

Coronary Artery Plaque Burden and Stenosis by Cardiovascular CT Correlate with Peripheral Gene Expression in 614 Patients: Results from the PREDICT and COMPASS Studies

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Background: We previously validated a composite peripheral blood gene expression score (GES) based on age, sex and 23 genes measured by real-time PCR to detect obstructive coronary artery disease (CAD), using invasive coronary angiography as gold standard ($\geq 50\%$ diameter stenosis). Coronary plaque and stenosis can be assessed by computed tomography-based coronary artery calcium (CAC) and coronary CT angiography (CTA).

Methods: A total of 614 symptomatic patients with no known CAD or diabetes from the COMPASS and PREDICT studies underwent CAC and CTA using institutional protocols. CAC was expressed as Agatston score. On CTA, each of the 17 segments was graded for stenosis by core laboratory (0: None; 1: Minimal [$<25\%$], 2: Mild [$25-49\%$], 3: Moderate [$50-69\%$], 4: Severe [$70-99\%$] or 5: Occluded [100%]). Segment involvement score (SIS) tabulated the number of involved segments; segment stenosis score (SSS) summed stenosis grades across all segments. Gene expression testing was done by Corus® CAD protocols in the CardioDx reference laboratory (Palo Alto, CA). ROC and correlation analyses were performed.

Results: In the 614 patients, mean age was 57; 50% were men. GES was significantly correlated with CAC ($r=0.35$; $p<0.001$). Furthermore, GES was significantly correlated with maximum stenosis, SIS and SSS ($r=0.41$, $r=0.39$ and $r=0.34$; respectively; all $p<0.001$; Figure). Increasing stenosis by CTA was associated with higher GES ($p<0.001$ based on one-way ANOVA; Figure). In multivariable analysis, CAC and GES were independently significant (all $p<0.01$) for prediction of obstructive CAD, max % stenosis, SIS, and SSS.

Conclusions: To our knowledge, this is the largest study demonstrating that a composite gene expression score based on age, gender and 23 genes measured by real-time PCR from the peripheral circulation is associated with plaque burden and stenosis by CAC and CTA. This composite GES may be of value in the diagnosis of obstructive CAD.

