ACC.12
61st Annual Scientific Session & Expo
ACC-i2 with TCT innovation in intervention

E395
JACC March 27, 2012
Volume 59, Issue 13

Acute Coronary Syndromes

AN AGGREGATE OF PATHWAY-RELATED BIOMARKERS PREDICT RISK OF ACUTE MYOCARDIAL INFARCTION AND DEATH

ACC Moderated Poster Contributions
McCormick Place South, Hall A
Sunday, March 25, 2012, 9:30 a.m.-10:30 a.m.

Session Title: Acute Coronary Syndromes: Clinical III
Abstract Category: 5. Acute Coronary Syndromes: Clinical
Presentation Number: 1167-177

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Introduction: Activation of diverse pathophysiologic processes that include thrombotic, inflammatory, and immune pathways contribute to plaque rupture and adverse outcomes in CAD. We hypothesized that an aggregate biomarker risk score comprised of C-reactive protein (CRP), fibrin degradation products (FDP), cytomegalovirus (CMV) antibody, and Heat Shock Protein 70 (HSP70) would improve future risk assessment of adverse events in subjects with risk factors for, or with established CAD.

Methods: 3,763 consecutive patients (60% with CAD; = 50% minimum stenosis in ≥1 artery) admitted for cardiac catheterization were enrolled in the Emory Biobank and followed for adverse cardiovascular outcomes over 2.5 years. Those with acute myocardial infarction (MI) and transplants were excluded. Serum biomarkers were measured using ELISA. Cox proportional hazard survival analyses and receiver operator statistics were performed with models adjusted for age, BMI, sex, race, smoking, diabetes, hypertension, and coronary severity score. Data were analyzed as continuous variables and with cut points.

Results: Preliminary analyses in a 1500 subject cohort revealed CRP, HSP70 and FDP significantly predicted outcome of death and MI. Definitive analyses were performed in 3550 subjects; hazard ratios (HRs) were calculated for two specific clinical situations: 1) subjects being evaluated for possible CAD; 2) those with angiographically documented CAD. In subgroup 2, HR for death and MI was: CRP ≥3.0 mg/L =1.48; HSP70 >0 =2.51; FDP ≥1.0 µg/ml =1.71 (p for each: <0.0001). For aggregate analyses: HR = 2.29 for 1 biomarker positive; 3.52 for 2 biomarkers; and 6.45 for 3 biomarkers (p for each: <0.0001). Annualized risk of death and MI was 18% in those with 3 positive biomarkers (4% of subgroup) compared to 2% in those with no positive biomarkers (35% of subgroup). For subgroup 2, the C-Statistic of 0.64 for a model based on traditional risk factors was improved to 0.74 (p<0.0001) with addition of the 3 biomarkers. Results were similar for subgroup 1.

Conclusions: An aggregate score based on serum levels of CRP, FDP and HSP70 is a strong predictor of future risk of death and MI in patients at risk of CAD and those with known CAD.