

Highlights of the IMPACT-CARD Trial

CORUS^{CAD}
Gene Expression Test By CardioDx

The Clinical Utility of Gene Expression Testing on the Diagnostic Evaluation of Patients Presenting to the Cardiologist with Symptoms of Suspected Obstructive Coronary Artery Disease: Results from the IMPACT (Investigation of a Molecular Personalized Coronary Gene Expression Test on Cardiology Practice Pattern) Trial

McPherson JA, Davis K, Yau M, et al.
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CARDIODX[®]

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IMPACT-CARD TRIAL OVERVIEW

(Investigation of a Molecular Personalized Coronary Gene Expression Test on Cardiology Practice Pattern) Trial

Each year approximately 10,000 patients per day present to primary care providers in the U.S. with symptoms suggestive of obstructive coronary artery disease (CAD)^{2,3}. Careful patient evaluation based on clinical factors and non-invasive imaging are utilized to determine the presence of obstructive CAD. Non-invasive imaging and invasive procedures carry risks from exposure to radiation and imaging agent intolerance while contributing considerable expense to the evaluation of patients. Despite the enormous burden to the healthcare system, stable coronary artery disease as the underlying cause of chest pain and related symptoms is found in only 10% of these patients.³ Assessment based on clinical factors in patients referred for advanced cardiovascular imaging has been shown to overestimate the presence of disease in patients with typical and atypical symptoms by 57% and 32% respectively.⁴ The challenge of accurately diagnosing obstructive CAD calls for a better, office-based, diagnostic approach, especially for patients referred to cardiology with low probability of disease, such as women and patients with atypical symptoms.

The IMPACT-CARD Trial prospectively evaluated the clinical utility of the Corus[®] CAD gene expression test in stable, nondiabetic patients referred to cardiology for evaluation of symptoms suggestive of coronary artery disease.** A total of 88 patients were enrolled to examine the cardiologists' diagnostic strategies before and after Corus CAD scores were known with 83 patients eligible for analysis. The IMPACT-CARD Trial evaluated the role of the Corus CAD test by assessing the test's ability to help identify whether or not a patient needs additional diagnostic cardiac testing, helping many patients avoid unnecessary non-invasive and invasive imaging procedures and the associated risks of exposure to radiation, imaging agent intolerance, and/or catheterization complications.

IMPACT-CARD TRIAL SYNOPSIS

- **Primary Analysis:** Measurement of the change in the diagnostic testing plan*** pre- and post-Corus CAD testing
- **Patient Population:** Nondiabetic patients with a history of chest pain, suspected anginal equivalent to chest pain, or atypical symptoms suggestive of obstructive CAD and without known prior myocardial infarction or revascularization
- **Enrollment:** 88 prospectively enrolled patients****
- **Secondary Analysis:** Assessment of patterns of change (decrease or increase) in diagnostic testing between low (≤ 15) and non-low (> 15) scoring groups*****
- **Principal Investigator:** John A. McPherson, MD, Vanderbilt University

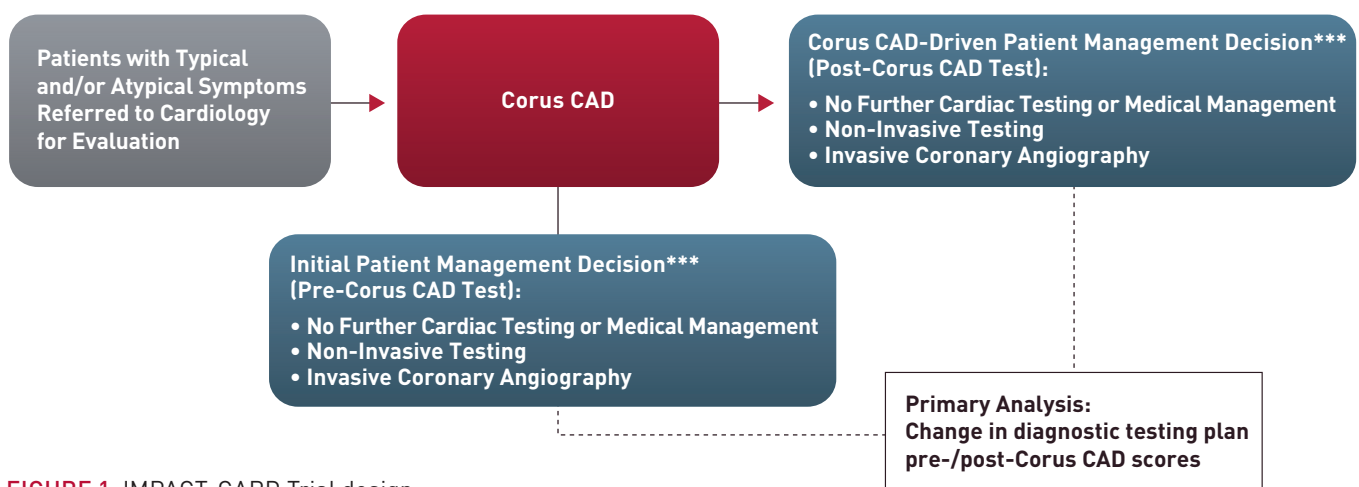


FIGURE 1: IMPACT-CARD Trial design

* ClinicalTrials.gov Identifier: NCT01251302

** Obstructive CAD defined in the trial as at least one coronary artery with $\geq 50\%$ luminal diameter stenosis as determined by quantitative coronary angiography (QCA)

*** Prospectively defined as 1) medical management or no further cardiac testing, 2) stress testing (with or without cardiac imaging) or coronary computed tomography angiography (CCTA), or 3) invasive coronary angiography (ICA)

**** 5 patients dropped out

***** Prospectively defined as low (≤ 15) or non-low (> 15)

KEY FINDINGS

Integrating Corus® CAD early in the assessment of symptomatic patients for obstructive CAD influences clinical decision making and helps identify whether or not patients need further cardiac evaluation

- Use of Corus CAD resulted in a clinically relevant, statistically significant change in non-invasive and invasive downstream cardiac testing[†]
- Following Corus CAD testing, cardiologists modified their diagnostic testing strategy in 58% of patients ($p < 0.001$) (SEE FIGURE 2)

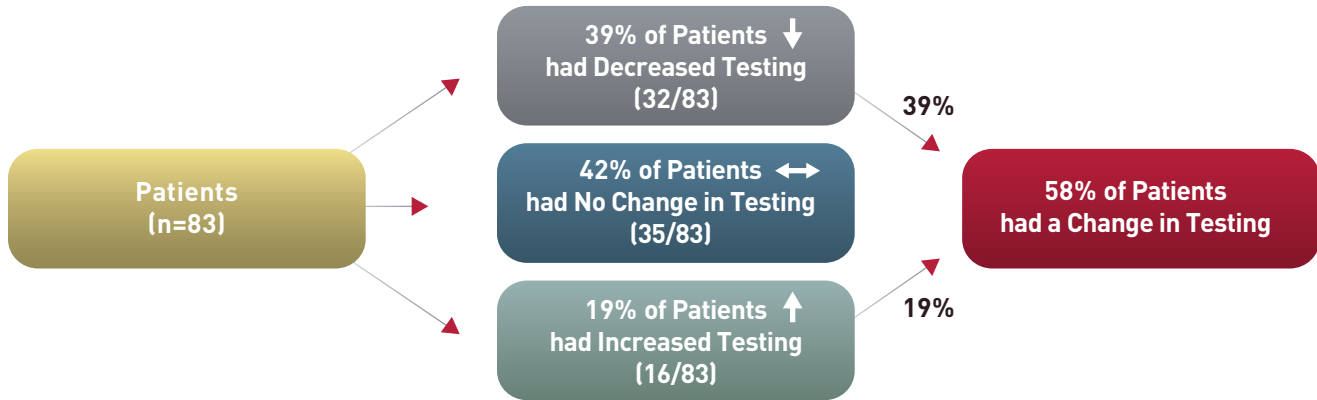


FIGURE 2: Change in cardiologists' diagnostic testing strategy post-Corus CAD testing

Corus CAD Scores Impact the Efficiency of the CAD Evaluation

- Among the prospectively enrolled patients with a change in diagnostic testing (n=48):
 - 91% (29/32) of patients with decreased^{||} diagnostic testing had low (≤ 15) Corus CAD scores
 - 100% (16/16) of patients with increased[¶] diagnostic testing had non-low (> 15) Corus CAD scores

	Corus CAD Score ≤ 15	Corus CAD Score > 15
Patients with Decreased Testing	91% (29/32)	9% (3/32)
Patients with Increased Testing	0% (0/16)	100% (16/16)

FIGURE 3: Change in diagnostic testing based on low (≤ 15) and non-low (> 15) Corus CAD scores

Corus CAD Simplifies the Diagnostic Workup of Patients With Symptoms Suggestive of Obstructive CAD

With a 96% NPV,[§] Corus CAD Excludes the Diagnosis of Obstructive CAD in Patients with Low (≤ 15) Corus CAD Scores

Corus CAD Helps Efficiently Exclude Cardiac Etiologies in Order to Pursue Non-Cardiac Causes

Corus CAD Demonstrated Safety with No Major Adverse Cardiovascular Events[‡] at 6-Month Follow-Up[#]

† Myocardial perfusion imaging (MPI), CCTA and/or ICA
 || Decreased testing: e.g. preliminary (MPI) vs. final (medical management) assessment; or preliminary (ICA) vs. final (MPI) assessment
 ¶ Increased testing: e.g. preliminary (medical management) vs. final (MPI) assessment; or preliminary (MPI) vs. final (ICA) assessment
 § Negative predictive value
 ‡ Major adverse cardiovascular events: death, MI (Q-wave and non-Q-wave myocardial infarction), stroke, revascularization by coronary artery bypass graft or percutaneous coronary interventions (PCI), and cardiac hospitalization
 # Patient follow-up in 78/83, (94%)

CardioDx®

CardioDx, Inc., a pioneer in the field of cardiovascular genomic diagnostics, is committed to developing clinically validated tests that empower clinicians to better tailor care to each individual patient. Strategically focused on coronary artery disease, cardiac arrhythmia and heart failure, CardioDx is poised to expand patient access and improve 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 the gene expression profile of cells found in peripheral blood specimens to be used as an aid to identify patients who are likely to have coronary artery stenosis of at least 50%. The test should be performed on patients with a history of chest pain, with suspected angina equivalent to chest pain, or with a high risk of coronary artery disease, 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, and/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 the expression levels of multiple genes using an algorithm with weighted functions to generate a quantitative score. The results of the test should be used by clinicians in conjunction with other tests and clinical information in their assessment of a patient's coronary artery disease.

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 coronary artery disease, to predict or detect response to therapy, or to help select the optimal therapy for patients.

REFERENCES:

- 1 McPherson JA, Davis K, Yau M, et al. The Clinical Utility of Gene Expression Testing on the Diagnostic Evaluation of Patients Presenting to the Cardiologist with Symptoms of Suspected Obstructive Coronary Artery Disease: Results from the IMPACT (Investigation of a Molecular Personalized Coronary Gene Expression Test on Cardiology Practice Pattern) Trial. *Crit Pathw Cardiol.* 2013;12(2):37–42.
- 2 National Ambulatory Care Survey: 2010. Centers for Disease Control.
- 3 Cayley WE. Diagnosing the Cause of Chest Pain. *Am Fam Physician.* 2005;72:2012-21.
- 4 Cheng VY, Berman DS, Rozanski A, et al. Performance of the Traditional Age, Sex, and Angina Typicality-Based Approach for Estimating Pretest Probability of Angiographically Significant Coronary Artery Disease in Patients Undergoing Coronary Computed Tomographic Angiography: Results from the Multinational Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry (CONFIRM). *Circulation.* 2011;124:2423-2432.
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