Validation of a Gene Expression Test Score Using Coronary Artery Calcium and CT-Angiography as Reference Standard for Plaque Burden and Stenosis Evaluation

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Abstract:

Background: We previously validated a real-time PCR 23-gene-expression test to assess obstructive CAD (≥50% stenosis by quantitative coronary angiography) in non-diabetic patients. Coronary plaque burden and stenosis can also be assessed by coronary artery calcium (CAC) and CT coronary angiography (CTA).

Methods: In the PREDICT study (NCT 00500617), a subset of patients without known CAD who had CTA with or without CAC were identified. Imaging was by institutional protocols; CAC was expressed as Agatston score. On CTA, patients were classified based on worst stenosis by local site and core-lab reads (None; Minimal [≤25%], Mild [25-49%], Moderate [50-69%], Severe [70-99%] or occluded [100%]). For case:control analyses, cases were defined as severe or occluded. Gene expression testing was done by Corus® CAD protocols in the CardioDx reference laboratory (Palo Alto, CA). ROC and correlation analyses were performed.

Results: Gene expression testing was completed on 256 patients with CAC (mean age: 62; 73% male) and 237 patients with CTA (mean age 58; 50% male). In the CAC cohort, CAC was significantly correlated with gene expression score (r=0.36, p<0.05). The gene expression score identified CAC>0 and CAC>399 in ROC analyses (AUC = 0.74 and 0.73, respectively, p<0.001). In the CTA-only cohort there were 14 cases by site read; ROC analysis for gene expression testing yielded AUC = 0.71 (p<0.001). At a previously defined gene expression score threshold of 15, sensitivity, specificity, NPV, and PPV were 93%, 44%, 99%, and 9%, respectively, with 42% of patients below this threshold. Increasing gene expression score was positively correlated with CTA-defined maximum stenosis (p<0.001), as previously seen for invasive angiography.
**Conclusion:** A validated gene expression test score significantly classified an independent set of CAC/CTA patients with respect to obstructive disease and correlated with CAC-derived plaque burden and CTA-derived stenosis.

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Iodine contrast media has not been approved for cardiovascular CT.