Highlights of the PREDICT Trial Gender-Specific Analysis

CORUS® CAD
Gene Expression Test By CardioDx

A Gender-Specific Blood-Based Gene Expression Score for Assessing Obstructive Coronary Artery Disease in Nondiabetic Patients: Results of the Personalized Risk Evaluation and Diagnosis in the Coronary Tree (PREDICT) Trial.

Lansky A, Elashoff MR, Ng V, et al.
American Heart Journal
September 2012;164:320-326.

CARDIODX®

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BACKGROUND OF CORUS® CAD TEST AND THE PREDICT TRIAL

Corus CAD is a blood-based gene expression test that can quickly and safely assess whether or not an individual patient's symptoms are due to obstructive coronary artery disease (CAD). Corus CAD measures the blood cell RNA levels of 23 genes that significantly correlate with obstructive CAD likelihood. Alterations in gene expression in peripheral blood cells have been shown to be sensitive to the presence and extent of obstructive CAD.[1]

In 2010, the results from the PREDICT validation trial, part of a 39-center, prospective, multi-center U.S. study designed to develop and validate a gene expression test for the assessment of obstructive CAD were published. This trial included stable nondiabetic patients who were referred for elective invasive coronary angiography (n=526)* with symptoms suggestive of CAD or were asymptomatic and at high risk for CAD.

Key findings from this trial:[2]

- Corus CAD demonstrated high sensitivity (85%) and a negative predictive value (NPV) of 83% for excluding obstructive CAD as the cause of patient's symptoms

PREDICT TRIAL GENDER-SPECIFIC ANALYSIS

Traditional noninvasive imaging, used to stratify patients appropriate for referral to invasive coronary angiography (ICA), has limitations related to variable site-dependent accuracy, high false-negative rates,[3] cost, exercise intolerance and risks related to radiation exposure and/or contrast agent effects.[4] As a result, the yield of ICA has been reported at 38% for a patient population comprised of both women and men.[5] Risk stratification is particularly challenging in women[3] due to:

- Atypical, non-specific symptoms
- Higher rates of false-negative and false-positive noninvasive cardiac test results than in men

In 2012, gender-specific results of 1160** patients enrolled in the PREDICT trial were published. Gender-specific data were utilized to compare the accuracy and added benefit of the Corus CAD gene expression score compared to traditional diagnostic methods (Framingham risk score [FRS]; Diamond-Forrester [D-F] classification; myocardial perfusion imaging [MPI]) for identification of obstructive CAD, using quantitative coronary angiography (QCA) as the gold standard.

Prevalence of Obstructive CAD Lower in Women than in Men

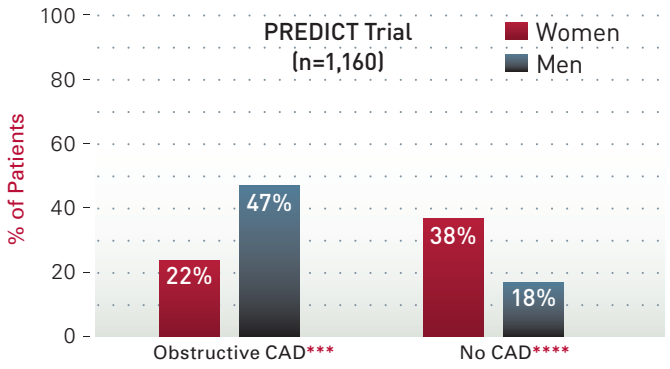

FIGURE 1: Percent of Women and Men with Obstructive CAD and No CAD as Defined by QCA

- The yield for obstructive CAD at ICA for women was less than half that of men (22% vs. 47% by QCA) **(SEE FIGURE 1)**
- The percentage of women without detectable CAD was more than twice that of men (38% vs. 18% by QCA) **(SEE FIGURE 1)**

* PREDICT validation cohort
** PREDICT development and validation cohort
*** Obstructive CAD was defined in the study as at least one atherosclerotic plaque causing ≥50% luminal diameter stenosis in a major coronary artery (≥2.0mm lumen diameter) as determined by quantitative coronary angiography (QCA)
**** No evidence of CAD was defined as <10% luminal diameter stenosis in at least 1 major coronary artery by QCA

KEY FINDINGS

Corus CAD Enhances Diagnostic Accuracy for the Assessment of Obstructive CAD in Women

- A positive MPI result was not a statistically significant indicator for obstructive CAD, maximum stenosis or total plaque burden in either women or men (SEE FIGURE 2)
- Typical chest pain symptoms (D-F classification) were an indicator of obstructive CAD in men (*P*=0.002), but were not predictive in women (*P*=NS) (SEE FIGURE 2)
- Corus CAD test performed equally well in women and men for assessment of obstructive CAD (SEE FIGURE 2)

	Obstructive Disease Odds Ratio (OR)		Maximum Stenosis (change in % stenosis)[¶]		No. of Lesions (change in number)		Total Plaque Burden (change in mm^3)	
	Women	Men	Women	Men	Women	Men	Women	Men
Chest Pain								
Atypical[§]	1.13; *P*=0.72	1.52; *P*=0.08	0.0; *P*=0.99	4.2; *P*=0.26	0.18; *P*=0.08	0.14; *P*=0.028	7.0; *P*=0.33	4.9; *P*=0.61
Typical[§]	1.52; *P*=0.20	2.0; *P*=0.002	2.1; *P*=0.61	13.1; *P*<0.001	0.13; *P*=0.22	0.25; *P*<0.001	11.9; *P*=0.13	34.6; *P*<0.001
MPI Positive[†]	1.21; *P*=0.53	1.48; *P*=0.09	2.6; *P*=0.49	4.6; *P*=0.21	-0.08; *P*=0.39	0.16; *P*=0.02	-4.7; *P*=0.46	14.0; *P*=0.14
Corus CAD[‡]	1.99; *P*<0.001	1.80; *P*<0.001	8.6; *P*<0.001	7.5; *P*<0.001	0.19; *P*<0.001	0.19; *P*<0.001	14.8; *P*<0.001	14.8; *P*=0.01

FIGURE 2: Gender-specific diagnostic accuracy of various assessment methods in identifying CAD

Statistically significant indicator in men only

Statistically significant indicator in women and men

Corus CAD Gene Expression Test is the Only Available Gender-Specific Diagnostic Test that Accurately Assesses Women and Men for Obstructive CAD.[6]

- Corus CAD scores were an independent indicator of obstructive CAD in the overall population (odds ratio [OR] 2.53, *P*=0.001) as well as in the female (OR 3.45, *P*=0.001) and the male (OR 1.99, *P*=0.001) subgroups separately (SEE FIGURE 3)
- Corus CAD test was the only significant indicator of obstructive CAD in women - MPI, clinical factors and symptoms were all non-significant (SEE FIGURE 3)

	(OR)	*P*	(OR)	*P*
	Female		**Male**	
Corus CAD Score (per 10-point increase in score)	3.449	<0.001	1.999	0.001
Typical chest pain	1.461	0.234	2.204	<0.001
Age (per 10 y)	4.665	0.174	10.018	0.001
Dyslipidemia	1.692	0.058	1.603	0.008
Hypertension	1.675	0.091	1.379	0.073
MPI positivity	0.737	0.244	0.946	0.748

FIGURE 3: Independent predictors of obstructive CAD in female and male subgroups

¶ Values reflect increase in % maximum stenosis
§ Relative to no angina
† Relative to MPI negative
‡ Values show increase for every 10-point rise in Corus CAD score, adjusted for clinical factors (FRS and D-F symptom characteristics)

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.

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