A prospective study by a group of several primary care clinics has found that CardioDx's coronary artery disease rule-out test, Corus CAD, significantly affected physician decision making in the primary care setting, changing doctors' treatment strategy for more than half of a cohort of 251 patients.

The results, published last month in the Journal of the American Board of Family Medicine, bolster a growing collection of clinical utility evidence CardioDx has continued to collect after launching and then receiving Medicare coverage for its test in 2012, including the company’s previous IMPACT-CARD trial, which looked at treatment decision making among cardiologists administering the test.

Lee Herman, first author on last month’s study and a primary care physician at Johns Creek Primary Care in Suwanee, Ga., told PGx Reporter he became interested in studying the effect of Corus CAD results on physician decision making after adopting the test into his own practice.

“I started feeling comfortable using [Corus CAD] and we found it very helpful. We were able to rule out a lot of heart disease and see signs of heart disease where we didn’t think we’d find it. And since about 10 percent of my practice is clinical trials, it made sense to get involved in clinical research on the test,” Herman said.

“The [IMPACT-CARD] trial previously helped show [Corus CAD] can be incorporated into cardiology offices. This study does that for primary care,” he added.

Corus CAD uses real-time PCR to gauge mRNA expression in 23 genes to help physicians exclude obstructive coronary artery disease as the cause of cardiac symptoms in stable non-diabetic patients. The test yields a score from one to 40. For patients who receive a score below 15, CardioDx recommends doctors not refer them to cardiologists for additional costly and more invasive procedures.

In the newly published study, IMPACT-PCP, Herman and his co-authors followed 251 patients seen at four primary care clinics in the southern US, and compared the treatment plans of physicians and other clinicians before receiving Corus CAD results to their planned and actual treatment strategies after receiving results of the assay.

All the recruited patients were tested upon enrollment, but before receiving Corus CAD results, clinicians made an initial determination of their patients’ probability of having CAD based only on clinical risk factors, symptoms, and prior ECG results if available.

The researchers recorded this initial assessment, as well as physicians' plans for further testing and intervention based on the evaluation.

Then the group asked the doctors to reconsider their determination based on the results of Corus CAD testing. On average, results were returned within two to three days, and the clinicians then completed a final assessment using the test results to...
The study compared these first and final assessments to note any changes — either upgrades or downgrades — in the physicians' plans for how to manage patients moving forward, for example with further cardiac testing, lifestyle changes, or invasive angiography.

The researchers also noted patient outcomes at 30 days after testing, and recorded whether physicians actually followed their final, post-test treatment plans.

Overall, clinicians changed their diagnostic/treatment plan for 58 percent of the patients in the study. More patients — about two thirds of the 145 for whom treatment plans were changed — saw a reduction, rather than an increase in their treatment plan post-testing.

This aligned closely, but not perfectly, with patients' Corus CAD scores. Among those whose follow-up plans were downgraded, 82 percent had low test scores, indicating low risk of CAD. For those whose follow-up plans were increased post-testing, 94 percent had an elevated score indicating high CAD risk.

According to the physicians' reported treatment plans, low Corus CAD test results caused them to plan to avoid cardiac stress testing in 48 patients for whom they originally planned it, and high test results led them to add stress testing for another 34 patients they had not originally intended to stress test.

The physicians stuck to their final treatment plans 85 percent of the time, according to the study authors. In the 30 day follow-up period, only one had an adverse cardiac event — a stroke — judged not to be related to the study protocol.

"I think this study does a good job showing that if used early in the diagnostic process, [Corus CAD] can help guide physicians to the correct diagnosis sooner and cost-effectively," Herman said.

"I understand skepticism with anything new," he added. "In the cardiology world, you have to remember, this test can be used to reduce the amount of cardiologic testing and stress tests, and consults are their bread and butter."

However, Herman noted that many cardiologists he has interacted with in his practice understand the utility of the test. "It helps funnel true disease to them," he said. "They have busy schedules, so this means they can concentrate on real disease instead of sending back panic disorder patients and reflux and such — problems that should be kept in the primary care office. And it also means we'll find a few [CAD patients] where we might not have before; for example, if you have a patient with strong anxiety symptoms, but then they have a high CAD score, that could be real disease," Herman said.

Unfortunately, Herman and his colleagues' study did not examine the association of Corus CAD scoring on long-term outcomes, so the results can only hint at whether physician's changes to their testing and treatment plan for patients might have adverse consequences.

The study also didn't analyze the potential cost savings of avoiding testing in patients deemed to be low-risk by Corus CAD who might otherwise have gone on to additional costly tests and procedures.

Corus CAD was clinically validated in two prospective, multicenter US trials, PREDICT and COMPASS. The PREDICT trial, published in the Annals of Internal Medicine in 2010, found that the Corus CAD gene expression score improved the accuracy of assessing CAD by 20 percent compared to using just the Diamond-Forrester score and by 16 percent compared to using an expanded clinical model.

The COMPASS trial data, published in Circulation: Cardiovascular Genetics in 2013, found that Corus CAD had better sensitivity than myocardial perfusion imaging (89 percent vs. 27 percent) and a better negative predictive value (96 percent vs. 88 percent) in determining a patient's likelihood of having CAD.

CardioDx, though first to market, is not alone in looking to heart disease rule-out as a target in the cardiology field, where integrating molecular diagnostics into clinical practice has been much more complicated than other disease areas like cancer.

Ruling out CAD and other diseases or incidents like heart attack in patients presenting with chest pain in various clinical settings could potentially save significant money spent on traditional workups and follow-up testing for patients that
may not need it, as well as help to alleviate logistical issues like emergency room overcrowding.

While Corus CAD is not intended for patients that require urgent evaluation, other emerging tests have targeted the emergency room setting.

Prevencio, a proteomics company working with technology licensed from the University of Pittsburgh, said last year that it was planning a multi-center validation study to support an application for US Food and Drug Administration approval of its multiplex protein test, HART, for ruling out obstructive CAD in patients presenting with chest pain in the emergency room.

At the American College of Cardiology meeting in Washington, DC, last weekend, Swedish researchers presented a large trial, published this week in the Journal of the American College of Cardiology, using measurement of the protein high-sensitivity cardiac troponin T (hs-cTnT) to rule out heart attack and reduce hospital admissions in patients presenting with chest pain in the emergency room of the Karolinska University Hospital.

The researchers found that "undetectable" hs-cTnT (levels lower than 5ng/l) in patients with no ischemic ECG changes had a negative predictive value of 99.8 percent for a heart attack within 30 days and a negative predictive value of 100 percent for death in the same time period.

In a press conference at the meeting discussing the study, one of the lead authors, Martin Holzmann, said his team believes that "up to 20 to 25 percent of all admissions to hospital because of chest pain may be prevented" using the group's method.

Molika Ashford is a GenomeWeb contributing editor and covers personalized medicine and molecular diagnostics. E-mail Molika Ashford.
could give both the frequency and phasing information because its read length covers the full length of the PCR product.

early [CRC] detection” he had seen. The FDA is not bound by advisory committee recommendations, but the agency often follows the advice.

a host of damaging consequences to global public health, patients’ lives, scientific careers, and the domestic economy,” GHTC said in the report.

based study that aims to identify the genetic and environmental determinants of immune phenotype variance and establish a path towards personalized medicine.

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