN (50μg) or saline (SA), given immediately after reperfusion. On hospital admission a 24-hour-Holter-ECG was initiated. Slopes of the linear QT/RR regression were determined for the time intervals before reperfusion and after reperfusion. A total of 6 patients in the EN group and 6 patients in the SA group had valid Holter-ECGs for QT analysis. Mean RR interval and QT interval were not significantly different between the EN and the SA groups before and after PCI. There were also no significant differences regarding QT/RR slopes between EN and SA groups before PCI. After PCI, QT/RR slopes significantly decreased in the EN group, whereas there were no significant alterations in the SA group.

Conclusion: Intracoronary EN therapy as an adjunct to direct PCI significantly decreases QT/RR slopes, suggesting a normalization of the coupling between heart rate and repolarization by improving electrical restitution. Thus, our findings offer new insights into possible beneficial effects of ACE inhibition on electrical stability in AMI.



1118-81 The Impact of Abciximab on Final Infarct Size and Left Ventricular Function of Patients With Acute Myocardial Infarction Undergoing Primary Stenting: Insights From the Abciximab and Carbostent Evaluation (ACE) Trial

Guido Parodi, Angela Migliorini, Roberto Sciagrà, Gentian Memisha, Renato Valenti, David Antoniucci, Careggi Hospital, Florence, Italy

OBJECTIVES: We sought to evaluate the impact of abciximab, as adjunctive therapy to routine infarct-related artery (IRA) stenting, on effectiveness of myocardial reperfusion. BACKGROUND: The impact of abciximab on left ventricular (LV) volumes and function of patients with acute myocardial infarction (AMI) undergoing IRA stenting is not yet defined. METHODS: Four hundreds unselected patients with AMI were randomised 1:1 to IRA stenting alone or stenting plus abciximab. One- month gated 99m-Tc Sestamibi SPECT had to be performed in a pre-specified subgroup of 250 patients to evaluate infarct size and LV volumes. RESULTS:Out of the 250 patients planned for the scintigraphic assessment, 8 died within the first month, 12 dropped out of the study protocol, 13 were excluded because gated acquisition was precluded by arrhythmias or technical reasons, and 35 had a previous myocardial infarction preventing the index infarct size evaluation. Thus, 182 patients represent the final study group (99 patients were randomized to abciximab therapy and 83 to stenting alone). There were no differences in the baseline clinical and angiographic characteristics, and in discharge therapy between the 2 groups. In the abciximab group infarct size was smaller than in stenting alone group (14.3±11.7 versus 19.1±13.0 %; p=0.01), resulting in smaller LV end-diastolic volume index (57.8±20.0 versus 64.6±20.8 mL/m^2; p=0.03), and LV end-systolic volume index (31.7±17.4 versus 37.5±18.6 mL/m^2; p=0.03). One-month LV ejection fraction was significantly higher in patients randomized to abciximab, as compared to stenting alone (47.4±11.3 versus 43.9±11.7 %; p=0.04). Reinfarction within 30 days occurred in 3 (4%) of patients of the stenting alone group as compared to none of the abciximab group (p=0.056). After excluding the 3 patients who experienced a reinfarction, the beneficial effect of abciximab on LV volumes and function still persists. **CONCLUSIONS:** The use of abciximab, as a standard adjunctive therapy to IRA, leads to the reduction in infarct size, resulting in smaller 1-month LV volumes and better LV function. The effect is not explained by the lower reinfarction rate.

1118-82 Distinct Modes of Cardiovascular Death Associated With Impaired Epicardial and Myocardial Perfusion Following Fibrinolysis for ST Elevation Myocardial Infarction

Stephen D. Wiviott, Marc S. Sabatine, David A. Morrow, Raphaelle Dumaine, Sabina A. Murphy, Kieth E. Boundy, Christopher P. Cannon, C. Michael Gibson, Brigham and Women's Hospital, Boston, MA

Background: Despite fibrinolysis for ST-elevation MI (STEMI), a significant mortality remains. A comprehensive analysis of cause of death and angiographic features could provide important information for therapeutic decision-making and understanding pathophysiology.

Methods: 3683 patients from an angiographic database STEMI fibrinolysis trials were analyzed. 180 deaths (4.9%) were observed. Angiographic features were measured by a blinded core lab.

Results: Causes of death included: CHF/Shock (22%), Stroke/ICH (18%), dysrhythmia (16%), cardiac rupture (13%), MI (12%), other cardiac (7%), hemorrhage (3%). Those with cardiac death compared to survivors were less likely to have TIMI flow grade (TFG) 2-3 (p<0.001) and TIMI Myocardial Perfusion Grade (TMPG) 2-3 (p=.004); had higher Corrected Frame Counts (CTFC, 68 vs.52, p<0.001), and were more likely to have 3 vessel CAD (p=0.001) or thrombus (p=0.001). Among cardiac deaths, TFG 0-1, higher CTFC, were associated with CHF/Shock (figure); TFG 0-1 and TMPG 0-1 were associated with dysrhythmia (figure) and cardiac rupture (p<0.05). There were no angiographic correlates of CVA/hemorrhage.

Conclusions: Impairment of epicardial and myocardial perfusion were associated with cardiovascular mortality. Angiographic features differed among causes of death. These angiographic correlates with mortality may aid in understanding the limitations of reperfusion therapy and the search for new modalities to reduce mortality in STEMI.