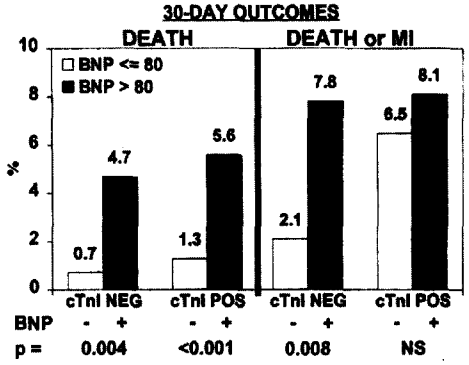
agement in the TACTICS-TIMI 18 trial. Decision-limits of 80 pg/ml for BNP and 0.1 ng/ml for cTnI were pre-specified based on prior work. **RESULTS**: Pts with baseline BNP > 80 ng/ml (n = 310) were at significantly higher risk of death by 30 days (5.2 vs. 1.2%, p<0.0001) and 6 months (8.7 vs. 1.7%, p<0.0001) after presentation. BNP predicted mortality independently of age, ST-segment depression, cTnI result, history of CHF and Killip class at presentation (p<0.0001). Importantly, BNP identified patients with negative cTnI who were at high risk for death (p=0.004) and death/MI (p=0.008) [FIG]. There was no significant difference in the benefit of INV vs. CON therapy among pts with positive vs. negative BNP with respect to death/MI at 30 and 180 days (p-interaction >0.5). **CONCLUSIONS**: BNP adds complementary information to cardiac troponin for risk assessment in unstable angina/non-ST elevation MI. Future research should aim at interventions which may reduce the risk associated with increased BNP.

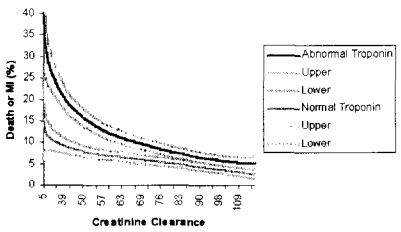


3:00 p.m.

822-5 **The Inter-Relationship Between Creatinine Clearance, Cardiac Troponin T And Outcomes in Patients With Acute Coronary Syndromes**

Ronnier J. Aviles, Arman T. Askari, E. Magnus Ohman, Kenneth W. Mahaffy, L. Kristin Newby, Peter Berger, Gang Jia, Robert M. Califf, Bertil Lindahl, Lars Wallentin, Eric J. Topol, Michael S. Lauer, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: Although abnormal cardiac troponin T (TnT) is predictive of poor outcome, the prognostic value of cardiac troponin T in patients with renal impairment remains controversial.
Methods: In GUSTO IV, 7800 with ACS were randomized to treatment with placebo, abciximab for 24 hours, or abciximab for 48 hours. The study cohort comprised 7637 subjects with complete TnT, creatinine clearance (CCl), and clinical data. Baseline TnT and CCl were analyzed. CCl was evaluated as categorical and as a continuous variable. Abnormal TnT: TnT > 0.1 mg/dL; abnormal CCl: CCl < median CCl (76 ml/min.). End point: composite of 30-day death and MI.
Results: Death/MI occurred in 648 subjects. There were 126 (6%) events in patients with abnormal TnT, 140 (8%) events in patients with abnormal CCl, and 311 (15%) in subjects with both abnormal TnT/CCl. The highest risk of death/MI occurred in patients with both abnormal TnT/CCl (OR, 4.4; 95% CI, 3.4 - 5.7; P < 0.001), suggesting that abnormal TnT is predictive of outcome in patients with abnormal CCl. Even after adjusting for age > 65 yrs, weight > 90 kg, ST depression, history of angina, MI, CHF, diabetes, hyperlipidemia, HTN, smoking, PCI, CABG, stroke, and treatment with IIb/IIIa, patients with both abnormal TnT/CCl had the highest risk of death/MI (OR, 3.3; 95% CI, 2.5 - 4.5; P < 0.001). TnT was predictive of outcome across the entire spectrum of CCl (Figure 1).



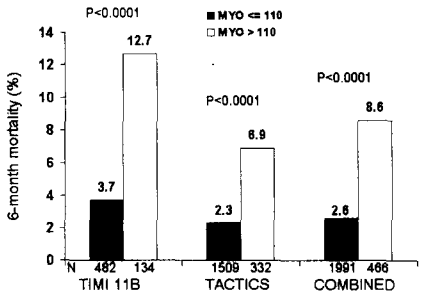
Conclusion: The prognostic value of TnT is not decreased in patients with impaired renal function who present with suspected ACS.

3:15 p.m.

822-6 **Elevated Serum Myoglobin Is Associated With Increased Long-Term Mortality, Independent of Cardiac Troponin I, Electrocardiographic Variables, and Other Baseline Variables: Combined Analyses From TIMI 11B and TACTICS/TIMI 18**

James A. de Lemos, David A. Morrow, Michael Gibson, Sabina A. Murphy, Nader Rifai, Mark S. Sabatine, Howard A. Cooper, Carolyn H. McCabe, Elliott M. Antman, Christopher P. Cannon, Eugene Braunwald, *University of Texas Southwestern Medical School, Dallas, Texas, TIMI Study Group, Boston, Massachusetts.*

Myoglobin (MYO) is a sensitive, but nonspecific early marker of myocardial injury. Few studies have considered the prognostic implications of increased MYO among pts with non-ST elevation acute coronary syndromes (ACS).
Methods: Baseline levels of MYO, cTnI, and CKMB were measured in 616 pts from TIMI 11B and 1841 pts from TACTICS/TIMI 18 (ACS:180, Bayer Diagnostics). Mortality at 6 months was compared between pts with MYO levels above and below the recommended diagnostic threshold (110 μg/L).
Results: Pts with elevated baseline MYO were older, more often male, and more likely to present with MI (vs unstable angina), ECG changes, increased CKMB and increased cTnI (p<0.01 for each variable). In multivariate analyses adjusting for index diagnosis, baseline variables, ECG changes, cTnI, and CKMB, elevated baseline MYO remained associated with higher 6-month mortality: TIMI 11B adjusted OR 2.9 [1.2-7.0]; TACTICS/TIMI 18 adjusted OR 2.7 [1.4-5.2]; combined dataset adjusted OR 2.8 [1.7-4.7]. There was no consistent association between MYO and nonfatal MI or recurrent ischemic events.
Conclusions: In two distinct groups of pts with ACS, elevated baseline myoglobin was associated with a statistically significant near 3-fold increase in the risk for long-term mortality, independent of other baseline risk predictors, including age, diabetes, ECG changes and biomarkers such as cTnI and CKMB. These findings suggest that myoglobin should be added to the panel of biomarkers routinely measured in pts with ACS.



ORAL CONTRIBUTIONS

828 Enhancing Fibrinolysis: Combination With Newer Antiplatelet and Antithrombotic Agents

Monday, March 18, 2002, 2:00 p.m.-3:30 p.m.
Georgia World Congress Center, Room 256W

2:00 p.m.

828-1 **Prevention of Reinfarction Using Half-Dose Reteplase and Abciximab: Observation From the GUSTO-5 Trial**

E. Magnus Ohman, Robert M. Califf, Michael Lincoff, Paul Armstrong, Neal Kleiman, Judith Hochman, Harvey White, Stefano Savonitto, Marion Piedmonte, Joan Booth, Eric J. Topol, *The University of North Carolina, Chapel Hill, North Carolina, The Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: An important caveat to successful reperfusion in acute myocardial infarction has been reinfarction occuring early after administration of fibrinolytic therapy. Reinfarctions are associated with major morbidity and a high mortality. The impact of newer combination reperfusion therapies on reinfarction rates remains to be determined. Methods: We examined the rate of reinfarction among patients randomized to either r-PA (10+10u) or low-dose r-PA (5+5u) and full dose abciximab in the GUSTO-5 trial. Results: A total of 479 patients (2.9%) had a reinfarction through discharge or 7 days, whichever was sooner. Patients randomized to combination therapy had significantly lower rate of reinfarction compared with r-PA alone (2.3% vs 3.5%, p<0.0001). Reinfarctions within the first 24 hours of randomization were more common among patients treated with r-PA (29% of all patients with reinfarctions after r-PA) compared with combination therapy (19%). Certain baseline characteristics were more common among patients with reinfarction versus those without, such as the elderly (over 75 years: 19% vs 13%), females (30% vs 25%), and in patients with prior MI (24% vs 15%), but less common among current smokers (33% vs 46%). In an adjusted analysis, patients randomized to combination therapy were less likely to suffer reinfarction (Odds Ratio: 0.67 95%CI: 0.56-0.80, p<0.001) compared to r-PA alone, even among patients who were more likely to have reinfarction such as older patients (p<0.001), and those with previous MI (p<0.001). Conclusions: Combina-

tion therapy with half-dose r-PA and abciximab reduces the rate of reinfarction across a broad range of patients compared with r-PA alone. The long-term implications of these findings on 1-year mortality awaits definition.

2:15 p.m.

828-2 The Abciximab ST-Recovery ON AMI (ASTRONAMI) GUSTO V Substudy: Enhanced Early Speed, Stability, and Quality of Reperfusion With Anti-Platelet Augmented Thrombolytic Therapy for ST-Elevation AMI

Mitchell W. Krucoff, Cynthia L. Green, Anatoly Langer, Brian Gibler, Paul W. Armstrong, Kathleen M. Trollinger, Suzanne W. Crater, Michael A. Lincoff, Robert M. Califf, Eric J. Topol, The ASTRONAMI-GUSTO V Investigators, *Duke University Medical Center/Duke Clinical Research Institute, Durham, North Carolina, Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: In the GUSTO V study combined Rx with abciximab and low dose rPA was compared to full dose rPA alone in pts with ST elevation MI. Mortality with Combo Rx was non-inferior. Mechanistic differences were not reported.
Methods: In the ASTRONAMI substudy the speed, stability and microvascular quality of reperfusion were quantified by blinded core lab analysis of ST recovery from Rozinn 152 continuous digital 12-lead ECG recordings as: 1) time (minutes) from onset of Rx to a) 1st 50% ST recovery from peak (**1st 50% ST**) and b) >4 hrs with >50% ST recovery (**STABLE ST**); 2) recurrent ischemia (**RE-ST**, as % of pts with ST re-elevation >150uV over recovery levels; and 3) ST level vs. time trend curve area (**ST AREA** in uV-min), respectively.
Results: A total of 4,992 pt hrs of monitoring totaling 299,520 ECGs were analyzed from 207 pts (108 Combo Rx, 99 rPA Rx). Clinical descriptors, time from chest pain to Rx, time to ST monitoring, duration of monitoring and peak ST levels were comparable. ST recovery results were:

Descriptor	rPA Rx	Combo Rx	P value*
1st 50% ST (%)	46 (19.0, 92.6)	34.0 (0, 66)	.042
STABLE ST (min)	100 (42, 162)	65 (0, 112)	.002
RE-ST (%)	40.2	30.1	.155
ST AREA (uV-min)	4782 (259, 9820)	2576 (0, 7716)	.047

* continuous variables: two-sample t-test, Wilcoxon rank sum test; discrete variables: likelihood ratio chi-square, Fisher's exact text.
Conclusion: Thus, combined Rx with abciximab and low dose rPA improves the speed, stability and microvascular quality of reperfusion in ST-elevation MI compared to rPA alone.

2:30 p.m.

828-3 Combination Tenecteplase and Abciximab Results in More Complete ST Resolution: Findings from the ASSENT 3 ECG Substudy

Yuling Fu, Galen Wagner, Shaun Goodman, Frans Van de Werf, Christopher B. Granger, Paul W. Armstrong, for the ASSENT 3 Investigators, *University of Alberta, Edmonton, Alberta, Canada.*

The ASSENT 3 study documented that the two experimental arms i.e. combination tenecteplase plus enoxaparin or half-dose tenecteplase and abciximab reduced the frequency of ischemic complications of acute myocardial infarction. The mechanism(s) for this benefit is unclear but combination therapy with fibrinolytic and glycoprotein IIb/IIIa inhibitors has previously achieved more effective early reperfusion in phase 2 angiographic trials whereas angiographic evaluation with low molecular weight heparin has shown less reocclusion.
Accordingly we analyzed sequential ECG's at baseline, 60 and 180 minutes after enrollment in all patients in the ASSENT 3 study, in order to evaluate the 3 treatment groups (tenecteplase and enoxaparin [TNK/ENOX]; half dose tenecteplase and abciximab [1/2 TNK/ABCX]; tenecteplase and unfractionated heparin [TNK/UH]). Amongst the 75% of the 6,095 patients who had technically suitable ECG data free of confounding factors, ST resolution compared to baseline is shown in the table.
These data, in a large comprehensively studied AMI population, suggest better early myocardial perfusion with combination TNK-abciximab than TNK with either ENOX OR UH alone. They also suggest the clinical benefit of enoxaparin in ASSENT 3 is modulated by a mechanism different than early reperfusion occurring later in the ischemic process.

	TNK/ENOX	1/2 TNK/ABCX	TNK/UH
60 min ECG	n=1,506	n=1,472	n=1,483
>=70% resolution	28.9	33.4*	31.9
30-70% resolution	33.9	32.5	31.4
<30% resolution	37.3	34.1	36.7
180 min ECG	n=1,463	n=1,461	n=1,416
>=70% resolution	50.0	59.1**	48.0
30-70% resolution	32.5	29.6	31.5
<30% resolution	17.5	11.3	20.5

*p=0.02 **p<0.001

2:45 p.m.

828-4 Differential Impact of Antithrombotic Treatments Combined With Tenecteplase in the Elderly With Acute Myocardial Infarction: Results From ASSENT-3

Christopher B. Granger, John H. Alexander, Emmanuel Lesaffre, Lars Wallentin, Paul W. Armstrong, Frans Van de Werf, *Duke Clinical Research Institute, Durham, North Carolina, Leuven Coordinating Centre, Leuven, Belgium.*

Background: Among patients with acute myocardial infarction (MI), the elderly are at particularly high risk for death and bleeding complications, including with more aggressive antithrombotic strategies.
Methods: In order to provide insight into risk and benefit in the elderly, we examined patients from the ASSENT-3 Trial with ST elevation MI, who were treated with tenecteplase (TNK) and randomized to unfractionated heparin (UFH), enoxaparin, or abciximab with low dose heparin (and half-dose TNK).
Results: Of the 6095 patients enrolled, 13% (767) were >75 years of age. Compared to younger patients, patients > 75 had higher rates of death (17.9 vs 4.3%), intracranial hemorrhage (ICH, 1.6 vs 0.8%), and bleeding. Older patients had higher rates of the efficacy + safety composite (death, reMI, refractory ischemia, ICH, and major bleeding) with abciximab than with enoxaparin or UFH (table), and the treatment effect of abciximab vs UFH was significantly less in older than in younger patients (interaction p<0.05).
Conclusions: Elderly patients with acute MI are at high risk of death and bleeding. Although TNK with either enoxaparin or abciximab appeared to be more effective than with standard UFH in younger patients, TNK with abciximab as dosed in this trial was significantly less effective and may be unsafe in the elderly. For elderly patients, development of treatments with greater safety and effectiveness remains a high priority.

>75 years (n=767)

	UHF	Enoxaparin	Abciximab	p
Death, reMI, refractory ischemia, ICH, major bleed (%)	28.0	25.5	36.9	0.01
30-day death (%)	15.9	15.6	22.3	0.11
ReMI (%)	6.3	2.3	3.0	0.07
Major bleeding (%)	4.1	7.2	13.3	0.001
ICH (%)	0.74	1.52	2.58	0.26

3:00 p.m.

828-5 Lack of Improvement in ST Segment Resolution After the Combination Treatment of Abciximab With Reteplase Compared to Reteplase Alone for Acute Myocardial Infarction: Results From the GUSTO V-RESTART Substudy

Fernando A. Cura, Marco Roffi, Narcis Pasca, Katherine E. Wolski, Eric J. Topol, Michael S. Lauer, *Cleveland Clinic Foundation, Cleveland, Ohio.*

Background: The combination of abciximab during reperfusion therapies is believed to enhance tissue level and microvascular perfusion. Resolution of ST-segment elevation after administration of thrombolytic therapy in patients with acute myocardial infarction is a marker of myocardial reperfusion and has an important predictive value of mortality. This study compared the extent of 60-minute ST-segment elevation resolution of patients treated with full dose of reteplase versus half-dose reteplase in combination with abciximab given at the normal dose from the GUSTO V-AMI trial.
Methods: From a total of 16.588 patients enrolled in the GUSTO V-AMI trial, 1764 were prospectively included in the RESTART substudy and were randomized to the combination of full dose abciximab and half dose of reteplase or full dose of reteplase alone. A baseline and 60-minute ECG was analyzed by a core lab to categorize 4 groups: complete resolution (>70%), partial resolution (<70%-30%), no resolution (<30%) and worsening ST-segment.
Results: There was no difference in the clinical baseline variables between the two treatment groups. The results are summarized in the table.

	Reteplase (n=871)	Reteplase + Abciximab (n=893)	p value
Complete Resolution (%)	32	34	0.37
Partial Resolution (%)	29	27	0.35
No Resolution (%)	19	18	0.59
Worsening ST-segment (%)	20	20	0.95
30-day Mortality (%)	5.1	4.7	0.73

Conclusion: Patients treated with reduced doses of reteplase when administered in combination with abciximab are associated with similar extent of ST-segment elevation resolution as those treated with full dose reteplase alone.

3:15 p.m.

828-6 Risk and Benefit of Half-Dose Lytic Plus Abciximab Versus Lytic Alone for ST-Elevation Myocardial Infarction: A Meta-Analysis

Freek W. Verheugt, *University Medical Center Nijmegen, Nijmegen, The Netherlands.*

Background Angiographic trials have shown improved 60 and 90 minutes coronary patency with half-dose lytic plus abciximab versus lytic alone in ST-elevation MI (STEMI). These strategies have recently been evaluated in 2 phase III megatrials for efficacy and