Corus CAD for Obstructive Coronary Artery Disease

MOL.TS.154.A
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Procedures addressed

The inclusion of any procedure code in this table does not imply that the code is under management or requires prior authorization. Refer to the specific Health Plan's procedure code list for management requirements.

Procedure addressed by this guideline	Procedure code
Corus CAD Gene Expression Test	81493

What is the Corus CAD test for obstructive CAD

Definition

Corus CAD is a blood-based test designed to exclude the presence of obstructive CAD in symptomatic patient.

- Heart disease is the leading cause of death for both men and women, accounting for 1 in 6 US deaths.[1] Coronary heart disease is the most common type of heart disease.[2]
- Patients with signs and symptoms of obstructive CAD, the result of a chronic inflammatory process that ultimately results in progressive luminal narrowing and acute coronary syndromes, may be evaluated with a variety of tests according to risk. Coronary angiography is the gold standard for diagnosing obstructive CAD, but it is invasive and associated with a low but finite risk of harm. Thus, coronary angiography is recommended solely for patients at high risk of CAD.[3]
- For patients initially assessed to be at low-to-intermediate risk, observation and noninvasive diagnostic methods, which may include imaging methods such as coronary computed tomography angiography (CCTA) or Myocardial Perfusion Imaging (MPI), may be recommended.
- Even noninvasive imaging methods, however, have potential risks of exposure to radiation and contrast material. Despite efforts to risk stratify patients with noninvasive testing, the subsequent yield of coronary angiography remains low. In one study of nearly 400,000 patients without known CAD undergoing elective coronary angiography, only approximately 38% were found to have obstructive CAD (if the definition of obstructive CAD was broadened to include stenosis of 50% or more in any coronary vessel, the prevalence increased to 41%).[4]

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- If symptoms are atypical, then they should be concurrent with at least one risk factor such as high cholesterol, hypertension, family history, smoking, post-menopausal state, morbid obesity, and known non-cardiac vascular disease. [4]
    - It is suggested as a first-line diagnostic modality in the ambulatory care setting ahead of noninvasive imaging to rule out obstructive CAD as the cause of a patient's symptoms.
    - Corus CAD is intended for use in adult patients with stable, non-acute presentation of symptoms suggestive of obstructive CAD who:[5]
        - are not diabetic
        - have not been diagnosed with prior myocardial infarction (MI) nor have had a previous revascularization procedure
        - are not currently taking steroids, immunosuppressive agents or chemotherapeutic agents
        - have a known history of obstructive CAD

Test information

- Corus CAD is a gene expression test that integrates the mRNA activity of 23 genes known to be involved in the development of and/or response to atherosclerosis into a single score, which can identify patients without obstructive CAD.[6]
    - Obstructive CAD is defined as:[7]
        - >50% stenosis in at least one coronary artery by Quantitative Coronary Angiography (QCA) core lab.
        - >50% QCA stenosis corresponds to 65 – 75% stenosis on clinical angiography.
- Some of these genes are sex-specific, accounting for key biological differences between men and women in the development of CAD.[6]
- A proprietary algorithm converts gene expression changes to a score that ranges from 1 to 40. The specific numeric value is translated into a percentage likelihood of the patient having obstructive CAD.[7,8]
    - Patients with scores less than or equal to 15 ("low score") have a low likelihood (<8%) of having obstructive CAD.[8]
- The test potentially eliminates 46% of patients (those with scores less than or equal to 15) from further cardiac workup due to the low likelihood of their symptoms being caused by obstructive CAD.[8]
- Test performance in the intended use population (disease prevalence of about 15%):[8]

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- Sensitivity = 89%
- Specificity = 52%
- Negative predictive value (NPV) = 96%

Guidelines and evidence

- Corus CAD is not mentioned in any of the current applicable American College of Cardiology (ACC) or American Heart Association (AHA) guidelines, policy statements or scientific statements. [9,10,11,12]
- Clinical validity studies:
  - PREDICT[7]
    - Prospective, multi-center, blinded study in 39 U.S. sites.
    - 1569 non-diabetic patients undergoing cardiac catheterization.
    - The predictive accuracy of the Corus CAD score was good, with AUC = 0.70± 0.02.
    - Corus CAD significantly improved the ability to detect underlying obstructive CAD compared with clinical assessment (based on the Diamond-Forrester [D-F] clinical risk score).
    - Test significantly improved MPI accuracy in identifying underlying obstructive CAD.
  - COMPASS[8]
    - Prospective, multi-center study in 19 U.S. sites.
    - 431 non-diabetic symptomatic patients scheduled for MPI.
    - Primary end point: Receiver-operating characteristics (ROC) analysis to discriminate less than or equal to 50% stenosis by QCA.
    - Corus CAD significantly improved the ability to detect underlying obstructive CAD compared to MPI.
    - Corus CAD outperformed clinical factors as assessed by D-F criteria and Morise score.
    - Six-month follow-up on 97% of patients showed that 27 of 28 patients with major adverse cardiovascular events (MACE) or revascularization had scores >15.
- Clinical utility studies:
  - IMPACT-CARD[13]

- Prospective, single-center study at Vanderbilt University Medical Center.
- 83 prospective non-diabetic symptomatic patients presenting to the cardiologist's office with 83 matched historical controls.
- A change in the diagnostic testing pattern pre/post Corus CAD testing was noted in 48/83 patients (58% observed vs. 10% expected change, p<0.001).
    - Low Score (less than or equal to 15): 56% decreased intensity of testing; 44% had no change.
    - High Score (>15): 52% increased intensity of testing; 39% had no change.
- 71% reduced testing rate in prospective group vs. historical cohort (p<0.001).
- Follow-up (chart review/phone call) in 180 d to ensure plan was followed & get MACE.
    - 0 patients of 161 (0.0%; 97% follow-up) had MACE.

- IMPACT-PCP[14]
    - Prospective, multi-center study of 4 practice sites.
    - 251 non-diabetic symptomatic patients presenting to the primary care physician's (PCP) office.
    - 51% of patients had a low score (less than or equal to 15).
    - A change in the diagnostic testing pattern pre/post Corus CAD testing was noted in 145/251 patients (58% observed vs. 10% expected change, p<0.001).
        - Low Score (less than or equal to 15): 60% decreased intensity of testing; 38% had no change.
        - High Score (>15): 40% increased intensity of testing; 47% had no change.
    - Follow-up (chart review/phone call) in 30 days to ensure plan was followed & record MACE.
        - 1 patient of 247 (0.4%) had "MACE" (hemorrhagic CVA 5 days after testing, later determined not to meet criteria for MACE).
- REGISTRY-1[15]
    - Prospective, multi-center chart review of non-diabetic patients with typical and/or atypical symptoms suggestive of obstructive CAD at 7 sites.
    - 342 patients presenting to PCP office.

        - Study designed for 670 patients with an interim look at 335.
        - Study stopped early due to meeting primary endpoint.
    - 49% of patients had a low score (less than or equal to 15).
    - Patients with low Corus CAD score (less than or equal to 15) had 94% decreased odds of referral versus patients with high score (> 15) ($p < 0.0001$).
        - For every 10 point decrease in score, had 14x decreased likelihood of referral to cardiology or advanced cardiac testing ($p < 0.0001$).
    - Referral rate: 6% for low scores, 70% for high scores.
    - Followed for minimum of 180 days (Avg. F/U = 267 days).
        - 21 cardiac caths, 2 from patients with low scores; 19 from patients with high scores.
        - MACE rate = 1.5% (5/342); 1 in low score group (percutaneous coronary intervention [PCI]), 3 in high score group (PCI x 2 and myocardial infarction [MI]) plus another not judged to be related to CV disease.
- Recently completed clinical trials
    - The PRESET Registry: A Registry to Evaluate Patterns of Care Associated With the Use of Corus® CAD in Real World Clinical Care Settings. ClinicalTrials.gov Identifier: NCT01677156.[16]
        - Primary outcome measures: "To describe referral patterns for cardiac care and testing within 1 month after gene expression testing. " [16]
    - Effect of Exercise Stress Testing on Peripheral Gene Expression Using CORUS™ CAD Diagnostic Test. ClinicalTrials.gov Identifier: NCT01486030.[17]
        - Primary outcome measures: "Gene expression score difference between peak exercise and baseline." [17]
    - PROspective Multicenter Imaging Study for Evaluation of Chest Pain - The PROMISE Trial. ClinicalTrials.gov Identifier: NCT01174550.[18]
        - Primary outcomes measures: "Time to primary endpoint as defined as a composite of death, myocardial infarction (MI), major complications from cardiovascular (CV) procedures or testing, and unstable angina hospitalization. The Kaplan-Meier events rates (cumulative percentage of participants with an event) were estimated for the anatomic and functional diagnostic test groups. " [18]
- While clinical utility studies have demonstrated that Corus CAD results can influence clinical decision making, there is insufficient data to demonstrate that

these decisions improve health outcomes as measured by the presence of major adverse cardiovascular events (MACE).

- The relatively small number of patients in the clinical utility trials (total n = 676) and the distribution of these patients (across less than a dozen practice sites) also raises questions about whether these results are generalizable to the entire US.

Criteria

- This test is considered investigational and/or experimental.
    - Investigational and experimental (I&E) molecular and genomic (MolGen) tests refer to assays involving chromosomes, DNA, RNA, or gene products that have insufficient data to determine the net health impact, which typically means there is insufficient data to support that a test accurately assesses the outcome of interest (analytical and clinical validity), significantly improves health outcomes (clinical utility), and/or performs better than an existing standard of care medical management option. Such tests are also not generally accepted as standard of care in the evaluation or management of a particular condition.
    - In the case of MolGen testing, FDA clearance is not a reliable standard given the number of laboratory developed tests that currently fall outside of FDA oversight and FDA clearance often does not assess clinical utility.

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