1053-4

Reduction in Percutaneous Coronary Intervention-Related Bleeding with Bivalirudin is Particularly Striking in Women

Tasneem I. Bhatt, Lisa Cho, A. Michael Lincoff, John A. Bittl, Eric J. Topol, Cleveland Clinic Foundation, Cleveland, Ohio; Osaka Heart Institute, Osaka, Florida.

Background: Female gender is a known poor risk factor for post-procedural bleeding among patients undergoing percutaneous coronary intervention (PCI).

Methods: Within a randomized clinical trial of coronary angioplasty comparing bivalirudin to unfractionated heparin patients were randomized to heparin or bivalirudin after completion of PCI. Major bleeding was defined as a combined endpoint of death, myocardial infarction (MI), revascularization, and major hemorrhage. In patients undergoing PCI (Table). Considering a combined safety and efficacy endpoint of death, MI, and revascularization, bivalirudin was associated with a 50% relative risk reduction in death and hemorrhage among patients undergoing PCI.

Results: Of the 4312 patients enrolled, 1367 (32.2%) patients were women. Compared to males, female gender was associated with a 19-fold increased risk of major hemorrhage—males: 13/1920 (0.7%) vs females: 14/1497 (0.9%) (p<0.0001). When stratified by gender, bivalirudin was associated with a significant reduction in bleeding in women. This effect was most striking among female patients (Table). Considering a combined safety endpoint of death, MI, revascularization, and major hemorrhage, bivalirudin was associated with a 50% relative risk reduction in adverse events in women: 14/1920 (0.7%) vs 69/1497 (4.5%) (p<0.0001). A trend toward a 50% relative risk reduction in major bleeding

Conclusions: Bivalirudin is associated with a substantial reduction in bleeding and major hemorrhage. Bivalirudin was associated with a 50% relative risk reduction in death and hemorrhage among patients undergoing PCI (Table). Considering a combined safety and efficacy endpoint of death, MI, and revascularization, bivalirudin was associated with a 50% relative risk reduction in death and hemorrhage among patients undergoing PCI.

Women

Men

Major Hemorrhage

Bivalirudin

Heparin

p Value

Women

(107/1920) 15.5% (37/1497) 5.3% <0.0001

Men

(207/1497) 13.9% (194/1497) 13.2% <0.0001

A New Rapid Ecarin Clotting Time Assay but Not Activated Clotting Time Strongly Correlates With Bivalirudin Concentration: A Percutaneous Coronary Intervention Study

Leslie Cho, Joel Reginelli, A. Michael Lincoff, Marco Roffi, Teresa Kaldus, Kandice Kottke-Marchant, Patrick D. Mize, David J. Moliterno, The Cleveland Clinic Foundation, Cleveland, Ohio; Pharmanetics Inc, Chapel Hill, NC.

Background: Recently, direct thrombin inhibitors (DTI) have been approved for anticoagulation in percutaneous coronary interventions (PCI). The accuracy of the activated clotting time (ACT), used for monitoring heparin, is uncertain for patients receiving DTI. A new point-of-care assay has been developed based on the ecarin clotting time (ECT), which specifically measures the activity of direct thrombin inhibitors. No prior study has examined the correlation of ECT and ACT sample (n=79, p<0.001). In contrast, there was relatively poor correlation between bivalirudin concentration and Hamochrom ACT (r=0.38, p=0.05) or pro-DMA ACT (r=0.41, p<0.001). There was also poor correlation between ECT and Hamochrom ACT (r=0.27, p=0.04) and ECT with pro-DMA ACT (r=0.52, p=0.001). There was poor correlation between pro-DMA and Hamochrom ACT (r=0.40, p=0.002). Conclusion: ECT is a reliable measurement of anticoagulation in patients receiving bivalirudin, while ACT has poor correlation with bivalirudin concentration. Assays need more correlation between ACT and ECT in such patients. These findings have important implications for guiding the extent of anticoagulation during PCI with DTI.

Poster Session

1054 Vascular and Cardiovascular Dysfunction

Poster Session

1054-13 Smoking, Thrombus, and Plaque in the Culprit Vessel in Patients With Acute Myocardial Infarction: Angiographic Findings

Toshiya Kurisumi, Atsushi Hirayama, Yasunori Ueda, Masahiko Shimizu, Tomohito Ohtani, Kazuhisa Kodama, Osaka Police Hospital, Osaka, Japan.

Background: Smoking is paradoxically associated with good prognosis in patients with acute myocardial infarction (AMI), and results in the higher successful thrombolytic therapy. Therefore, we investigated the hypothesis that smoking status is closely associated with amount of thrombus culprit lesion. Methods: The prevalence of plaques and amount of thrombus in the major coronary arteries were successfully evaluated in 62 patients (male: 55, mean age: 60.2). All patients were underwent percutaneous coronary intervention (PCI), and the residual amount of thrombus after PCI were semi-quantitatively divided into 2 groups (massive: n=33 or little: n=29) by angiography. Furthermore, we analyzed the color of plaque on culprit lesion (4 grades from white to yellow), and the number of plaque in infarct related artery (IRA). Results: 65% of the smoking patients had a higher prevalence of thrombus culprit lesion, compared with non-smoking patients (45% vs. 17%, p=0.049). The mean plaque thrombus was higher, compared with non-smoking patients (65% vs. 22%, p<0.01). The number of plaque in IRA (3.9±2.0 vs. 3.3±1.8), max plaque score (2.7±0.9 vs. 2.7±0.9), and the color of plaque in culprit lesion (2.7±0.9 vs. 2.6±1.1) were not significantly affected by smoking status. As coronary risk factors, Total cholesterol (205 vs. 180 mg/dl, p<0.05) and triglyceride (138 vs. 114 mg/dl, p=0.05) was significantly higher, and the prevalence of hypertension (50% vs. 35%, p<0.01) was significantly lower in smoking patients. Conclusion. This is first evidence to assess the association of smoking status and the amount of thrombus in culprit lesion directly, and also these findings may provide the explanation of the smoker's paradox.

Poster Session

1054-14 Possible Mechanism of Coronary Thrombosis Caused by Vasospasm in Angiographically Nearly Normal Coronary Artery: Evaluation by Plaque Appearance and Malondialdehyde-Modified Oxidized LDL

Shigenasa Tanii, Ikioyoshi Watanabe, Takeshi Fuji, Kazutoshi Ishikawa, Michiaki Matsumoto, Takeshi Mimamoto, Ken Naagao, Katsuo Kameyama, Department of Cardiology, Nihon University Sunpadigak Hospital, Tokyo, Japan, and Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan.

Background: Investigators have demonstrated that focal vasospasm has a high incidence of acute coronary syndrome (ACS) compared to diffuse vasospasm. Recently circulating malondialdehyde-modified oxidized LDL(MDA-LDL) was reported to activate thrombosis formation. Therefore we investigated the differences in plaque appearance and plasma MDA-LDL between two patterns of vasospasm. Methods and Results: Blood samples were collected from aortic root(Ao) and coronary sinus before provocation of left coronary spasm. After release of spasm, IVUS study was performed and volumetric analyses of plaque lesions were evaluated with Neta-3D IVUS system. More abundant soft plaque was localized just at the lesion with focal vasospasm even in the absence of significant angiographic disease, whereas in diffuse vasospasm, internal thickness dilated slightly after stenting the coronary artery. Data is presented in Table 1. Conclusion: Plasma MDA-LDL levels associated with triggering vasospasm were significantly elevated in the coronary circulation focal in vasospasm. Under this condition, dramatically increased % plaque volume during focal vasospasm might play an important role in the mechanism of thrombogenicity leading to ACS.

Poster Session

1054-15 Insulin Resistance as an Independent Predictor of Acute Coronary Syndrome: An Intravascular Ultrasound Study With Clinical Correlations

Takeshi Yoshitama, Masato Nakamura, Taro Tsunoda, Yoko Kitagawa, Masanori Shiba, Guguru Yajima, Masahisa Wada, Taisuke Iijima, Toshiro Naito, Hideto Tanagi, Hiroshi Anzai, Takahiro Nishida, Tetsu Yamaguchi, Masao Tani, Hideyoshi Watanabe, Takeshi Fujii, Kazutoshi Ishikawa, Michiaki Matsumoto, Takeo Anazawa, Takanori Anazawa, Shiga University Hospital, Otsu, Japan, 2nd Department of Internal Medicine, Nihon University School of Medicine, Tokyo, Japan.

Background: Insulin resistance has been implicated as an important initiating factor in coronary atherosclerosis. However, associations between insulin resistance and acute coronary syndrome (ACS) remain unclear.

Methods: Before intervention, 7% patients with 8% culprit lesions underwent intravascular ultrasound (IVUS) examination by which cross-sectional area (CSA) within the elastic membrane (EEM), lumen CSA, and plaque CSA were evaluated. Positive remodeling...
ling (lesion EEM CSA more than 5% greater than at the proximal reference segment) and negative remodeling (lesion EEM CSA more than 5% less than at the distal reference segment) also were evaluated. Insulin resistance was determined by homeostasis model assessment (HOMA) and defined as values above the 75th percentile (i.e., 1.71). Patients were divided into two groups: group 1: n=13, patients with ACS; group 2: n=62, patients with stable angina. Clinical and IVUS variables with a p value less than 0.1 in univariate analysis were entered into the multivariate models. Results: The data was as follows.

The Significant Predictors for ACS

<table>
<thead>
<tr>
<th>No. of segments</th>
<th>ACS Stable angina Univariate p value</th>
<th>Multivariate p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n=13</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=72</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive remodeling</td>
<td>6 (46%)</td>
<td>0.03</td>
</tr>
<tr>
<td>Hypertension</td>
<td>6 (46%)</td>
<td>0.04</td>
</tr>
<tr>
<td>Insulin resistance</td>
<td>10 (77%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Positive remodeling, absent of hypertension and insulin resistance were the predictors for ACS. However, multivariate logistic regression analysis showed insulin resistance was the most powerful predictor.

1054-16 Distribution of Vulnerable Plaque in the Human Coronary Artery: Angiographic and Intravascular Ultrasound Analysis of Occult Atherosclerosis in Proximal Sites in the Three Major Coronary Arteries

Tetsuji Matsutani, Masahiro Kajiguchi, Masashi Ogita, Masahiro Muto, Takumi Yamada, Toshiyuki Tan, Syuji Yamaoka, Kazuki Iwata, Yoshimasa Murakami, Mitsuhiro Okamoto, Junji Toyama, Aichi Prefectural Owari Hospital Cardiovascular Center, Ichinomiya, Aichi, Japan.

Objective: To use intravascular ultrasound (IVUS) to examine the distribution of vulnerable atherosclerotic plaque (VP) in human coronary arteries and clarify the morphological features of occult atherosclerosis in these sites that may develop into VP.

Methods and Results: In 307 consecutive acute coronary syndrome cases (226 acute myocardial infarction, 79 unstable angina, culprit lesion distribution, under coronary angiography, was found to be RCA 94, LAD 179, and LCx 34. We then assessed the location of these lesions to evaluate the distribution of VP. In the RCA and LAD, VPs were most frequently observed at proximal sites in the RCA, 39 lesions (41.6%), and LAD, 17 lesions (60.4%). In the LCx, VPs were more frequently observed at mid-site (20, 59.9%) than at proximal site. To assess evidence of which occult atheroscleroses might develop into VPs in these sites, we also used IVUS to examine proximal sites with no angiographic stenosis (50%-25%) during 70% of the patients. A total of 71 distal target lesions in each morphological features of occult atherosclerosis in proximal sites of the three major coronary arteries were shown below (table). Conclusion: Vulnerable plaque tends to develop at proximal sites in the RCA and LAD. Significant occult atherosclerotic lesions, associated with calcification and echolucence, may be more likely to develop in the proximal RCA and LAD that in the proximal LCx.

The morphological features of occult atherosclerosis in proximal sites of coronary arteries

<table>
<thead>
<tr>
<th>%Plaque Area</th>
<th>Plaque Eccentricity</th>
<th>Calcification</th>
<th>Echolucent Area</th>
<th>RCA (n=26)</th>
<th>LAD (n=35)</th>
<th>LCx (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>61.3±10.1%</td>
<td>15/26(57.7%)</td>
<td>20/26(76.9%)</td>
<td>8/26(30.8%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>52.1±14.5%</td>
<td>27/35(77.1%)</td>
<td>29/35(85.7%)</td>
<td>9/35(25.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LCx (n=17)</td>
<td>33.1±16.5%</td>
<td>0/17(0%)</td>
<td>0/17(0%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

1054-17 Treatment With Statins Results in Decreased Heat Production From the Culprit Atherosclerotic Lesions In Patients With Stable and Unstable Angina

Christodoulos Stefanadis, Konstantina Toutouva, Panagiota Tsamis, Ioannis Kallikazaros, Sophia Vaino, Manolis Vavouranakis, Kostas Tsirouf, Christos Pitsavos, Athanasios Tzikas, Pavlos Toutouzas, Hippokration Hospital, Athens, Greece.

Background: Previous ex vivo and in vivo studies have shown that inflammation leads to heat production from atherosclerotic lesions. Administration of statins may further stabilizes atherosclerotic plaques, due to an additional anti-inflammatory effect. The aim of our study was to investigate the effect of statins on the inflammatory process of atherosclerotic plaques by measuring the temperature of atherosclerotic plaques. Methods: In the study we included 62 patients (pts), 36 pts with unstable angina (UA) and 26 pts with stable angina (SA) who were hospitalized and underwent diagnostic catheterization. Balloon angioplasty was on physician's decision. Statins were administered for a period of one week. No evidence for acute coronary syndromes were found in the nonstenotic segments, ranging from 46% to 66% (mean ± 72±12%) of the total plaque volume. There was no difference when postevmy remodeled stenoses (p<0.001) were compared to intermediately/normaly remodelled stenoses (EEM CSA mean reference). The percentage of the plaque contained in the nonstenotic segments correlated inversely with lesion length (r=-0.62, p=0.0254), and woolly, but directly with nonstenotic segment length (r=0.05, p=0.15). Conclusions: In arteries with single, focal stenosis, 3/4 of the atherosclerotic plaque burden is contained in the non-stenotic segments.

1054-18 Progress With the Calibration of a 3F Near Infrared Spectroscopy Fiber Optic Catheter for Monitoring the pH of Vulnerable Vascular Tissue: A Feasibility Study Approach for Detection of Active Vulnerable Plaque

Tanak Khan, Babu Soller, Peter Meling, Mohammad Mogadd, Ward Casscells, Moraza Namaar, Center for Vulnerable Plaque Research, University of Texas-Houston, and Texas Heart Institute, Houston, Texas.

We hypothesized that localization of vulnerable plaque can be enhanced by physiological factors such as low pH, high temperature (T), NO, hypoxia, and oxycydrualics, which have been shown to shift NIR spectra. We have previously found that pHH of regions of plaques are lower in pH. Therefore, we chose pH to calibrate our spectroscopy catheter. Methods: Ulteriant probe sizes were used to study variable penetration depth. Eventually, using a unique miniaturized fiber optic side-viewing catheter, we demonstrated the feasibility of performing the correlation. 10 human carotid endarterectomized plaques were collected and placed immediately in a humified, 37°C controlled T glove-box type incubator. Optical reflectance spectra (400 - 1100 nm) were taken with the prototype catheter connected to a spectrometer. Partial Least Squares multivariate calibration techniques were used for the correlation. Results: The R² of the determination of tissue pH from the optical NIR calibration was 0.63 and the Root Mean Squared Deviation (RMSD) was 0.14 pH units.

Conclusion: This feasibility study suggests that tissue pH can be determined with NIR spectroscopy in both ex vivo and in vivo plaque tissues. Further improvements in signal-to-noise ratio will be required to meet the long-term goal of detection of vulnerable plaques based on pH. Our new multi-probe catheter allows multiple radial reading of NIR spectra of the vessel wall. This enables pH spectrographic imaging of vulnerable plaque.