

Validation of a Gender-Dependent Blood-Based Gene Expression Test for Diagnosis of Obstructive Coronary Artery Disease in Non-diabetic Patients

Meeting:

PCNA 2010

Authors:

Brenda Garrett RN, Saint Joseph's Hospital, Atlanta, Georgia, James A. Wingrove PhD, Michael R. Elashoff, PhD, Susan E. Daniels PhD, Steven Rosenberg PhD, CardioDx, Inc, Palo Alto, CA., William E. Kraus MD, Duke University School of Medicine, Durham, NC, Szilard Voros MD, Piedmont Heart Institute, Atlanta, GA, Robert S. Schwartz MD, Minneapolis Heart institute, Minneapolis, MN, and Eric J. Topol MD, Scripps Translational Research Institute, La Jolla, CA, for the PREDICT Investigators

Abstract:

Background: The current diagnosis of significant coronary artery disease (CAD) in stable chest pain patients without prior known disease follows a varied clinical path, and is especially challenging in women. Using whole blood samples from the PREDICT trial, a clinical angiographic population, a gender-specific gene expression- test, has been developed.

Methods: Total blood RNA was isolated from PAXgene[®] tubes drawn from subjects undergoing coronary angiography participating in the PREDICT multi-center trial. Cases had $\geq 50\%$ stenosis in >1 major coronary artery; controls had $< 50\%$ luminal stenosis as determined by quantitative coronary angiography. A 23 gene RT-PCR and demographics based classifier was developed from data on 640 patients in the PREDICT trial. The algorithm consists of gender and age specific gene-expression terms, gene-expression- ratios and is reported on a 1-40 scale. The performance characteristics of the test were prospectively determined in 526 non-diabetic patients (192 cases and 334 controls; 57% male)

Results: ROC analysis yielded an overall AUC = 0.70, ($p=10^{-16}$) with significant performance in both the male and female subsets, ($p < 0.001$ in each gender). The algorithm was significantly additive to clinical variables (Diamond-Forrester method (AUC 0.72 vs. 0.66, $p < 0.01$) in ROC analysis; classification of clinically defined patient disease status was also significantly improved ($p = 0.004$). At a threshold algorithm score of 14.75, the test sensitivity was 85% with a specificity of 43%. In this population, 34% of the patients had scores below this threshold.

Conclusion: This whole blood gene expression test provides clinicians with a new and novel, non-invasive diagnostic approach in assessing stable chest pain in non-diabetic patients. It incorporates age and gender in the diagnostic algorithm and appears to improve upon the personalized risk stratification for obstructive CAD.