ABSTRACTS - Myocardial Ischemia and Infarction

Tuesday, April 01, 2003, 2:00 p.m.-3:30 p.m.
McCormick Place, Room S103

853 Enhancing Microvascular Perfusion in Acute Myocardial Infarction

C-Michael Gibson, Lisa K. Jennings, Robert P. Giugliano, Robert A. Harrington, Matthew P. Roe, Sabina A. Murphy, Shila Cholera, Kenneth W. Baran, Hans-Peter Hobbach, Eugene Braunwald, TIMI Study Group, Boston, MA, University of Tennessee Health Science Center, Memphis, TN

Background: While inhibition of platelet (plt) aggregation is a surrogate measure of drug efficacy, the percent of plt glycoprotein (GP)IIb-IIIa receptors occupied by a GP IIb-IIIa inhibitor (plt receptor occupancy (RO)) is a more direct and fundamental measure of its underlying biologic activity. We hypothesized that improved patency, tissue level perfusion and ST segment resolution would be associated with higher levels of RO. Methods: Patients (n=70) treated with low dose TNK - eptifibatide as part of the INTEGRITI study were included in the RO substudy. Results: The percent RO at 60 min, as measured by D3 mAb binding, was higher among patients with a patent artery (TFG 2/3) at 60 minutes after lytic compared with an occluded artery (TFG 0/1) (p=0.005) (Table). The percent RO was also higher among patients with normal TIMI Myocardial Perfusion Grade (TMPG) 3 compared with incomplete myocardial reperfusion (TMPG 0/1/2) (p=0.04), and among patients with complete (>70%) ST resolution compared with incomplete resolution (p=0.006). Conclusions: This study links restoration of epicardial flow, tissue level perfusion and ST segment resolution with higher levels of plt glycoprotein IIb-IIIa receptor occupancy following therapy with eptifibatide when given in combination with TNK. These data provide a pathophysiologic link between RO and therapeutic efficacy of combination therapy.

853-1 Increased Platelet Receptor Occupancy Following Eptifibatide Therapy Is Associated With Improved Patency, Tissue Level Perfusion, and ST-Segment Resolution in ST-Segment Elevation Myocardial Infarction: An INTEGRITI Substudy

C-Michael Gibson, Lisa K. Jennings, Robert P. Giugliano, Robert A. Harrington, Matthew P. Roe, Sabina A. Murphy, Shila Cholera, Kenneth W. Baran, Hans-Peter Hobbach, Eugene Braunwald, TIMI Study Group, Boston, MA, University of Tennessee Health Science Center, Memphis, TN

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853-2 Clinical Implications of Myocardial Perfusion Status Assessed by Myocardial Blush After Primary Angioplasty In Acute Myocardial Infarction: Analysis From the CADILLAC Trial

Costantino C. Costantino, Alessandra J. Laks, Kazuaki Shirai, Esterina Cristea, Cristina Brearowski, Steve Stack, Martin Faby, Cindy L. Grimes, John D. Carroll, Stacey Thomas, Giulio Guagliumi, Barry Rutherford, Mark Turco, David Mathias, Marlin B. Leon, Greg W. Stone, Cardiovascular Research Foundation, New York, NY

Background: Two single-center retrospective studies have suggested that myocardial perfusion as assessed by the angiographic blush score is of major prognostic importance after primary PCI. The implications of myocardial blush grade (MBG) in a randomized trial of PCI for AMI have not been reported. Methods and Results: In the CADILLAC trial, 2,082 pts of any age with AMI <12 hours without shock were randomized to PTCA + a glycoprotein IIb/IIIa antagonist or to stenting with a stent. All films have been recalled to the angiographic core laboratory for independent blinded evaluation of blush. Of the 856 films reviewed to date, myocardial perfusion was absent or minimal (MBG 0/1) in 44% of pts, moderate (MBG 2) in 20%, and normal (MBG 3) in 20%. Predictors of reduced blush included male sex (p=0.01), LAD location (p=0.001), longer time from symptoms onset to first balloon inflation (p=0.01), thrombus (p>0.007), low LVEF (<0.40), and baseline TIMI 0/1 flow (p=0.0027). Mortality as a function of MBG appears in the table.

<table>
<thead>
<tr>
<th>All patients</th>
<th>MBG 0/1</th>
<th>MBG 2</th>
<th>MBG 3</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>30 days</td>
<td>3.2%</td>
<td>1.3%</td>
<td>0.6%</td>
<td>0.07</td>
</tr>
<tr>
<td>1 year</td>
<td>5.9%</td>
<td>2.4%</td>
<td>2.3%</td>
<td>0.03</td>
</tr>
</tbody>
</table>

439A ORAL CONTRIBUTIONS
Conclusions: In this large prospective, multicenter randomized trial of contemporary mechanical reperfusion strategies, normal myocardial perfusion was achieved in only 20% of pts, and correlated with short and long-term survival. These data validate the utility of the myocardial blush score as a prognostic index after primary PCI in AIC.

853-3

A New Endpoint to Evaluate the Success of Reperfusion Therapy Following ST-Elevation Myocardial Infarction

Robert P. Giugliano, Marc S. Sabatine, C. Michael Gibson, Matthew T. Roe, Robert A. Harrington, Ghislaine Ptasiaa, David A. Morrow, Elliott M. Antman, Eugene Braunwald, Brigham & Women’s Hospital, Boston, MA, Florida Clinical Research Institute, Florida, NC

Background. TIMI epicardial flow grade (TFG) predicts mortality after fibrinolysis. It is not known whether concurrent assessment of two independent measures of tissue-level reperfusion (TIMI myocardial reperfusion - TMPG, ST-segment resolution - STRES) adds to TFG.

Methods. Patients with acute myocardial infarction enrolled in three consecutive TIMI trials underwent coronary angiography and assessment of ST segment resolution 60 minutes following fibrinolytic plus GP IIb/IIIa inhibitor. PCI was performed after 60 minutes at the cardiologist’s discretion. Complete restoration of myocardial and epicardial flow was defined as patients who had TFG=3 and TMPG=3 and complete STRES at 60 minutes.

Results. Data for all three measurements were available in 682 patients (mean age 58, 28% women, 14% diabetic). Complete restoration of both myocardial and epicardial flow occurred in 117 patients (18%), and clinical events by 30 days were rare (1 [0.9%] patient with reinfarction, 4 [3.4%] patients with recurrent ischemia requiring urgent revascularization) and significantly lower in this group (Figure).

Conclusions. A combined assessment of epicardial and myocardial reperfusion using TFG, TMPG, and ST-resolution at 60-minutes identifies patients at very low risk for clinical events. We propose this new endpoint to evaluate the success of reperfusion therapy.

3:00 p.m.

853-4

ST-Segment Elevation Resolution as a Predictor of Mortality in Patients With Thrombolysis in Myocardial Infarction III Flow in the Infarct Artery After Primary Angioplasty: The CADILLAC Trial

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Background. ST elevation resolution (STR) is a measure microvascular reperfusion and has been correlated with outcomes. Platelet GP IIb/IIIa inhibitors (PI) enhance STR with lytic therapy, but the effects of PI and stents on STR after primary PCI are unknown.

Methods. Pts with AMI and ≥2 mm ST elevation treated with primary PCI from 1984-2001 (n=634) were stratified into 3 categories of STR based on ST elevation post-PCI: complete (<0.5 mm, n=331), partial (0.5-1.5 mm, n=275), and poor (≥2 mm, n=228). Clinical follow-up was obtained in 98% of pts at 6.2 yrs.

Results: Complete vs. partial vs. poor STR correlated with peak CK/MB release (173 vs. 200 vs. 221, p=.003), 7 no ejection fraction (57% vs. 54% vs. 51%, p=0.001), and late cardiac survival (87% vs. 76% vs. 69% at 10 yrs, p<.002). Complete STR was seen less often in diabetics (39% vs. 42%, p=0.035), non-smokers (28% vs. 44%, p=0.03), anterior MI (16% vs. 55%, p<0.0001), Killip Class II-IV (19% vs. 43%, p=0.001), TIMI 0-1 flow post-PCI (36% vs. 51%, p<0.001), and TIMI 2-3 flow post-PI (16% vs. 41%, p=0.004). Complete STR was correlated with PI and stent use: no PI, no stent (30%); PI, no stent (45%); stent, no PI (62%); and stent and PI (58%) (p=0.001) (Figure). PI and stenting were independent predictors of complete STR (OR 2.2, 95% CI 1.4-3.4; stenting: OR 1.9, 95% CI 1.2-2.9).

Conclusion: Stents and PI improve STR after primary PCI and may enhance microvascular reperfusion. These observational results need to be confirmed in randomized trials.