

Peripheral Blood Gene Expression Reflects Differences Between Coronary Artery Calcification and Stenosis as Assessed by Coronary Artery Calcium Scanning and Ct Angiography

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Abstract:

Background:

We previously validated a composite peripheral blood gene expression score (GES) based on age, sex and 23 genes to detect obstructive coronary artery disease (CAD), using invasive coronary angiography as gold standard ($\geq 50\%$ diameter stenosis). Plaque and stenosis can also be assessed by cardiovascular CT.

Methods:

614 symptomatic patients with no known CAD or diabetes from the COMPASS and PREDICT studies underwent CAC and CTA by institutional protocols and GES was measured according to Corus® CAD protocols in the CardioDx CLIA laboratory (Palo Alto, CA). CAC was expressed as Agatston score. For qualitative analysis, each of the 17 segments was graded for stenosis as 0: none, 1: minimal, 2: mild, 3: moderate and 4: severe; segment involvement score (SIS) was calculated by adding all segments with any plaque and segment stenosis score (SSS) by summing individual segment scores. Patients from COMPASS (N=394) also underwent quantitative measurements of calcified, high-density and low-density non-calcified plaque, as previously described. Expression levels of the 23 genes were analyzed by age and sex-adjusted logistic regression.

Results:

In the 614 patients, mean age was 57 ± 10 ; 50% were men. Overall GES was significantly correlated with CAC ($r=0.35$) and MPS ($r=0.41$), both $p < 0.001$. Individual gene expression level analysis showed that genes from the myeloid lineage, including S100A12/8, were significantly increased and T cell genes decreased with increasing MPS, whereas only innate immunity (myeloid and NK, S100A12/8, SLAMF7) genes were significantly increased with increasing calcification. In the quantitative analysis set (N=394, mean age: 55 ± 12 , 50% men) a similar pattern was observed with only neutrophil genes significantly upregulated with calcification, whereas both B and T cell genes were downregulated with increasing MPS.

Conclusions:

Gene expression and qualitative and quantitative cardiac CT data showed that peripheral blood gene expression changes for overall maximum percent stenosis and calcification differ. MPS was associated with increased expression of innate immune genes and decreased lymphocyte gene expression, while calcification was associated with increases in innate immune gene expression.