

**INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN (IGFBP) 2: A
NOVEL METABOLIC BIOMARKER STRONGLY PREDICTIVE OF
FUTURE CARDIOVASCULAR EVENTS**

Svati Hasmukh Shah, Jie-Lena Sun, Karen Pieper, Carol Haynes, Michael Muehlbauer, James R. Bain, Elizabeth R. Hauser, William E. Kraus, Christopher B. Newgard, Christopher B. Granger, Robert M. Califf, and L. Kristin Newby
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 MYOCARDIAL ISCHEMIA AND INFARCTION

INSULIN-LIKE GROWTH FACTOR BINDING PROTEIN (IGFBP) 2: A NOVEL METABOLIC BIOMARKER STRONGLY PREDICTIVE OF FUTURE CARDIOVASCULAR EVENTS

ACC Oral Contributions

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Monday, March 15, 2010, 2:15 p.m.-2:30 p.m.

Session Title: Novel Biomarkers and New Applications of Existing Tools with Practical Implications

Abstract Category: Unstable Ischemic Syndrome/Long-Term Outcome

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Background: Many cardiovascular risk factors are metabolic. As part of the MURDOCK Cardiovascular genomics study, we hypothesized that novel metabolic biomarkers would add to standard clinical predictors of future cardiovascular events in patients undergoing evaluation for CAD.

Methods: Consecutive patients (N=2002) undergoing cardiac catheterization at Duke University Medical Center formed the base population. Clinical and procedural data and longitudinal follow-up were collected through the Duke Databank for Cardiovascular Disease. Conventional assays were used for measurement of 11 metabolic biomarkers (adiponectin, AgRP, ghrelin, HGH, IGF1, insulin, leptin, PYY, IGFBP1, IGFBP2, and IGFBP3) in fasting plasma samples. Multivariable Cox proportional hazards modeling was used to assess the independent relationships between biomarker levels and time to death and time to death or myocardial infarction (MI), adjusting for previously identified clinical predictors of these events from a validated multivariable model.

Results: Over a median follow-up of 3.1 years, there were 232 deaths and 294 death or MI events. Most metabolic markers predicted cardiovascular events in univariable analyses for both death and death or MI ($p < 0.05$) except IGF1 and insulin for death or MI, and leptin, IGF1 and insulin for death alone. In the multivariable clinical model for death, IGFBP2 (insulin growth factor binding protein-2) levels (median 601.2, interquartile range 691.0 ng/mL) were independently associated with mortality (HR for every 100 ng/mL increase 1.02 [95% CI 1.01-1.03], $p < 0.0001$, Wald $\chi^2 = 22.0$). IGFBP2 levels were also independently associated with death or MI (HR for every 100 ng/mL increase 1.02 [95% CI 1.01-1.03], $p < 0.0001$, Wald $\chi^2 = 27.4$). In both models, IGFBP2 levels were more strongly predictive of cardiovascular events than all individual clinical variables except ejection fraction.

Conclusions: IGFBP2 levels are strongly predictive of future cardiovascular events independent from standard clinical predictors. IGFBP2 has previously been implicated in cell mobility and the metabolic syndrome. These observations provide insight into novel mechanisms of risk and risk markers.

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