The Compass Trial (NCT01117506): A Prospective Multi-center, Double-blind Study Assessing A Whole Blood Gene Expression Test For The Detection Of Obstructive Coronary Artery Disease In Symptomatic Patients Referred For Myocardial Perfusion Imaging

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Abstract:
Background: First-time patients referred for elective invasive angiography (cath) often do not have obstructive CAD. We previously validated a whole-blood 23 gene expression score for obstructive CAD (≥50% stenosis by quantitative coronary angiography (QCA)) in an angiographic population. The current study evaluated gene expression testing in a lower risk population clinically referred for myocardial perfusion imaging (MPI).

Methods: COMPASS is a prospective multi-center trial of symptomatic patients without known CAD with blood samples obtained prior to MPI. Gene expression testing was performed in a CLIA approved reference laboratory (CardioDx, Palo Alto CA). Subjects with abnormal MPI were encouraged to undergo cath; those with normal MPI or who declined a clinically-indicated cath had research coronary CT angiography (CTA). Adjudication of obstructive CAD was hierarchal with QCA as primary reference standard followed by core-lab CTA. The prespecified primary endpoint was area under the curve (AUC) of gene expression score in ROC analysis with CAD cases defined as ≥50% stenosis by QCA and CTA; a secondary case analysis used 50% by QCA and 70% stenosis by CTA.

Results: From 537 patients enrolled, 431 were analyzed having completed MPI, cath or CTA, and gene expression testing (mean age 56, 48%F). There were 63 cases (15%) in the primary analysis. The study met its primary and secondary endpoints: gene expression score AUC was 0.79 (p<.001) and was superior to MPI (AUC = 0.59; p<.001, Figure). At a gene expression score threshold of 15, sensitivity and negative predictive value (NPV) were 89% and 97%; MPI
sensitivity and NPV were 27% and 88%. For the secondary case analysis, the gene expression AUC was also higher than MPI (0.77 vs 0.64, p<0.01)

**Conclusions:** Gene expression testing can assess obstructive CAD in a population referred for MPI and appears superior to MPI in diagnosing obstructive CAD (p<.001) in a low disease prevalence population.

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