Reduced Shear Stress and Large Shear Stress Gradient Cause Coronary Aneurysm and Thrombus Formation in Children With Kawasaki Disease

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We tested whether reduced shear stress (SS) and large shear stress gradient could be caused coronary artery aneurysm (AN) formation at coronary branching site and thrombus formation in AN in patients with Kawasaki disease (KD). 139 children (2y - 16y) who had coronary abnormality revealed by D-ECHO were subjected. All patients had different sized AN without any significant stenosis in proximal and distal portion of AN and were divided into four groups by the maximum diameter of AN; Group S: < 1.5-fold the diameter of the adjacent non-annealing vessel, n=34; Group M:1.5 < t < 4.0-fold, n=31; Group L: 4.0-fold, n=29; Group N: normal-looking vessels by CAG, n=45. All patients had Aspirin and / or Warfarin. The averaged peak velocity (APV) was measured at the middle of ANs in groups L, M and S, at the branching site of segment 5-6 in group M, and at the normal-looking proximal lesion of AN in all 4 groups. SS was calculated by the simplified formula as: shear stress = 4µV/4µR2, where µ is blood viscosity, R is maximum inner diameter of AN or coronary vessel. SS gradient was calculated by the formula as: SS gradient = SS at normal-looking lesion / SS at AN or coronary branching site. Also, CAG and IVUS were performed for detection of thrombus and localization of ANs.

Results:

- In group M, SS in normal-looking vessels were 26.6 ± 3.1 µPa s/m in AN and 26.6 ± 3.1 µPa s/m in controls: 284.9 ± 14.7 µPa s/m.
- APV in group M were 14.5 ± 7.4 cm/s in AN and 14.5 ± 7.4 cm/s in controls: 26.8 ± 10.7 cm/s.

Conclusion:

Reduced shear stress and large shear stress gradient may play a critical role of giant aneurysm and thrombus formation intra coronary aneurysms in Kawasaki disease.

Physiologic and Anatomic Evaluation Prior to and After Stent Implantation in Small Coronary Vessels: Final Results of PHANTOM Trial

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Background: Long-term outcomes after PCI of small coronary artery disease remain suboptimal, but there is no diagnostic tool available to define (appropriate)ness of PCI in this setting. This prospective multicenter study assesses the role of intravascular ultrasound (IVUS), quantitative coronary angiography (QCA) and fractional flow reserve (FFR) in patients with small coronary arteries.

Methods: Sixty patients with small coronary arteries (reference diameter ≥2.8 mm) and coronary stenoses between 40-70% were included. A 0.241-mm pressure guide wire (Wave Wire) was used for FFR measurements after 2 minutes of IV infusion of adenosine (11 mg/m2). Volume 30-IVUS and angiographic data were analyzed in an independent core laboratory. PCI was deferred if FFR >0.75. Optimal stenting was defined by IVUS (minimal luminal area (MLA) instant >80% of reference MLA). Clinical follow-up was scheduled at 6 and 12 months.

Results: Mean age was 62.4 ± 10y; 40% had diabetes and 84% had HTN. There were no procedure complications. Mean RD (reference diameter) was 2.1mm. Sixty percent of the patients had normal FFR (>0.75). Seventy percent of patients with a CSA obstruction >70% by IVUS had an FFR ≤0.75, while 100% with CSA obstruction >75% had FFR ≤0.75. Angiographic MLD was not correlated with FFR. Forty-four percent had post-stenting FFR ≤0.90 in spite of optimal IVUS result. Fifty six patients completed at least 6 month follow-up (25 completed 12-month). Among patients who did not undergo index PCI because of an FFR ≤0.75 (n=27 out of 56 with follow-up), none required follow-up revascularization. There were 5 repeat PCI in the cohort of patients initially treated with PCI (n=25). Complete follow-up data will be presented. Conclusion: The majority of intermediate lesions in small vessels may not require PCI. There is a poor correlation between physiological and anatomical parameters in patients with small vessel disease. Deferring PCI based on FFR ≤0.75, appears to be associated with moderate stenosis in small coronary vessels. Considering the high incidence of restenosis, FFR represents a valuable tool to define the appropriateness of PCI in small vessels.

Hypersensitivity is Associated With Coronary Endothelial Dysfunction in Obese and Non-diabetic Patients

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Background: The American Heart Association (AHA) has recently classified obesity as a modifiable risk factor for coronary heart disease. Therefore, we evaluated the impact of obesity on insulin resistance and coronary endothelial function in overweight patients with normal or mild coronary artery disease. Methods: A total of 38 consecutive non-diabetic patients with normal or mildly diseased coronary arteries at angiography underwent coronary vascular reactive evaluation using intracoronary administration of papaverine, acetylcholine and nitroglycerin using a Doppler guidewire. Patients were divided into two groups based on body mass index (BMI): Group 1 patients with a BMI<25 (n = 19, normal weight); and Group 2, patients with a BMI≥25 (n = 13, overweight). The level of fasting immuno-reactive insulin (FIRI) and fasting blood glucose (FBS) were measured in each subject. Homeostasis model assessment (HOMA-IR) was used as an indicator of insulin resistance. Results: FIRI and HOMA-IR in Group 2 were significantly greater than those in Group 1 (4.4±2.7 vs. 14.5±4.1 µU/ml, p=0.01; 1.0±0.62 vs. 3.5±2.77, p=0.01, respectively), whereas FBS was similar when comparing the two groups (95±11 vs. 98±13 mg/dl). The percent change in coronary blood flow and coronary artery diameter induced by acetylcholine in Group 2 had a significant negative correlation with both HOMA-IR and FIRI (HOMA-IR: r=0.69, p<0.01; r=0.94, p=0.02; FIRI: r=0.69, p<0.01; r=0.72, p<0.01, respectively) but displayed no significant correlation in Group 1. Conclusions: Obesity with hypersensitivity caused by increased insulin resistance is associated with coronary endothelial dysfunction in non-diabetic patients.

A Novel Anti-restenosis Effect of Paclitaxel-Eluting Stents

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Background: Coronary stenting is a known, potent stimulator of adventitial angiogene-

These post stent angiogenesis may help neointimal growth and maintenance. Cell migration and proliferation blockage are two known mechanism of Pacltixel limiting neointimal hiperplasia. Pacltixel is a knwon angiogenesis inhibitor in other tissues, like tumors, nonetheless this effect on coronary arteries has not yet been studied. We thus examined adventitial neovascularization in porcine coronary arteries following paclitaxel eluting stent implant and compared them with control stents.

Methods: Forty-three stented arteries, 26 paclitaxel stents (1ug/mm2) and 17 controls were examined blindly. Adventitial vessels (vasa vasorum) were identified as arterial structures with endothelial cells surrounding a lumen, with or without erythrocytes. Adventitial vessel density was determined by manual counting using a curved geometric shape 600x1500 microns placed in the adventitia bordering the external elastic lamina. Intimal thickness was measured from the back of each strut to the lumen and calculated an average for each artery.

Results: Paclitaxel-stented arteries showed a marked decrease in adventitial vessels compared with control stented vessels (1.5±1.2 versus 3.1±2.2 vessels/20,000 sq micros, p<0.003). There was no statistical difference in minimum intima thickness between the treated and control groups in this mild injury model (paclitaxel: 308.9±57.3, controls:284.3±59.0 micros, p>0.5).

Conclusions: Paclitaxel elution from stents is associated with markedly decreased adventitial angiogenesis. In addition to its anti migratory and antiproliferative effects, pacltixel may prevent neointimal growth by preventing adventitial vasa vasorum, limiting oxygen and nutrient supply to the neointima. If true, this opens novel therapeutic strategies for limiting neointimal hyperplasia.

Proteomic Profiling of Restenotic Lesions Unveils Increased Expression of Structural Proteins That Are Inhibited by Intramural Delivery of Ramipryn

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Restenosis is the major limiting factor of balloon angioplasty.Identiying genes that regulate neointima formation is ongoing, facilitated by cDNA array profiling of the arterial wall. This study utilizes proteomic profiling to identify gene products involved in arterial remodeling that occurs as a consequence of restenosis. We specifically identified proteins inhibited by ramipryn since this drug is being used clinically for its anti-restenotic properties.

Intramural infusion of ramipryn or its vehicle was delivered through a balloon catheter directly into the vessel wall during angioplasty. After 3 weeks, proteomic profiles of arterial wall segments were obtained. On average, 485 protein spots were consistently