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

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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 (≥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=1.4x10^-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=3x10^-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.