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Coronary Shear Stress Induces Endothelial Dysfunction and Impaired Vascular Remodeling in Patients with Mildly Diseased Coronary Arteries

Keishi Saihara, Shuichi Hamasaki, Masahiro Kamekou, Fumio Nakano, Takashi Yoshitama, Sanemasa Ishida, Akiko Yoshikawa, Tetsuro Kataoka, Masakazu Ogawa, Hideki Okui, Tei Chuwa, Kagoshima Univ, Kagoshima, Japan

Background: Remodeling in normal vessels is regulated by the endothelium in response to altered shear stress. Although the association between coronary vascular remodeling and endothelial function in humans is not fully elucidated. Thus, we examined the relation of shear stress to both endothelial function and vascular remodeling by a simultaneous intravascular ultrasound (IVUS) and Doppler flow study. Methods and Results: Patients (n=72) with a discrete and mildly stenotic lesion (% diameter stenosis<30%) underwent IVUS examination of the left anterior discending coronary artery. Vascular reactivity was examined using intracoronary acetylcholine (Ach), papaverine and nitroglycerine in the left anterior descending coronary artery using Doppler Guidewire. Vessel area (VA), lumen area (LA), and plaque area (PA) were evaluated at the same position as the top of the Doppler Guidewire. Patients were divided into two groups according to the % area stenosis: group 1: n=17, patients with a lesion of % area stenosis<40%; group 2: n=55, patients with a lesion of % area stenosis ?40%. VA significantly increased with PA in both group. The increase in VA for every 1-mm2 increase in PA in group 1 was significantly greater than that in group 2 (2.46 vs. 1.68, p<0.01). The percent increases in coronary blood flow and coronary artery diameter induced by Ach in group 1 were significantly greater than those in group 2 (64+/-70 vs. 16+/-75%, p<0.05; -7+/-18 vs.-32+/-31%, p<0.01, respectively). Coronary wall shear stress in group 1 was significantly smaller than that in group 2 (131+/-53 vs. 166+/-71 dynes/cm2 , p<0.05). Conclusions: Coronary shear stress increases in response to plaque accumulation and induces endothelial dysfunction and impaired vascular remodeling in patients with mildly diseased coronary arteries.

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Is Angiographic TIMI Frame Count an Index of Endothelial Function?

Luisa Gregorini, Experimental Surg & Transplantation, Milan, Italy; Jean Marco, Bruno Farrah, Clin Pasteur, Toulouse, France; Carlo Palombo, Internal Medicine Dept, Pisa, Italy; Monique Bernies, Clin Pasteur, Toulouse, France; Micaela Kozakova, Internal Medicine Dept, Pisa, Italy; Guido Pomidossi, Experimental Surg & Transplantation, Milan, Italy; Daniela Mari, Massimo Cugno, Internal Medicine Dept, Milan, Italy; Gianni B Anguissola, Adalberto Grossi, Experimental Surg & Transplantation, Milan, Italy

The angiographic phenomenon of slow flow occurring after coronary revascularization (PCI) or after thrombolysis predicts poor LV functional recovery. Whether the TIMI frame count (FC) correlates with blood flow velocity (APV) obtained by Doppler flow wires is unknown. In 46 patients undergoing coronary stenting we measured APV by intracoronary flow wires, coronary cross sectional area (CSA) by QCA and we calculated CFR after having induced hyperemia by intracoronary (24μg) or intravenous (140μg/kg/min x 5min) adenosine. APV was continuously recorded during the revascularization procedure, except for the short times necessary to change balloons. The extent and the time-course of post-occlusion hyperemia were also evaluated, since it may reflects the endothelial response to shear stress and may be an index of endothelial dysfunction. Results. Before revascularization FC was in PCI and non-PCI vessels 46.4+/-13.7 and 40.6+/-14.9, respectively (P<0.05). After adenosine FC became 39.5+/-14.9 and 33.1+/-12.4, respectively, (P <0.05, mean+/-SD). After revascularization FC became 37.2+/-12.6 (P<0.05) and 33.2+/-5.3, in PCI and non-PCI vessel, respectively. Adenosine significantly reduced but did not normalize FC. APV was before PCI 13.3+/-5.2cm/sec and became 32.0+/-12.6 after adenosine (P<0.05). After revascularization APV increased to 21.1+/-8.9 (P<0.05) and 47.5+/-18.4 after adenosine (P<0.05). No correlations were found between APV or CFR and FC. Before revascularization baseline blood flow (ml/min) was 29.4+/-16.4 and 83.2+/-55.9 after adenosine (+187.6+/-81.9%). At balloon deflation became 101.0+/-39.2 8 ml/min corresponding to +300+/-163% increase. FC correlated with the hyperemic blood flow observed immediately after balloon deflation (P =0.001, Rsp=0.188). Conclusions. In our patients the FC did not correlate with APV, CFR, but the FC obtained before revascularization correlated with the hyperemic flow. FC may be an index of endothelial function and reflect the capacity of the reperfused endothelium to produce NO.

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Induction of Coronary Artery Spasm by Two Pharmacologic Agents: Comparison between Intracoronary Injection of Acetylcholine and Intracoronary Administration of Ergonovine

Shozo Sueda, Hiroaki Kohno, Hiroshi Fukuda, Saijo Saiseikai, Saijo City, Japan

Backgrounds: There have been few studies comparing the clinical usefulness for the induction of coronary artery spasm between acetylcholine (ACh) and ergonovine (ER). Objectives: This study examined whether or not intracoronary injection of ACh was similar to intracoronary administration of ER for the induction of coronary artery spasm. Methods and Results: We performed selective intracoronary administration of both ER and ACh in the same 171 patients (106 men, 62±10 years) with <50% stenosis. Under no medication, ACh was injected first in incremental doses of 20–100 mg. Ten minutes later, ER was administered in total doses of 40–64 mg. Positive spasm was defined as > 99% luminal narrowing. Coronary spasms were induced by either pharmacologic agents in 134 vessels from 70 patients. In the overall results, no difference was existed in the incidence of provoked spasm between the 2 agents (ACh: 33% vs. ER: 32%, ns). However, ER provoked more focal spasms, whereas ACh provoked more diffuse spasms. Seventy-four (56%) of all 134 vessels had coronary spasms on the same coronary arteries. Coincidence of both provoked spasms and spasm configuration on the same coronary artery was observed in only 16%(22/134). Coincidence of this study was 94% of all vessels, whereas the remaining 6% of vessels were different each other. Non-coincidence rate of RCA was significantly higher than that of LCA (9% vs. 4%, p<0.01). No serious or irreversible complications were observed during two sequential tests. Conclusions: We recommend the supplementary use of these two agents for the induction of coronary vasospasm in the cardiac laboratory. As a spasm provocation test, there is no difference between ACh and ER.

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Physiologic Interrogation of Transplant Arteriopathy

William F Fearon, Mamoo Nakamura, David P Lee, Mehrdad Rezaee, Randall H Vagelos, Sharon A Hunt, Paul G Yock, Alan C Yeung, Stanford Univ, Stanford, CA

Background: Assessing transplant arteriopathy by measuring fractional flow reserve (FFR) with a coronary pressure wire has not been previously evaluated. Coronary flow reserve (CFR), using a validated coronary thermodilution technique, can now be measured simultaneously using the same pressure wire. Methods: In 19 asymptomatic cardiac transplant recipients (mean 2.5 years since transplant), coronary angiography and intravascular ultrasound (IVUS) imaging of the left anterior descending artery (LAD) were performed. Using a coronary pressure wire, FFR of the LAD was measured after 48 micrograms of intracoronary (IC) adenosine. With the same wire, and modified software, proximal and distal coronary temperature was monitored, and the mean transit time of room temperature saline injected down the LAD was calculated based on the thermodilution curve at rest and after 15 mg of IC papaverine. The ratio of the resting to hyperemic mean transit times has been shown to correlate with Doppler wire derived CFR. A blinded core lab performed quantitative coronary angiography (QCA) and 3-D IVUS analysis. Results: QCA revealed no stenosis >35%. The average FFR was 0.89; 68% (13/19, p<0.0001) of the patients had an FFR below the normal cutoff of 0.94; and 11% (2/19, p=NS) had an FFR less than the ischemic threshold of 0.75. There was a significant inverse correlation between FFR and IVUS derived % plaque volume (r=-0.70, p=0.0008). FFR did not correlate with IVUS derived minimum lumen diameter or area (r<0.5, p=NS), although there was a correlation with maximum lumen area (r=0.64, p=0.003). The average thermodilution derived CFR in 17 patients was 1.9; in 59% (10/17, p<0.0001) the CFR was below the normal cutoff of 2.0. In 18% the FFR was normal (>0.94) and the CFR was abnormal (<2.0), suggesting pure microcirculatory dysfunction. FFR and CFR did not correlate (r<0.5, p=NS). Conclusions: FFR correlates with IVUS findings and is abnormal in a significant proportion of asymptomatic cardiac transplant patients with normal angiograms. Simultaneous measurement of CFR with the same pressure wire using a novel coronary thermodilution technique is feasible and adds information to the physiologic evaluation of these patients.

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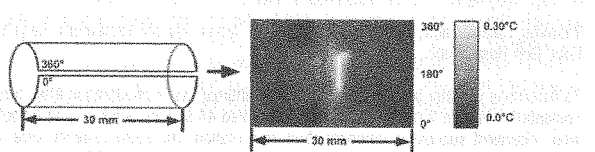
In Vitro Surface Temperature Images from a Guidewire-Based Thermography System

Brian K Courtney, Mamoo Nakamura, Ross Tsugita, Rachna Basisht, Yasuhiro Honda, Paul G Yock, Peter J Fitzgerald, Stanford Univ Medical Ctr, Stanford, CA

Introduction: Heterogeneity of arterial wall temperature, as measured with catheter-based systems to identify thermally-active vulnerable plaques, has been shown to correlate with adverse coronary events in clinical scenarios. Guidewire-based systems may provide an alternative method with greater spatial resolution and ease of use. Methods and Results: A thermocouple sensor (Imetrx Inc.) in the tip of a guidewire coupled to a rotary pullback device enabled sampling of temperature along a spiral path against the inner surface of a thin-walled silicone tube. An external heat source was placed eccentrically against the outer wall to simulate a heat-generating lesion. 36 heated and 12 control pullbacks were performed. Temperature vs. time data was mapped to an image of the vessel wall surface as shown below. No changes in temperature of greater than 0.08 deg C were detected in the controls. The simulated lesion was detected in all 36 heated cases with peak temperature changes in each case ranging from 0.13 to 0.64 deg C. Conclusions: Guidewire-based thermography is technically feasible for the detection of vulnerable plaques. Thermographic imaging can display biologic features that may assist in plaque characterization.



Prevention of Restenosis With Systemic Approaches

Subspecialty: PCI

Tuesday

McCormick Place Hall D

Abstracts 2922–2932

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Cilostazol Reduces Restenosis in Lesions without Stent Implantation, but Does Not Reduce Restenosis in Lesions with Stent Implantation

Yuichi Noguchi, Takeyasu Noriyuki, Yuko Fumikura, Kimito Ishikawa, Tsukuba Medical Ctr, Tsukuba, Japan; Shigeyuki Watanabe, Iwao Yamaguchi, Institute of Clin Medicine, Univ of Tsukuba, Tsukuba, Japan

The aim of this study was to evaluate the efficacy of cilostazol on restenosis after percutaneous coronary intervention(PCI). Between Aug.1996 and Dec.2000,750 consecutive patients(pts)