

Highlights of the COMPASS Study

CORUS[®] CAD

A Blood-Based Gene Expression Test for Obstructive
Coronary Artery Disease Tested in Symptomatic
Nondiabetic Patients Referred for Myocardial
Perfusion Imaging: The COMPASS Study

Thomas GS, Voros S, McPherson JA, et al.
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ClinicalTrials.gov Identifier: NCT01117506



CARDIODX[®]

Highlights of the COMPASS Study¹

COMPASS STUDY OVERVIEW

(Coronary Obstruction Detection by Molecular Personalized Gene Expression)

The COMPASS study was designed to provide additional independent clinical validation of the Corus[®] CAD test in a real-world patient population presenting with symptoms suggestive of obstructive coronary artery disease (CAD)* and referred for myocardial perfusion imaging (MPI), a common noninvasive test for CAD. The study builds on the results of the previous PREDICT clinical validation study, assessing the Corus CAD test earlier in the diagnostic algorithm to determine the accuracy of the test in its ability to help clinicians rule out obstructive CAD in stable, symptomatic patients.

COMPASS STUDY SYNOPSIS

- Analysis cohort comprised of 431 nondiabetic patients with non-acute typical or atypical symptoms suggestive of CAD referred for MPI; exclusion criteria included history of CAD, myocardial infarction, or revascularization
- Prospective, blinded, multicenter study (19 U.S. clinical sites)
- Enrollment between May 2010 and March 2011
- Prior to MPI, Corus CAD testing was performed, with study investigators blinded to results; following MPI, patients were referred to either invasive coronary angiography (ICA) or coronary computed tomography angiography (CCTA) (SEE FIGURE 1)
- Pre-specified primary endpoint was the receiver operator characteristics analysis to evaluate the ability of the Corus CAD test to identify patients unlikely to have obstructive CAD
- Lead Investigator: Gregory Thomas, MD, MPH, University of California, Irvine

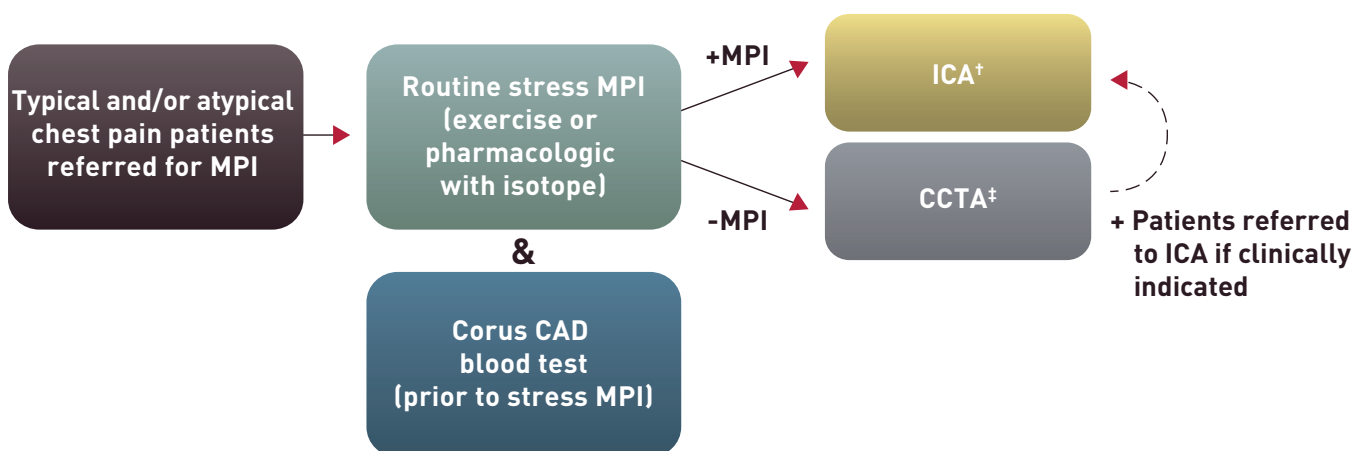


FIGURE 1: COMPASS study design

The Corus CAD test outperformed MPI in assessing the likelihood of obstructive CAD with an area under the curve (AUC) of 0.79 compared to MPI site and core-lab read AUCs of 0.59 and 0.63, respectively ($p < 0.001$).¹ The COMPASS results were consistent with earlier findings from the PREDICT multicenter U.S. validation study demonstrating that the Corus CAD score is proportional to the presence and extent of obstructive CAD.

*Obstructive CAD is defined as at least one atherosclerotic plaque causing $\geq 50\%$ luminal diameter stenosis in a major coronary artery (≥ 1.5 mm lumen diameter) as determined by invasive quantitative coronary angiography or coronary computed tomography angiography (≥ 2.0 mm lumen diameter).

†Data analyzed by quantitative coronary angiography core lab

‡Data analyzed by computed tomography angiography core lab

KEY FINDINGS

The Corus® CAD Test Helps Clinicians Accurately[§] Rule out Obstructive CAD in Symptomatic Patients

- The Corus CAD test outperformed MPI by demonstrating a significantly higher sensitivity ($p < 0.001$) and a significantly higher negative predictive value (NPV) ($p < 0.001$) for assessing the presence of obstructive CAD in the overall population of men and women referred to MPI (SEE FIGURE 2)

The Corus CAD Test Scores Correlated with the Likelihood of Obstructive and Non-obstructive CAD

- 96% of patients with low (≤ 15) Corus CAD test scores did not have obstructive CAD (SEE FIGURE 3)
- The higher the Corus CAD test score, the higher the likelihood of obstructive ($\geq 50\%$ stenosis) CAD (SEE FIGURE 3)

	Corus CAD	Site-read MPI	Core-lab MPI
Sensitivity	89%	27%	36%
NPV	96%	88%	88%

FIGURE 2: Comparison of sensitivity and NPV for the Corus CAD test and MPI. The Corus CAD test performance values are given at the pre-specified score threshold of 15.^{||} In COMPASS, 46% of patients scored at or below this threshold.

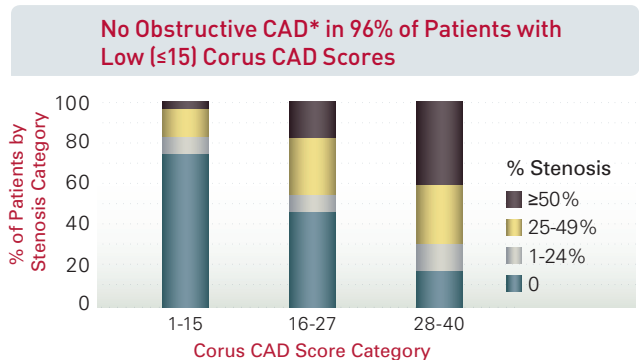


FIGURE 3: Relationship between coronary artery stenosis and Corus CAD score

The Corus CAD Test is an Accurate[§] and Safe Decision-making Tool Helping Clinicians to Determine Next Steps for Patient Management

- At six-month follow-up, there were 28 patients with MACE[¶] or revascularization; only one patient with a Corus CAD test score of ≤ 15 had a revascularization, resulting in an NPV of $>99\%$ for patients with scores ≤ 15
- As shown in the clinical algorithm below, based on COMPASS results, the diagnostic accuracy of the Corus CAD test would help patients avoid unnecessary noninvasive or invasive cardiac procedures (SEE FIGURE 4)
 - 46% of patients (scores ≤ 15) would not require further noninvasive diagnostic testing
 - A 29% reduction in ICA compared to use of MPI alone would occur
 - A 47% diagnostic yield at ICA compared to 35% with MPI alone would occur

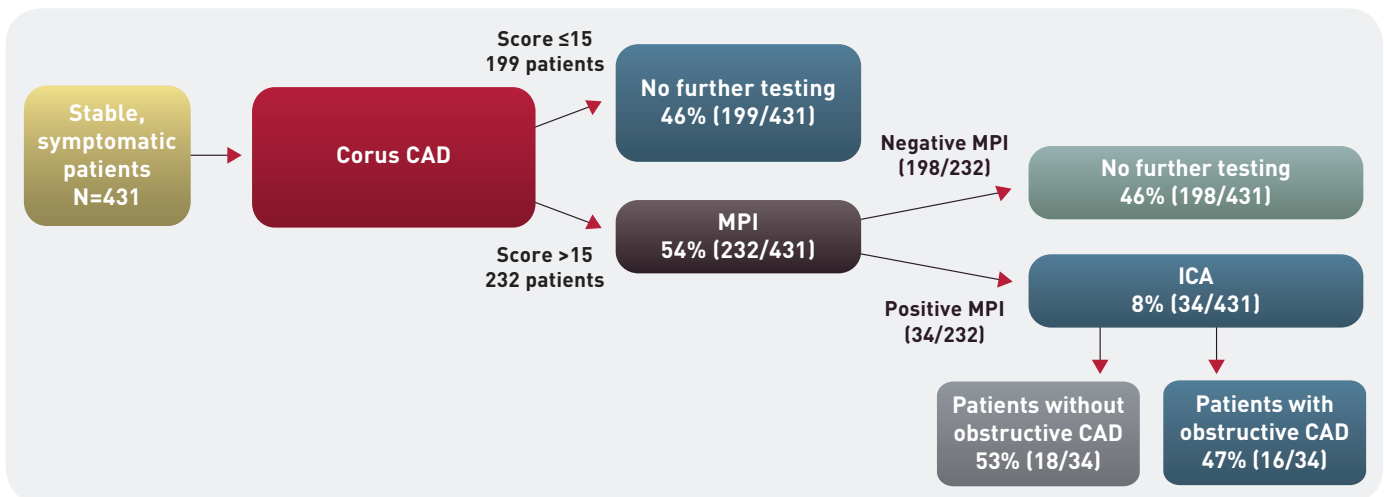


FIGURE 4: Clinical algorithm based on sequential use of the Corus CAD test and MPI. Based upon COMPASS study results.

[§]The COMPASS study found that the Corus CAD algorithm has a sensitivity of 89% and an NPV of 96% at the pre-specified threshold of 15 in the overall population of men and women referred to MPI.

^{||}Threshold of 15 includes the overall population of men and women

[¶]MACE: non-fatal MI, stroke/transient ischemia attack, and all-cause mortality

CardioDx®

CardioDx, Inc., a molecular diagnostics company specializing in cardiovascular genomics, is committed to developing clinically validated tests that empower clinicians to better tailor care to each individual patient. Strategically focused on coronary artery disease, CardioDx is committed to expanding patient access and improving healthcare quality and efficiency through the commercialization of genomic technologies.

Corus® CAD Intended Use

The Corus CAD test is a quantitative in vitro diagnostic test performed in a single laboratory, using age, sex, and the gene expression profile of cells found in peripheral blood specimens to help a clinician identify the likelihood that a patient has coronary artery stenosis of at least 50%. The test should be performed on patients with a history of chest pain, with suspected anginal equivalent to chest pain, or with a high risk of coronary artery disease (CAD), but with no known prior myocardial infarction or revascularization procedures. The test is not intended for patients with acute myocardial infarction, high-risk unstable angina, systemic infectious or systemic inflammatory conditions, diabetes, or who are currently taking steroids, immunosuppressive agents, or chemotherapeutic agents.

The test is performed on a blood specimen obtained from the patient. The test incorporates age, sex, and the expression levels of multiple genes using an algorithm with weighted gene expression levels to generate a quantitative score. The results of the test should be used by clinicians in conjunction with other tests and clinical information when assessing a patient's CAD.

The Corus CAD test is for prescription use only. The test is not intended to be used to screen for stenosis among patients who are asymptomatic and not considered at high-risk for CAD, to predict or detect response to therapy, or to help select the optimal therapy for patients.

REFERENCE:

1. Thomas GS, Voros S, McPherson JA, et al. A Blood-Based Gene Expression Test for Obstructive Coronary Artery Disease Tested in Symptomatic Nondiabetic Patients Referred for Myocardial Perfusion Imaging: The COMPASS Study. *Circ Cardiovasc Genet.* 2013;6(2):154-162.

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