

3:00 p.m.

ORAL CONTRIBUTIONS

849FO-5

Angiotensin Converting Enzyme Inhibition Reduces Elevated C-Reactive Protein in Patients With Angiographic Coronary Artery Disease

Chloe A. Allen Maycock, Joseph B. Muhlestein, Benjamin D. Horne, Robert R. Pearson, Tami L. Bair, Tobin H. Lim, Heath U. Jones, Sandra P. Reyna, Stephanie V. Moore, Dale G. Renlund, Jeffrey L. Anderson, LDS Hospital, Salt Lake City, UT, University of Utah, Salt Lake City, UT

Background: Inflammation is hypothesized to play a role in all stages of atherosclerosis, and C-reactive protein (CRP), a marker of inflammation, is associated with greater cardiovascular risk. The inflammatory process is upregulated by the renin-angiotensin system (RAS), which suggests that inhibition of the RAS may affect CRP expression. The objective of this study was to determine if angiotensin converting enzyme inhibition (ACEI) or angiotensin receptor blockade (ARB) reduces high-sensitivity (hs)CRP concentrations in a large prospective cohort undergoing coronary angiography.

Methods: Baseline blood samples and patient histories were obtained from 507 patients (pts) not receiving ACEI or ARB who were hospitalized for coronary angiography; 71% had significant ($\geq 70\%$) CAD. After an average follow-up period of 3 years (range: 2 to 4 years), repeat blood samples and recent medical histories were obtained, including any initiation of ACEI or ARB. Hs-CRP was measured (Dade Behring) at baseline and at last follow-up (> 2 years). Potential confounders (age, smoking history, gender, and beta-blocker, aspirin, and/or statin therapies) were examined together with hsCRP in multivariable regression.

Results: 118 subjects (mean age: 64 ± 11 years, 74% male) reported ACEI use, 38 pts (mean age: 67 ± 10 y, 68% male) reported ARB use, and 351 (mean age: 66 ± 10 y, 68% male) reported neither. Median hsCRP at baseline was 0.21 mg/dL (range: 0.02-15 mg/dL). Pts taking ACEI experienced a greater hsCRP reduction than non-ACEI/non-ARB controls (median change: -0.05 mg/dL vs 0.0 mg/dL; $p=0.008$). A trend in hsCRP reduction for the smaller ARB groups was not significant (median change: -0.03 mg/dL vs 0.0 mg/dL; $p=NS$). In multivariable regression, only ACEI therapy ($p=0.007$) and statin therapy ($p=0.034$) were selected as independent predictors of hsCRP change.

Conclusion: In a coronary high-risk cohort, initiation of ACEI significantly and independently reduced plasma hsCRP, even after controlling for statin therapy and other confounders. A vascular anti-inflammatory effect may represent an additional mechanism by which ACEI are associated with benefit to patients with or at risk for CAD.

3:15 p.m.

849FO-6

A Risk Score for Predicting Coronary Artery Bypass Surgery in Patients With Non-ST Elevation Acute Coronary Syndromes

Saihari Sadanandan, Christopher P. Cannon, C. Michael Gibson, Rajen Desai, Sabina A. Murphy, Peter M. DiBattiste, Eugene Braunwald, for the TACTICS TIMI-18 Investigators, Brigham & Women's Hospital, Boston, MA

Background: Routine early use of clopidogrel in patients with unstable angina/non-ST elevation myocardial infarction (UA/NSTEMI) undergoing early coronary artery bypass surgery (CABG) is associated with increased risk of peri-operative bleeding. A simple clinical risk score on admission to predict the likelihood of CABG during index hospitalization in such patients might be useful.

Methods: We evaluated 2220 patients with UA/NSTEMI randomized to early invasive (INV) or conservative (CON) strategy in the TACTICS TIMI-18 trial. Patients with h/o prior CABG ($n=484$) were significantly less likely to undergo in-hospital CABG (OR 0.34, $p<0.0001$) and they were excluded. A logistic regression model was developed to identify clinical variables independently associated with CABG. A p -value of <0.05 was required for retention in the model. The model was validated using UA/NSTEMI patient population from TIMI 11B ($N=3229$) and TIMI 3B ($N=694$) trials.

Results: Of the 1736 patients studied, 326 (18.8%) underwent CABG following index hospitalization. The median time to CABG in the overall population was 3.8 days (2.5, 6.0); INV pts 3.4 days (1.9, 4.9) and CON pts 5.0 days (3.7, 7.9). We identified 8 variables independently associated with CABG; (+) tn T or I (OR 4.3), h/o peripheral vascular disease (OR 2.0), ST segment deviation >0.5 mm (OR 1.8), prior h/o stable angina (OR 1.7), male gender (OR 1.6), prior aspirin use (OR 1.4) and hyperlipidemia (OR 1.4). A risk score was generated by assigning a score of 3 for (+) tn T or I and 1 for each other variable. The association of the risk score with CABG was highly significant ($p<0.0001$, C-statistic 0.72). CABG rates increased significantly with increasing risk score (6.8% for risk score 1-3, 18.4% for 4-6 and 41.1% for >6.0). The association of the risk score with CABG remained significant in the validation model from TIMI 11B ($p<0.0001$; C-statistic 0.63) and TIMI 3B ($p<0.0001$; C-statistic 0.65) trials.

Conclusion: In patients with UA/NSTEMI, a simple risk score based on admission clinical variables predicts the need for CABG. A risk score > 6.0 is associated with high likelihood of CABG during index hospitalization.

853 Enhancing Microvascular Perfusion in Acute Myocardial Infarction

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

2:00 p.m.

853-1

Increased Platelet Receptor Occupancy Following Eptifibatid 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 T. 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 GPIIb/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 + eptifibatid 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 ($p=0.005$). **Conclusions:** This study links restoration of epicardial flow, tissue level perfusion and ST segment resolution with higher levels of plt GPIIb/IIIa receptor occupancy following therapy with eptifibatid when given in combination with TNK. These data provide a pathophysiologic link between plt RO and therapeutic efficacy of combination therapy.

Platelet Receptor Occupancy

Characteristic	Characteristic Present	Characteristic Absent	p-value
60 min TFG 2/3	76.2% +/- 9.2%, median 77%, n=63	63.9% +/- 29.7%, median 70%, n=7	0.005
60 min TMPG 3	79.6% +/- 9.5%, median 80%, n=40	73.0% +/- 16.2%, median 73%, n=30	0.036
Complete ($>70\%$) ST Resolution	81.3% +/- 8.3%, median 81%, n=27	73.1% +/- 17.4%, median 74.5%, n=24	0.034

2:15 p.m.

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 O. Costantini, Alexandra J. Lansky, Kazuyuki Shirai, Ecaterina Cristea, Cristina Brestowski, Steve Slack, Martin Fahy, Cindy L. Grines, John D. Carroll, Stuckey Thomas, Giulio Guagliumi, Barry Rutherford, Mark Turco, David Mathias, Martin B. Leon, Gregg 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 \pm abciximab vs. stenting \pm abciximab. 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 35%, and normal (MBG 3) in 20%. Predictors of reduced blush included male sex ($p=0.01$), LAD location ($p<0.0001$), longer time from symptoms onset to first balloon inflation ($p=0.01$), thrombus ($p=0.007$), low LVEF ($p<0.0001$), and baseline TIMI 0/1 flow ($p=0.0007$). Mortality as a function of MBG appears in the table.

	MBG 0/1	MBG 2	MBG 3	P Value
All patients				
30 days	3.2%	1.3%	0.6%	0.07
1 year	5.9%	2.4%	2.3%	0.03