

A Validated, Peripheral Blood Gene Expression Pattern Correlates with Coronary Arterial Plaque Burden by Quantitative Coronary Angiography and Coronary Artery Calcium Scoring

Meeting:

ACC.11

Session Title:

Genetics and Cardiovascular Outcomes

Abstract Category:

48. Genetics and Clinical Outcomes

Presentation Number:

924-4

Citation:

J. Am. Coll. Cardiol. 2011;57;E1157

Authors:

Szilard Voros, Michael R. Elashoff, Amy J. Sehnert, Hsiao D. Lieu, James A. Wingrove, Susan E. Daniels, Steven Rosenberg, Alexandra Lansky, Robert S. Schwartz, William E. Kraus, Eric J. Topol, Piedmont Heart Institute, Atlanta, GA, CardioDx Inc, Palo Alto, CA

Abstract:

Background: Coronary plaque burden can be measured indirectly by quantitative coronary angiography (QCA) and by coronary artery calcium (CAC) scoring by CT. We previously validated a real-time-PCR-based 23-gene-expression test, Corus CAD, to predict obstructive CAD using QCA ($\geq 50\%$ stenosis).

Methods: In the validation cohort of the PREDICT study (NCT 00500617), 526 patients had gene expression score and QCA-derived plaque burden available and in 79 patients (49 cases, 30 controls), CAC score also. Plaque burden was defined as the sum of occluded luminal volumes for all QCA lesions; occluded volume is calculated from lesion length and reference and minimal vessel luminal diameter, assuming a symmetrical hourglass shape. Linear regression analysis was used to evaluate relationships.

Results: In the 526 patients, there was significant correlation between gene expression score and QCA-derived plaque burden ($p=1.4 \times 10^{-8}$, $R=0.38$). In the CT subset, gene expression and CAC scores (range 0-3189; median=270) were correlated with $R=0.63$ ($p=3 \times 10^{-10}$). ROC analysis for the prediction of non-zero CAC by gene expression score showed an AUC 0.92. Both scores were significantly associated with disease burden by QCA ($R=0.57$ and 0.51 ,

respectively) and were significant in a combined linear model ($R=0.63$, $p=0.0004$ and 0.002 for CAC and gene expression). For the detection of obstructive CAD, ROC analysis of case:control status in the CT subset yielded AUCs of 0.71 , 0.70 , and 0.75 for gene expression score, CAC, and the combination, respectively (all $p<0.001$). Logistic regression with case:control status as the dependent variable and CAC and gene expression scores as independent variables showed that both were significant ($p=0.007$ and 0.002 , respectively); in a combined multivariate model, only gene expression score retained significance ($p=0.019$, CAC $p=0.134$). Extension of these studies to a larger CTA cohort of 430 patients from PREDICT will be reported.

Conclusion: Peripheral blood gene expression pattern measured by a validated test was significantly correlated to coronary plaque burden, as defined by QCA and CAC. A combined score is a better predictor, indicating they provide independent information.