POSTER SESSION

1082

Biology of the Atherosclerotic Plaque: Clinical Studies

Monday, March 08, 2004, Noon-2:00 p.m.
Morial Convention Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1082-177   Impact of NAD(P)H Oxidase-Derived Reactive Oxygen Species on Plaque Formation and Vascular Remodeling: Comparison of Histochemical Characteristics and Intravascular Ultrasound Finding of Atherosclerotic Lesions

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Background: Oxidative stress induced by reactive oxygen species (ROS) in the vessel wall plays an essential role in atherogenesis. Recently, we demonstrated that the generation of ROS via NAD(P)H oxidase was correlated with plaque instability using coronary specimens obtained by directional coronary atherectomy (DCA). In this study, the relation of ROS generation and vessel remodeling was studied using a combination of preintervention intravascular ultrasound (IVUS) and measurement of ROS corresponding to DCA specimens.
Methods: On the pre-DCA IVUS images of 30 patients, lesions and reference segments were analyzed for vessel area (VA) and plaque area (PA). Positive vascular remodeling was defined as lesion VA > both proximal and distal reference VAs, and remodeling index was calculated as lesion VA / an average of proximal and distal reference VA. The degree of ROS generation and expression of NAD(P)H oxidase p22phox in DCA specimens were evaluated by the dihydroethidium method and immunohistochemistry as the ratio of positive area to total surface area in each specimen.
Results: ROS generation in coronary specimens was closely associated with expression of p22phox, and it was significantly correlated with lesion PA and remodeling index (r=0.60, p<0.001, r=0.79, p<0.001, respectively, Fig.). Positive remodeling was observed more frequently in patients with high ROS generation, compared to those with low ROS generation (75.0% vs 11.1%, p<0.001).
Conclusions: ROS generation is correlated with both plaque volume and vascular positive remodeling. NAD(P)H oxidase-derived ROS may have a significant role in the progression of atherosclerosis and the associated remodeling process.

1082-180   Compensatory Enlargement Delay Vascular Healing of the Culprit Lesion Following Acute Myocardial Infarction

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Background: Although there have been many reports on the mechanism of plaque disruption leading to acute myocardial infarction (MI), the process by which the culprit lesion subsequently heals has not been well described. We hypothesized that positive remodeling of the culprit lesion at the onset of acute MI may retard the healing of the vessel 6 months later.
Methods: We studied 28 acute MI patients (26 men, 60.8+/-9.2 years) within 24 hours after onset. In all cases, both angioscopy (Clinical Supply Co.; Vecmova) and intravascular ultrasound (IVUS, Boston Scientific Scimed, Inc.; ULTRA CROSS 3.2) were performed immediately before percutaneous coronary stenting (Multi-Link or S670/S660) and at 6 months followed-up after onset (193+/-18 days) in stented segments. At onset, IVUS was used to evaluate compensatory remodeling of the culprit lesion, which was defined as vessel area at culprit lesion 5% greater than that of reference segment . Six months later, angioscopy was used to classify the culprit lesions as containing remaining thrombi (T) or no thrombi (N). In addition, the medications used in groups T and N were noted.
Results: Six patients were classified into group T and 22 into group N. Group T showed a higher incidence of compensatory enlargement of the culprit lesion at MI onset (100.0% vs. 40.9%; p=0.018) compared with group N. Fewer patients with group T had received an angiotensin-converting enzyme (ACE) inhibitor (16.7% vs. 68.2%) or a statin (16.7% vs. 45.5%) compared with group N. All patients were taking aspirin.
Conclusion: Six months later from onset, 21.4% of MI patients have remaining thrombi in the culprit lesion. Vascular healing following acute MI may be retarded by compensatory enlargement of the culprit lesion, which continues to be a potent source of instability and thrombogenicity. Moreover, administration of an ACE inhibitor or a statin appears to be effective for stabilization of the culprit lesion.

1082-181   Production of Reactive Oxygen Species by Mononuclear Cells Correlates With the Severity of Coronary Heart Disease and NADPH Oxidase Expression

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Background: Reactive oxygen species (ROS) have been implicated in the development of atherogenesis. ROS production in phagocytic and nonphagocytic cells largely depends on NAD(P)H-oxidase, which consists of several subunits among which is p22phox. We now investigated whether ROS release by mononuclear cells, which contribute to atherogenesis, correlates with the extent of coronary heart disease. We also assessed the role of the C242T p22phox polymorphism, which has been hypothesised to affect NADPH-oxidase dependent ROS release. Methods: In 154 male patients who underwent coronary angiography because of suspected coronary heart disease (CHD) the coronary arteries were assessed using the extent-score, which reflects the total atherosclerotic burden of the vessels, the severity-score and the Gensini-score. In all patients, NADPH-oxidase dependent ROS release from mononuclear cells, isolated by Ficoll separation, was quantitated by luminol enhanced chemiluminescence after phorbol-lester stimulation. The C242T polymorphism was assessed by restriction fragment length polymorphism. p22phox-mRNA from mononuclear cells was measured by quantitative PCR.
Results: Peak ROS release in mononuclear cells was significantly different (p<0.001) between patients with (n=123) and without (n=31) CHD. ROS release was largely dependent on NADPH oxidase as indicated by inhibition with diphenylene iodonium. The extent-score, but not the severity- and the Gensini-score, showed a positive significant correlation with peak ROS-release from mononuclear cells (p<0.001). Multivariate analysis, correcting for effects of lipid-levels, age, concomitant medication, blood pressure and diabetes confirmed the independent correlation. The amount of p22phox-mRNA from mononuclear cells significantly correlated with ROS release (p<0.01). No correlation was found for the distribution of the p22phox 242C- and the 242T-polymorphism and CHD or ROS release.
Conclusion: These data demonstrate a correlation between coronary atherosclerotic burden and NADPH-oxidase dependent ROS-production. The present findings support the concept of oxygen-radicals as important risk factors for atherogenesis.
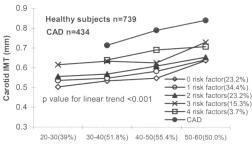
1082-182   Carotid Intima-Media Thickening as Surrogate Atherosclerosis Marker: Is It Relevant to the Asians?

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Background: Carotid intima-media thickening has emerged as a surrogate marker of atherosclerosis, predictive of stroke and cardiovascular events in asymptomatic Western populations, but its relevance in Chinese has not been documented.
Methods: 739 asymptomatic Chinese, aged 18-70 year, were studied in southern China (Pan Yu, Hong Kong and Macau), Sydney and San Francisco. Risk factors screened included smoking, obesity (body mass index >25), dyslipidemia (high density cholesterol <0.9mmol/l, low density cholesterol >4.1mmol/l or triglycerides >4.5mmol/l), hypertension and diabetes. Intima-media thickness (IMT) of common carotid artery was measured by high resolution ultrasound, using a validated automatic edge-detection and thickness measurement computer package. A group of 434 coronary artery patients (CAD) were studied similarly for comparison.
Results: Their mean age was 43±9 years and 48% were male. 214 subjects (28.8%) were smokers, and mean LDL-cholesterol was 2.9±1.0mmol/l. 254 subjects (34.4%) had 1 risk factor and 42.2% had >1 risk factors. Mean carotid IMT was 0.60±0.12mm, being significantly higher with increased age and with prevalence of risk factors (p value for linear trend <0.001). CAD patients had significantly higher (p<0.01) carotid IMT at all age.
Conclusions: Carotid IMT is a relevant surrogate atherosclceoritc marker in the Asians, supporting its wide applications in epidemilogical and clinical research.