The Use of a Personalized Gene Expression Test to Improve Decision Making in the Evaluation of Patients with Suspected Coronary Artery Disease

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Abstract:
Statement of Problem or Question: The evaluation of patients (pts) with suspected coronary artery disease (CAD) is highly variable and is associated with test overutilization, high costs, and iatrogenic complications.

Objectives: The main objective of the program is to assess the clinical utility of a personalized gene expression score (GES) among pts with suspected CAD in medical decision making by primary care physicians around referral to a cardiologist. We also assessed downstream use of cardiac noninvasive and invasive testing in these referred and non-referred pts.

Description of Program: The GES is a validated quantitative diagnostic test for non-diabetic pts, measuring expression levels of 23 genes from peripheral blood to determine the likelihood of a pt having at least one vessel with $\geq$ 50% coronary artery stenosis. The GES has a negative predictive value of 96% in a recent study evaluating pts referred for myocardial perfusion imaging. We selected three community-based primary care practices for evaluation: these sites underwent education and training in the use and interpretation of the GES. Stable pts with chest pain with suspected CAD had a peripheral blood sample drawn, which was sent to a central reference lab: this lab reported the GES to the physician within 3-4 days. A total of 184 pts presented to these practices with chest pain and underwent gene expression testing from January to September 2011. We extracted information on GES, patient demographics, and chest pain symptoms as well as diagnostic tests and cardiology referrals ordered. All pts are being followed for late major adverse cardiac events.

Measures of Success: We measured percentage of low GES ($\leq15$) pts, rate of cardiology referrals, rate of noninvasive and invasive cardiac testing, and diagnostic yield at cardiac catheterization.

Findings to Date: The median age was 56 years old, and 49% were female. The cohort included 184 pts with typical and atypical symptoms (112, 61%), asymptomatic pts with $\geq 3$ risk factors (64, 35%) and asymptomatic pts with $< 3$ risk factors for CAD (8, 4%). There were 88 (48%) pts with low GES (mean=9) and 96 (52%) with non-low GES (mean=25). The primary analysis was the proportion of referrals to a cardiologist among low and non-low GES pts. A total of 47 (25%) pts were referred to cardiology: 6% (n=5) of low GES and 44% (n=42) of non-low GES. The odds ratio by logistic regression for referral among low GES pts was 0.17 (p=0.011), controlling for age,
gender, type of symptoms, and practice site. Additional cardiac testing was noted in 6% (n=5) of low GES pts and 36% (n=35) of non-low GES pts. Of note, there were 7 angiograms performed in the low (n=1) and non-low (n=6) GES pts: 2/7 pts (all non-low GES scores) were found to have clinically significant obstructive CAD.

**Key Lesson for Dissemination:** The use of the personalized gene expression test was efficient in separating patients into low (48%) and non-low (52%) GES groups. Patient with low GES were ~6 times less likely to be referred to a cardiologist. The low GES was associated with lower downstream cardiac testing effects as well. The findings suggest that this clinical practice innovation involving personalized gene expression scores may be used by primary care physicians to rule out low risk patients as well as identify appropriate patients needing further testing.

**Reference:**


**Abstract Highlights:**

- This study examined the association between the gene expression score (GES) and patient referrals to cardiology in four community-based primary care practices.
- The use of the gene expression test was helpful in separating stable, symptomatic patients with suspected CAD into low* (48%) and non-low† (52%) GES groups.
- Patients in the low GES group were 73% less likely to be referred to the cardiologist, after adjusting for clinical factors.
- A low GES was associated with significantly lower utilization of downstream cardiac testing.
- The GES may be helpful in improving the management of patients presenting with symptoms of obstructive CAD in the primary care setting.

*Low GES is defined as score ≤15
† Non-low GES is defined as score >15

Should you have any questions related to this study or abstract, please contact CardioDx Medical Affairs at medicalaffairs@cardiodx.com or 866-941-4996.