1048-90 Pregnancy Associated Plasma Protein-A Levels Are Elevated in Patients With Unstable Angina

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Background: Pregnancy-associated plasma protein A (PAPP-A), recently identified as an insulin like growth factor (IGF) binding protein proteinase, is a high molecular weight zinc binding metalloproteinase secreted by vascular smooth muscle cells. Increased PAPP-A activity leads to enhanced IGF bioactivity and may contribute to the progression of atherosclerosis. Thus, the current study was designed to test the hypothesis that circulating PAPP-A levels are elevated in patients (pts) with unstable angina (UA). **Methods**: Blood samples were taken from 333 pts undergoing cardiac catheterization at the Mayo Clinic. PAPP-A levels were analyzed using a biotin-tyramide-amplified enzyme immunoassay. UA was defined as the new onset of anginal symptoms (<6 weeks), rest pain, or post infarction angina (within 3 weeks of infarction). Control pts were those who had coronary disease and did not meet the requirements for UA or were undergoing routine cardiac catheterization for preoperative cardiac surgery such as valve repair/replacement. Thirty-two pts with UA were identified and the circulating levels of PAPP-A were compared to the remaining pts. Clinical characteristics were identified through patient interview and chart review. Coronary angiograms were reviewed for the extent of the disease, which was defined as the number of major vessels with >70% stenosis. **Results:** The study group consisted of 333 pts, 223 (67%) were males, mean age 64±11. There were no differences in the age, gender, presence of diabetes, hypertension, family history, cholesterol levels, smoking history of the pts with or without UA. The PAPP-A levels in the UA pts were significantly higher than in the pts without UA (7.1 ± 4.0 vs. 5.5 ± 3.4 mIU/L, p= 0.01, two sided p=0.036). PAPP-A levels were associated with older age (p<0.001), male gender (p=0.005) and lower levels of high-density lipoprotein (p=0.002). PAPP-A levels were not associated with the extent of the coronary artery disease. **Conclusion:** Patients with unstable angina have higher levels of circulating PAPP-A than patients without unstable angina. PAPP-A may be marker for plaque instability.

1048-91 Elevated C-Reactive Protein Levels Are Associated With Myocardial Ischemia Early in the Course of Non-ST Elevation Coronary Syndromes

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Background High plasma levels of C-reactive protein (CRP) are associated with short- or long-term ischemic complications in patients with unstable coronary artery disease. However, a possible direct relationship of plasma CRP with spontaneous myocardial ischemia early in the course of non ST elevation acute coronary syndromes (NSTACS) was not thoroughly investigated.

Methods To evaluate this issue 172 consecutive patients with NSTACS with no elevated plasma cardiac troponin T levels upon admission (cTnT<0.1 μg/dl) who underwent a 24 hour continuous 12-lead electrocardiographic (ECG) monitoring were studied. The association of plasma CRP levels upon admission with either the incidence or duration of the recorded myocardial ischemia (ST-segment shifts) was evaluated. Patients divided into three groups according to the tertiles of CRP values upon admission.

Results During 3,896 hours of continuous 12-lead ECG monitoring, 169 ST-segment shifts were recorded in 48 patients with a mean number of 3.5±2.0 shifts per patient and a mean duration of 29.8±23.8 min per episode, corresponding to a total duration of 124.4±143.8 min per patient. There was a significant gradual increased risk for either the incidence (p<0.001) or the total duration of ST-segment shifts with increasing of CRP tertiles (p=0.01). Multivariate analysis showed that CRP tertiles were independently and positively related to the occurrence of ST-segment shifts.

Conclusions High plasma levels of CRP may be associated with a higher incidence of myocardial ischemia early in the course of NSTACS, suggesting a direct relationship of inflammation in this process.

1048-92 Coronary Expression of Heat Shock Protein 60 and Serum Antibody Levels in Patients With Acute Coronary Syndrome

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Background- The production of heat shock protein (HSP) in coronary arteries provokes an autoimmune reaction with the anti-HSP antibody. We examined the relation between the instability of ischemic heart disease (IHD) and inflammatory cell infiltration and HSP expression in coronary tissues as well as the serum levels of HSP antibody. **Methods and Results-** Coronary specimens from 73 symptomatic patients (acute coronary syndrome [ACS, n=33]; stable IHD, n=40) who had undergone a coronary atherectomy were immunohistochemically tested for the expression of human and chlamydial HSP60, HSP70, CD68 (macrophages) and CD3 (T lymphocytes). Specimens from ACS patients exhibited a significantly broader area of staining for CD68, CD3, and chlamydial and human HSP60, compared with stable IHD patients (8.4±0.6% vs 2.9±0.4%, 4.2±0.3% vs 2.0±0.3%, 6.0±0.4% vs 2.4±0.3%, p<0.001, respectively, 11.3±0.9% vs 7.7±0.7%, p<0.005). A discriminant function analysis revealed that the expression of CD68 plus chlamydial and human HSP60 in the same lesions could clearly differentiate coronary specimens from ACS patients and specimens from stable IHD patients (accuracy 86.3%, F-value, 33.82). When blood samples were obtained from ACS patients (n=54) and stable IHD patients (n=520), the levels of anti-human HSP60 antibodies were significantly higher in ACS patients than in stable IHD patients (0.808±0.022 vs. 0.757±0.010, p<0.05). **Conclusions-** The coexistence of inflammatory cells and HSP60 associated with elevated serum levels of HSP60 antibodies may be related to the etiologic mechanisms of unstable plaque.

1048-93 Coagulation Activation and Long-Term Outcome in Acute Coronary Syndromes

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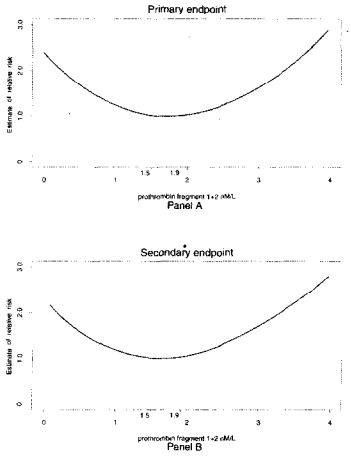
Rationale. After an episode of unstable angina or myocardial infarction, a high proportion of patients show biochemical signs of coagulation activation, expressed as persistently elevated thrombin generation, in their blood. It is not known whether this has any influence on long-term outcome.

Objective. In this prospective multicenter cohort study we assessed the relation of persistently elevated thrombin generation to outcome in patients with acute coronary syndromes. A total of 319 consecutive patients with acute coronary syndromes enrolled in GUSTO IIb trial.. Plasma prothrombin fragment 1+2 levels, an index of "in vivo" thrombin generation, was measured during the acute phase and after one, six and 12 months, and its relation to outcome was assessed during a median 29-month follow-up.

Findings: The primary end-point of cardiac death or myocardial (re)infarction occurred in 61 patients (19%). There was a U-shaped relation between plasma prothrombin fragment 1+2 levels and the risk of developing the primary end-point: intermediate levels (1.5-1.9 nmol/L) were associated with the lowest risk, whereas both higher (> 1.9 nmol/L) and lower (<1.5 nmol/L) values were associated with an increased risk (RR 1.56, 95% confidence interval 1.25-2.28; RR 1.35; 95% confidence interval 1.11-1.86; respectively)**Conclusions**: After an episode of acute coronary syndrome, both high and low levels of thrombin generation are predictors of an increased risk of an unfavourable outcome.



1048-94 IL-6 Genotypic Polymorphism and IL-6 Levels in Acute Coronary Syndromes With and Without ST-Segment Elevation

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Background: Inflammation plays an important role in the pathogenesis of acute coronary syndromes (ACS) with ST-segment elevation (STSE) and without ST-segment elevation (NSTSE). Interleukin-6 (IL6) is an inflammatory marker with prognostic value in patients with coronary artery disease (CAD) and is elevated in ACS.

Methods: We studied 68 consecutive patients (aged 61±11years, 58 males) admitted to our institution with ACS. Forty-seven patients (aged 63±8, 39 males) presented with NSTSE and 21 (aged 57±15, 19 males) with STSE ACS. Clinical, electrocardiographic and laboratory parameters were recorded. Genotypic analysis of IL6 gene polymorphism G/C-174 was performed with the PCR-SSP technique. Quantitative assessment of serum IL6 levels was performed on a blood sample drawn within 48 hours from the last episode of chest pain.

Results: The two groups had similar clinical characteristics and risk factors for CAD. Patients with STSE had a higher incidence of the C/C-174 polymorphism compared with NSTSE patients, who had a higher incidence of the G/G-174 polymorphism.

In multivariable analysis, independent markers of STSE group were the IL6 polymorphism (OR=5.4, 95% CI 1.8-16.2, p=0.003) and age (OR=0.91, 95% CI 0.84-0.97, p=0.006).

Conclusion: The genotypic polymorphism G/C-174 of IL-6 gene may be related to the type of ACS (STSE or NSTSE). This association may be due to higher IL-6 production in patients with the C allele in the IL-6 gene.