TIMP-1 and MMP-9/TIMP-3 were still higher in the lesions from unstable (0.24  $\pm$  0.07 and 1.47  $\pm$  0.39) than in those from stable (0.09  $\pm$  0.05 and 0.53  $\pm$  0.19) patients. Immunohistochemistry localized both MMP-9 and TIMPs in macrophages some of which were expressed in the fibrous cap of the ruptured plaque.

Conclusions: Upregulation of MMP-9 in the plaques from unstable coronary patients was disproportional to that of TIMPs, suggesting that active degradation of extracellular matrix persists in advanced coronary lesions particularly in those from clinically unstable natients

1042-80

## Ischemia Modified Albumin Improves the Sensitivity and Negative Predictive Value of Standard Cardiac Biomarkers for the Diagnosis of Myocardial Ischemia

<u>Saif Anwaruddin</u>, James L. Januzzi, Jr., Kent B. Lewandrowski, Elizabeth Lewandrowski, Massachusetts General Hospital, Boston, MA

**Introduction:** We examined the utility of ischemia modified albumin (IMA), both alone and with standard biomarkers of cardiac myonecrosis, for the assessment of patients with suspected myocardial ischemia in the emergency department.

Methods: 200 consecutive patients presenting to the emergency department with symptoms suggestive of myocardial ischemia were evaluated. Measurement of troponin I (Tnl), creatine kinase-MB (CK-MB), and myoglobin (Myo) were performed on each patient using a quantitative bedside point of care assay (Biosite, LaJolla, CA) as well as measurement of the IMA with the Albumin Cobalt Binding (ACB) assay (Ischemia Technologies, Denver, CO). Every case (including history, physical, electrocardiogram, stress test and angiography, if applicable) was reviewed, in a blinded fashion, by a cardiologist. A clinical diagnosis of ischemia was assigned based on these data, and then correlated to the results of the biomarker testing.

Results: 13% of the patients were judged to have myocardial ischemia by clinical data. Compared to those patients without ischemia, patients with a clinical diagnosis of ischemia were older (70.5 ± 16.9 vs 65.4 ± 16.9 years, p<0.001), and were more likely to have had a prior diagnosis of coronary artery disease (67% vs 26%, p<0.001) or prior revascularization (28% vs 10%, p=0.002). Furthermore, those patients with ischemia were more likely to have congestive heart failure (20% vs 6%, p=0.002). Utilizing a cutpoint of 90 unit/ml, we found the ACB assay to have 83% sensitivity and 30% specificity for the diagnosis of ischemia, with a negative predictive value of 92%. Among the same group of patients, the triple screen of CK-MB/Tnl/Myo had a sensitivity of only 57%. The combination of IMM/CK-MB/Tnl/Myo increased the sensitivity for the detection of ischemia to 97%, with a negative predictive value of 92%.

Conclusion: When used in patients with suspected myocardial ischemia, the ACB assay for IMA has high sensitivity and negative predictive values. Furthermore, IMA measurement improves the sensitivity of CK-MB/Tnl/Myo for the detection of acute coronary ischemia

1042-81

## Increased Expression of Myeloid Related Protein in Infiltrated Neutrophils in Coronary Atherosclerotic Plaques of Patients With Unstable Angina

<u>Shoichi Miyamoto</u>, Masaki Ikemoto, Makiko Ueda, Takahiko Naruko, Akira Itoh, Koji Hasegawa, Masatoshi Fujita, Kyoto University, Kyoto, Japan, Osaka City University, Osaka, Japan

Background: Myeloid related protein (MRP) is expressed in infiltrated neutrophils and macrophages during inflammatory reactions. The purpose of this study was to investigate: (1) whether serum MRP levels are increased in patients with unstable angina (UA). (2) whether MRP levels are upregulated in coronary atherosclerotic plagues of patients with UA. Methods: Serum MRP levels were measured using a sandwich enzyme-linked immunosorbent assay system which was newly developed in our laboratory in 53 patients [64±13 (SD) years] with UA (Braunwald's classification II and III) and 39 patients (64±11 years) with stable angina (SA), and serum C reactive protein (CRP) levels were also measured. In addition, we immunohistochemically studied the presence of MRP in directional coronary atherectomy specimens, obtained from the different 25 patients (59±10 years) with UA and 26 patients (56±12 years) with SA. The presence of MRP immunoreactivity was quantified using a computer-aided planimetry. For the identification of the cell types which stain positive for MRP, immunodouble staining was also performed. Results: There were no significant differences between the two groups regarding age, sex, risk factors, and angiographic findings. Serum MRP levels were significantly higher in patients with UA than in SA  $(3.25\pm3.08\mu g/ml\ vs.\ 0.77\pm0.31\mu g/ml,\ p<0.0001)$ . Serum CRP levels were also significantly higher in patients with UA than in SA (3.11±6.14mg/dl vs. 0.19±0.20mg/dl, p<0.005). The percentage of MRP positive area was significantly higher in patients with UA than in those with SA (18.3±14.2% vs. 1.3±2.4%, p<0.0001). In patients with UA, the immunodouble staining clearly revealed that MRP was expressed in infiltrated neutrophils and occasional macrophages. Conclusion: The measurement of serum MRP levels and the immunohistochemical approach are useful for the differentiation between UA and SA. MRP may be involved in vulnerability of coronary atherosclerotic plaques in patients with UA.

1042-82

White Blood Cell Count Predicts Higher Risk of Intermediate-Term Outcomes in Patients Stabilized After Acute Coronary Syndromes: Observations From the SYMPHONY and 2<sup>nd</sup> SYMPHONY Trials

Gustavo B.F. Oliveira, L. Kristin Newby, Lauren Lindblad, Leopoldo S. Piegas, Freek W. Verheught, Robert A. Harrington, Judith S. Hochman, Harvey D. White, Frans Van de Werf, Christopher B. Granger, Duke Clinical Research Institute, Duke University Medical Center, Durham, NC, Instituto Dante Pazzanese de Cardiologia, Sao Paulo, Brazil

Background: As a marker of inflammation, the white blood cell count (WBCc) is widely available, has WHO-defined laboratory assay standards and excellent interassay precision (coefficient of variation <3%), and has been shown to be associated with acute coronary syndromes (ACS) at presentation and clinical outcomes. Little is known about later WBCc in initially stabilized ACS patients, Methods: Our hypothesis was that WBCc would be an independent predictor of death (at 90 days and 1 year), and recurrent ischemic events at 90 days, in patients with unstable angina or myocardial infarction who were clinically stable for at least 12 hours. WBCc were collected at 3 days (median) in 9015 patients from the SYMPHONY and 2<sup>nd</sup> SYMPHONY trials. The continuous and dichotomized (median 7600/mm<sup>3</sup>) relationships of WBCc with baseline characteristics and outcomes were examined. Results: Patients with higher WBCc were younger and heavier, more often male, diabetic and current smokers, had higher estimated creatinine clearance, more congestive heart failure, but less often had prior ACS. Statins, betablockers, aspirin and percutaneous coronary intervention were used more frequently in these patients. In adjusted models, the HRs per 10-increase in continuous WBCc were 2.4 (1.35-4.28) and 1.89 (1.14-3.12) for 90-day and 1-year death, respectively (Pvalue<0.0001). Conclusion: WBCc is a strong predictor of death and recurrent ischemic events in the full spectrum of ACS patients, even after an initial stabilization.

## Outcomes by Baseline WBC Count

	WBC≥_ 7600/mm <sup>3</sup>	WBC< 7600/mm <sup>3</sup>	Hazard Ratio (95% CI)	P-value
90-day Death, %	1.9	1.1	3.0 (1.70-5.34)	0.0002
90-day Death or MI, %	7.1	5.9	1.5 (1.13-2.10)	0.007
90-day Death /MI /SRI, %	9.3	8.1	1.4 (1.05-1.82)	0.02
1-year Death, %	2.8	1.1	2.0 (1.23-3.31)	0.005

1042-83

Detection of Increased Blood Temperature in the Coronary Sinus of Patients With Coronary Artery Disease: The Impact of Temperature Measurements on Prognosis

<u>Sophia Vaina</u>, Konstantinos Toutouzas, John Mitropoulos, Eleftherios Tsiamis, Christos Pitsavos, Harissios Boudoulas, Christodoulos Stefanadis, Hippokration Hospital, Athens, Greece

Background: Widespread inflammation is observed in patients (pts) with coronary artery disease (CAD), possibly resulting in increased temperature in the coronary sinus (CS) blood. Our study aimed to test whether increased CS blood temperature in pts with CAD is related to prognosis. Methods: We enrolled 47 pts undergoing coronary angiography, for evaluation of recent onset of chest pain. Temperature measurements were performed by a CS thermography catheter (Medispes, ZWG, Switzerland), previously validated, As temperature difference (\Delta T) was designated the difference between CS and right atrium (RA) blood temperature. Study's end-points were: recurrent angina, myocardial infarction (MI) and cardiac death. Mean follow-up period was 8.7±3 months. Results: The mean blood temperature was lower in the RA compared to the CS (38.07±0.3 vs.38.28±0.4°C,p<0.001). During follow-up 2 pts suffered from MI, 1 died after coronary artery bypass surgery and 6 had a repeat revascularization procedure. The incidence of adverse cardiac events in pts with  $\Delta T$ >0.25°C was 34.78% and in pts with  $\Delta T$ <0.25°C was 4.16%(p<0.01). The relative risk of adverse cardiac events in pts with  $\Delta T > 0.25$ °C was significantly increased (RR = 8.36,p<0.05). A Cox survival plot stratified for the cutoff point showed a clear relationship between  $\Delta T$  and event-free survival (Figure). Conclusions: This study suggests, that increased blood temperature in the CS is a predictor for adverse cardiac events in a mid-term follow-up period in pts with CAD.

