Does Genetic Polymorphism for Platelet Glycoprotein IIb/IIIa Impact Early and Long-Term Outcomes After Effective Percutaneous Coronary Interventions?

Gina Wexler, Roxana Mehran, Eugenia Nikolovsky, Eva D. Aymong, Sotir Poltera, Izat Hsipt, Issam Moussa, Edward Kreps, Gregg W. Stone, Jeffrey W. Moses, Martin B. Leon, George Dangas, Lenox Hill Hospital Heart and Vascular Institute of New York and Cardiovascular Research Foundation, New York, NY

Background: Genetic polymorphism (PI A2) of the platelet GP IIb/IIIa protein has been associated with increased thrombus formation and myocardial infarction compared to the A1A1 status; the rare A2A2 status confers the greatest risk, while the A1A2 status confers rather modest risk. The association of PI A2 with adverse events after percutaneous coronary intervention (PCI) is unknown.

Patients and Methods: We followed 153 consecutive patients with normal baseline CK-MB, who underwent elective PCI for symptomatic coronary artery disease for 1 year. All patients were tested for PI A2 polymorphism. Adverse events were recorded and adjudicated by an independent committee blinded to the polymorphism status. All patients received ASA and Clopidogrel for one month post PCI.

Results: The normal (A1A1) and heterozygous (A1A2) variants were found in 108 (70.6%) and 45 (29.4%) of the patients respectively; the homozygous variant was not detected in this population. Baseline patient and lesion characteristics, as well as platelet aggregation assay, maximum activated clotting time value and use of GP IIb/IIIa blockers were similar between the two groups. There were no differences in outcome between groups (Table).

Conclusion: Heterozygous genetic polymorphism PI A1A2 was found in approximately one third of patients undergoing elective PCI and it was not associated with any increase in early or late adverse outcomes after PCI compared to the normal homozygous PI A1A1 status.

A1A1, n=108  A1A2, n=45  p-Value
Intra-procedural no flow/thrombus 1 (1%) 0 (0%) 1.0
Any CPK-MB elevation (> normal) 23 (20%) 9 (20%) 0.65
CPK-MB elevation (>5 X normal) 1 (2%) 2 (4%) 0.21
MACE at 30-days 4 (3.7%) 0 (0%) 0.22
MACE at 1 year 6.6% 7.9% 0.72

Diabetes Achieve Lower Activated Clotting Time When Given the Same Dose of Heparin as Non-diabetics During Percutaneous Coronary Intervention

Michael S. Lee, Vaninder Singh, Salvatore Rametta, Tom Nero, Marshall Fox, James R. Wittenst, St. Luke's-Roosevelt Hospital Center, New York, NY

Background: It is well established that adverse clinical outcomes and complications of percutaneous coronary intervention (PCI) are more common in diabetics than in non-diabetics. The use of glycoprotein IIb/IIIa receptor antagonists has improved clinical outcomes. Current PCI guidelines recommend an initial 70 IU/kg intravenous dose of unfractionated heparin, and compared initially-achieved ACT in diabetics versus non-diabetics. Diabetics may be less sensitive to heparin compared to non-diabetics. The use of glycoprotein IIb/IIIa receptor antagonists has improved clinical outcomes. Current PCI guidelines recommend an initial 70 IU/kg intravenous dose of unfractionated heparin, and compared initially-achieved ACT in diabetics versus non-diabetics. Diabetics may be less sensitive to heparin compared to non-diabetics.

Methods: We retrospectively studied 265 PCI patients treated by intention to receive 70 IU/kg of unfractionated heparin, and compared initially-achieved ACT in diabetics versus non-diabetics.

Results: Achieved initial ACT in the diabetic group was significantly lower than that in the non-diabetic group (269.5±46.5 vs. 333.6±53.6 s, p<0.001). The results suggest that diabetics are less sensitive to heparin compared to non-diabetics. We hypothesized that an initial heparin dose of 70 IU/kg is not sufficient to achieve adequate anticoagulation in diabetics undergoing PCI. Methods: We retrospectively studied 265 PCI patients treated by intention to receive 70 IU/kg of unfractionated heparin, and compared initially-achieved ACT in diabetics versus non-diabetics. Results: Achieved initial ACT in the diabetic group was significantly lower than that in the non-diabetic group (269.5±46.5 vs. 333.6±53.6 s, p<0.001). The results suggest that diabetics are less sensitive to heparin compared to non-diabetics. We hypothesized that an initial heparin dose of 70 IU/kg is not sufficient to achieve adequate anticoagulation in diabetics undergoing PCI.

Conclusion: Current heparin dosing of 70 IU/kg for PCI leads to suboptimal initial ACT in diabetics. Diabetics may need a higher dose of unfractionated heparin to reach optimal levels of anticoagulation during PCI. Further investigation is warranted to determine optimal combinations of antithrombotic and antiplatelet therapies especially in diabetic patients.

Diabetics Achieve Lower Activated Clotting Time When Given the Same Dose of Heparin as Non-diabetics During Percutaneous Coronary Intervention

Coating of Intracoronary Stents With AC133+ Endothelial Progenitor Cells

Balt Koester, Markus Guntenkohl, Ursula Gehling, Sonja Loges, Wulf Iiz, Jan Kaehler, Dieter Hoessel, Walter Fiedler, Thomas Meienitz, Thomas Meinren, University Hospital Eppendorf, Hamburg, Germany

Background: Rapid regeneration of endothelium after coronary stenting reduces restenosis and thrombosis. Endothelialization may be delayed after treatment with brachytherapy or drug eluting stents. Endothelial progenitor cells (EPC) have a high regenerative potential which could enhance reendothelialization at site of stenting. The aim of these experiments was to identify an optimal stent coating for adherence and growth of EPC. Methods: AC133+ EPC were isolated from leukapheresis products. Mononuclear cells were isolated by density gradient centrifugation, incubated with AC133-conjugated microbeads and processed through a magnetic column. Purified EPC were cultivated in IMDM with supplements. 316L steel stents, coated with heparin, aluminum oxide, fibronectin, vitronectin, osteonectin, collagen type I and IV, laminin and uncoated 316L steel stents were incubated with EPC for two weeks. Cell layers were evaluated by microscopy. Results: Cell density was scored in 4 categories according to visual assessment of mean cell density within three representative microscopic fields and analysis in quadruplicates (categories: 1: 0-20; 2: 21-40; 3: 41-60; 4: 61-80 cells/field). Results: Within one week of culture EPC become adherent on heparin-, fibronectin-, vitronectin-, osteonectin- and collagen-coated stents, whereas there was no visible cell attachment to uncoated 316L steel. The highest numbers of cells were counted on heparin-, aluminum oxide-, and collagen type IV-coated stents (>41 cells/field), whereas cell numbers were significantly lower on collagen type I- and fibronectin-coated stents (>21 cells/field). Lowest numbers or no cells were detected on osteonectin-, laminin-coated stents and on 316L stents without coating (<0 cells/field). Morphological features revealed AC133+ derived cells grown to confluence as endothelium. Conclusions: Endothelial progenitor cells are suitable for coating of coronary stents. Stent coating with heparin or aluminum oxide enhances their attachment and growth. Endothelial progenitor cells may offer therapeutic potential in irradiated lesions or lesions treated with antiplatelet drugs.

The Impact of Sirolimus-Eluting Stents on the Outcome of Patients With Difussion Lesions

Kenpo Tanabe, Pedro A. Lemos, Chi-hang Lee, Muzzaffer Degertekin, Evelyn Reyser, Akis C. Arampatzis, Ron T. van Dornburg, Pin de Feyer, Willem J. van der Giessen, George Sianos, Peter C. Smits, Paul Cummins, Arno Rutter, Francesco Saia, Patrick W. Serruys, Thoraxcenter, Rotterdam, The Netherlands

Background: Although stents have improved procedural success rate, the treatment of bifurcation lesions is still problematic with an increased restenosis rate and need for repeat revascularization. Sirolimus-eluting stents (SES) have recently proved to virtually