

## **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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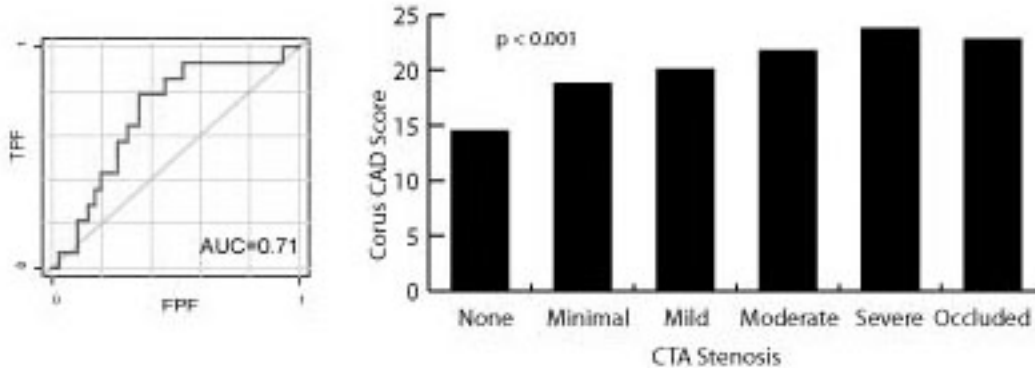
### **Abstract:**

**Background:** We previously validated a real-time PCR 23-gene-expression test to assess obstructive CAD ( $\geq 50\%$  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<sup>®</sup> 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.



**Disclosures:** **S. Voros:** Employment; Significant; Integrated Cardiovascular Research Group. Research Grant; Significant; Abbott Vascular, Abbott Laboratories, Volcano, Inc, Toshiba America Medical Systems, Cardiogenesis, Merck, Inc, CardioDx, Inc. Speaker's Bureau; Significant; Merck, Inc. Honoraria; Significant; Toshiba America Medical Systems, Marquis Imaging, HDL, Inc. **M.J. Budoff:** None. **M.R. Elashoff:** Employment; Significant; CardioDx. **A.J. Sehnert:** None. **H. Lieu:** Employment; Significant; CardioDx. **J. Wingrove:** Employment; Significant; CardioDx. **A. Johnson:** Employment; Significant; CardioDx. **S.E. Daniels:** Employment; Significant; CardioDx. **S. Rosenberg:** Employment; Significant; CardioDx. Ownership Interest; Significant; CardioDx. **R.S. Schwartz:** None. **W.E. Kraus:** None. **E.J. Topol:** None.

Iodine contrast media has not been approved for cardiovascular CT.