1:48 p.m.

1169MP-130 Myocardial Apoptosis Following Short Periods of Ischemia in the Isolated Rat Heart: A Hypothetical Cut Off Point for Experimental Simulated Angina?

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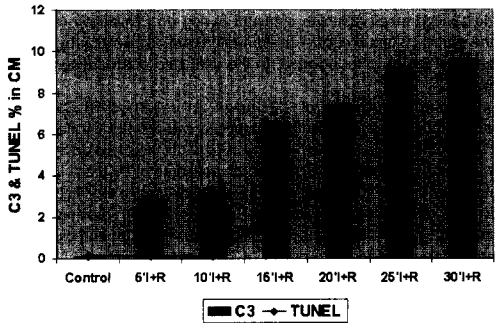
Background: Apoptosis (AP) affects myocytes (CM) of ischaemic-reperfused hearts occurring primarily during reperfusion (R), after a period of ischaemia (I) sufficiently long to induce irreversible cardiac damage. The present study was undertaken in order to verify whether short periods of I can initiate AP and, if so, to identify a cut-off point beyond which the process is clearly triggered.
Methods & Results: Isolated rat hearts were exposed to increasing periods of global I followed by the same length of R (See Graph). Sections were stained by TUNEL (T), propidium iodide and either anti-desmin or -active caspase 3 (C3) antibodies. Confocal microscopy (CFM) and electron microscopy (EM) analysis were performed. 5 and 10 M I resulted in C3 processing independently from DNA fragmentation. T staining was seen first after 15 M I and colocalized with C3 labelling. The percentage of T positive CM progressively rose with increasing length of I. These findings were confirmed by EM and C3 activity measurement.
Conclusions: Very brief periods of I (5 and 10 M) induce C3 processing without leading to DNA fragmentation. In contrast, periods of I longer than 10 M do allow completion of AP. These findings indicate that caspase activation can occur independently from AP. Additionally, our data, though requiring validation in an in vivo model of "simulated angina', seem to suggest the existence of an ischaemic threshold beyond which still relatively short periods of I can cause irreversible damage leading to AP.



POSTER SESSION

1170 Novel Factors: Affecting Myocardial Response in Acute Coronary Syndromes

Tuesday, March 19, 2002, Noon-2:00 p.m.
Georgia World Congress Center, Hall G
Presentation Hour: 1:00 p.m.-2:00 p.m.

1170-33 Elevated Plasma Levels of C-Reactive Protein May Modulate Myocardial Damage in Patients With Acute Myocardial Infarction Underwent Successful Percutaneous Coronary Intervention

Akihiro Nakagomi, Kouichi Akutu, Satoshi Aoki, Yoshito Yamane, Hiromichi Takagi, Nobuhiko Fujita, Hitoshi Takano, Yoshiki Kusama, Morimasa Takayama, Teruo Takano, *Nippon Medical School, Tokyo, Japan.*

Background: Recent evidence suggests that high concentrations of C-reactive protein (CRP;>5mg/dl) induce proinflammatory cytokines such as TNF-alpha and IL-6 on monocytes, which may cause myocardial damage. In contrast, several investigators showed CRP inhibited neutrophil chemotaxis and superoxide production in a dose-dependent manner (0.5 to 5.0mg/dl). Elevated CRP (but not CRP>5mg/dl) may minimize tissue damage at sites where CRP accumulates, and may modulate myocardial damage after percutaneous coronary intervention (PCI).
Methods:240 patients with acute myocardial infarction (AMI) within 6 hours of onset on admission were enrolled in this study. All patients underwent successfull PCI (TIMI flow grade 3 at the end of the procedures) and repeated coronary angiography and left ventriculography at 3 weeks. Patients were divided into 3 groups according to the levels of CRP on admission (time from AMI onset to blood sampling;3.8±1.2 hour); Group L (n=105,CRP<0.5mg/dl), Group M (n=97,0.5≤CRP≤5.0mg/dl) and Group H (n=38, CRP>5.0mg/dl). Clinical characteristics including preinfarction angina within 48 hours of onset of AMI (pre-AP), blood chemical variables, medications, angiographic findings and ejection fraction (EF) after PCI and at 3 weeks were evaluated.
Results: Maximum CK level in Group H (3121±2835 IU/l) was significantly higher than that in Group L (1145±1592) and Group M (1019±1524) (p<0.01). EF at 3 weeks was 56.0±18.7% in Group L, 57.7±17.6% in Group M and 50.8±17.4% in Group H (p<0.01). Delta EF (EF at 3 weeks minus EF after PCI) was -2.8±10.1%, 3.5±11.5% and 1.5±11.9%, respectively (p=0.06). There were no significant differences in age, medications, infarct-related lesions, the number of diseased vessels (>70% stenosis), collateral vessels and reperfusion time after the onset of AMI among 3 groups. Multivariate analysis demonstrated that CRP levels (0.5 to 5.0mg/dl) on admission (Odds ratio;2.6,95%CI;1.9-4.1;p=0.05) and pre-AP (Odds ratio;3.1;95% CI;1.9-4.5;p=0.03) were independently associated with good delta EF.
Conclusion: These data indicated that elevated CRP (0.5 to 5.0mg/dl) may modulate myocardial damage in patients with AMI underwent successful PCI.

1170-34 Increased Collagen Degradation Predicts Early Ventricular Remodelling Following Acute Myocardial Infarction

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Background: Early ventricular remodelling following myocardial infarction (AMI) is characterised by infarct expansion and is a product of the balance between collagen degradation and synthesis. Serological markers of collagen turnover may be useful in predicting those at risk of remodelling. C-propeptide for type-I collagen (PICP) and C-telopeptide for type-I collagen (CITP) are markers of collagen synthesis and degradation respectively.
Methods: 51 patients recruited with ECG criteria for thrombolysis. Plasma PICP & CITP measured on admission (O/A), 12 hours, 24 h, days 2, 3, 4 & 30. Echocardiography performed on days 4 & 30 for analysis of wall motion index (WMI) and Doppler derived mitral deceleration time (Dt) as indicators of remodelling.
Results: 23 had normal WMI, 28 abnormal WMI. Mean Dt-200ms. Both groups showed sequential increases in PICP & CITP over first 4 days. However, mean CITP O/A was higher in abnormal WMI group, 4.5 vs 3.1ng/ml (p<0.05) as was peak, 6.3 vs 4.9 (p<0.05). Conversely, PICP O/A was lower in abnormal WMI group 114 vs 144ng/ml (p<0.05), as was peak, 161 vs 193 (p=0.1). Admission CITP correlated with WMI, r = 0.53, p<0.001, predicting WMI in a multiple regression model independent of age, infarct site and creatinine. Ratio of admission CITP:PICP higher in abnormal WMI group, 1:31 vs 1:57 (p<0.01). CITP >3.2ng/ml (normal mean +2 SD) had a 74% positive predictive value for abnormal WMI, negative predictive value 65%. CITP O/A negatively correlated with Dt, r = -0.38, p<0.01. CITP >3.2 was also associated with a lower Dt - 184ms vs 223ms, p<0.05.
Conclusions: There is increased collagen synthesis and degradation following AMI. However, the balance of collagen turnover is different in patients who undergo adverse ventricular remodelling, manifested by abnormal WMI and reduced early mitral deceleration time. These patients have a relative increase in degradation coupled with a relative reduction in synthesis, altering the balance in favour of collagen breakdown. These changes occur early. Serological evidence of increased breakdown on admission is predictive of remodelling. This supports the potential role of serological markers in identifying patients at risk of remodelling.

1170-35 Diagnosis of Coronary Vasospasm by Detection of Postischemic Regional Delayed Relaxation or Diastolic Asynchrony Using Echocardiographic Evaluation With Color Kinesis

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Background: Coronary vasospasm has been diagnosed by an invasive provocative procedure during coronary arteriography. It would be useful in daily practice to have a reliable, noninvasive and safe diagnostic method for coronary vasospasm. Regional diastolic dysfunction may remain without apparent regional systolic dysfunction after transient severe myocardial ischemia. Color Kinesis (CK) has been recently developed to facilitate the echocardiographic evaluation of regional wall motion. Method: In order to determine the usefulness of this method for objective diagnosis of post-ischemic regional delayed relaxation or diastolic asynchrony in patients with coronary vasospasm, consecutive 26 patients with diagnosed coronary spastic angina (CSA) and 25 patients with chest pain syndrome (CPS), with the most recent chest symptom within 2 weeks (4±5 days), were subjected to the CK study. Coronary vasospasm was diagnosed by intracoronary acetylcholine test during coronary arteriography. Regional fractional area change during the first 30% of the left ventricular filling time in percentage of global end-diastolic area (CK-diastolic index: CKDI) was used to objectively identify diastolic endocardial motion asynchrony. Results: Delayed diastolic endocardial motion or decreased CKDI <40% (normal value: 75±10%) in at least one area was observed in 25 (96%) of CSA, whereas abnormal CKDI was noted in only 2 (8%) of CPS. The sensitivity and specificity for the diagnosis of CSA by detection of diastolic asynchrony using CKDI were 96% and 92%, respectively. The sensitivity for detecting the angina-provoking coronary artery by this method were 95%, 100%, and 89% for the left anterior descending coronary artery, the left circumflex branch and the right coronary artery, respectively. In 17 (65%) of CSA, decreased CKDI was detected in more than one vascular territory, suggesting multivessel spasm. Decreased CKDI was noted in none (0%) of CSA after a month attack-free period. Conclusion: Analysis of CK images allows identification of regional left ventricular diastolic dysfunction or wall motion asynchrony in patients with coronary vasospasm, differentiating them from patients with chest pain syndrome.