

Gene Expression Scores For CAD Are Stable Over One Year: Results From the COMPASS Trial

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Background: Peripheral whole blood cell gene expression measurements have significant promise in diagnosis and monitoring of progressive inflammatory disorders such as atherosclerosis. However, the sensitivity of gene expression to environmental and clinical factors and thus stability over time have not been evaluated, and are key to clinical utility. We previously validated a gene expression score (GES, 1-40 scale) for obstructive CAD diagnosis in non--diabetic patients in the COMPASS (NCT01117506) trial and found a threshold of 15 to have a 96% negative predictive value. We also found real--time PCR laboratory based GES variation of 0.97 score units was substantially less than population variation of 10.5. In the current study we sought to determine the frequency and magnitude of changes in this GES over 1 year.

Methods: Subjects at the 4 highest enrolling COMPASS sites were contacted approximately 1 year after their initial GES and CAD evaluation requesting a second blood draw. The GES was measured using validated Corus CAD protocols (CardioDx, Palo Alto, CA).

Results: A total of 195 (66%) of 295 eligible patients were enrolled; mean age 57, 49% female; GES was obtained on 192 (98%). Of these 17 had revascularizations or an event between index and 1 year sampling. For the remaining 175 without these procedures or events, mean scores increased from 15.9 to 17.3, corresponding to a 2.5% increase in obstructive CAD likelihood by logistic regression. Only 4 patients (2%) had score changes >10. A total of 12 patients (7%) had scores that crossed the 15 threshold between index and 1 year samples, 9 increased and 3 decreased, none which had obstructive CAD. The number of cardiovascular medications prescribed during the study period increased in 31 patients without a significant change in their GES compared to those without medication changes.

Conclusions: A validated whole blood gene expression score for obstructive CAD was relatively stable over one year, demonstrating on average only a 2.5% absolute

increase in obstructive CAD likelihood. A small fraction of patients had large score changes or had score changes which crossed the pre-specified threshold.

Reference: Thomas GS, McPherson J, Rhee B, et al. Gene Expression Scores for CAD Are Stable Over One Year: Results From the COMPASS Trial. *J Am Coll Cardiol.* 2014;63(12_S).