

Study 'opens the door' to troponin, diabetes link

Valerie Neff Newitt

May 2017—Clinicians and laboratories have only begun to wade into the depths of the FDA's long-awaited clearance of a new-generation, high-sensitivity cardiac troponin T (hs-cTnT) assay for rapid diagnosis of acute myocardial infarction. Roche's Elecsys TnT Gen 5 STAT assay received just such clearance in January. Yet researchers are already deep into investigations that may float new opportunities for high-sensitivity troponin T testing to the surface of medical diagnostics.

One such effort, carried out by investigators from the Johns Hopkins Welch Center for Prevention, Epidemiology and Clinical Research, demonstrated that high levels of hs-cTnT may also indicate a substantial risk factor for incident diabetes and cardiovascular disease.



Dr. Whelton

The prospective study, "High-sensitivity cardiac troponin T (hs-cTnT) as a predictor of incident diabetes in the Atherosclerosis Risk in Communities (ARIC) study" (*Diabetes Care*. 2017;40[2]:261-269), emerged from "other excellent studies out of ARIC showing a strong relationship between troponin and cardiovascular outcomes," says lead investigator Seamus Whelton, MD, MPH, Pollin cardiovascular prevention fellow at the Johns Hopkins Ciccarone Center for the Prevention of Heart Disease.

"We have known there is an overlap between diabetes and cardiovascular disease and that diabetes is a strong risk factor for CVD," he tells CAP TODAY. "We wanted to utilize hs-cTnT because the subclinical cardiac microvascular damage it represents may be at least partially due to hyperglycemia, and hs-cTnT may serve as a marker of the cumulative long-term exposure to pathophysiologic changes that occur before diabetes is diagnosed. This could be one reason why glucose-lowering trials in diabetes have not, in general, shown a reduction in cardiovascular outcome."



Dr. Lazo

Study coauthor Mariana Lazo, MD, PhD, ScM, assistant professor of medicine and epidemiology in the Johns Hopkins Division of General Internal Medicine, says she and colleagues wanted to expand the knowledge of the overlap between CVD and diabetes. "We do not yet fully understand if there is a common root cause to both. Some would argue that diabetes comes first and then cardiovascular disease develops. Others see it the other way around, believing CVD might lead to diabetes, although there has been less evidence of that. Still others consider that the two have a common root cause; perhaps they both evolve together."

In the hopes of finding an answer, the researchers hypothesized that hs-cTnT, a recognized marker of subclinical myocardial damage and predictive of CVD, might also be predictive of incident diabetes and the major cardiovascular complications associated with it. “If so, that finding might support the possibility of a marker of long-term exposure to changes in the body that occur before the onset of diabetes and CVD,” Dr. Lazo says.

The Johns Hopkins study took advantage of Atherosclerosis Risk in Communities study data and blood samples obtained from 1996 to 1998 from 8,153 study participants with no known CVD or diabetes. “The blood had been collected, frozen, and stored at a time when hs-cTnT had not yet been developed,” Dr. Lazo says.

The investigators prospectively analyzed these individuals who had been followed for a median of 13 years during the ARIC study. Over that time, 1,830 participants developed diagnosed diabetes. “As diseases in these subjects developed, we—now armed with hs-cTnT—could go back to their blood samples and run an assay,” Dr. Lazo says. Roche Diagnostics’ Elecsys TnT Gen 5 STAT, capable of detecting troponin levels as low as 3 ng/L, was used. Roche donated reagents for the study.

“We asked, ‘Is the presence of high levels of hs-cTnT also indicative of risk of diabetes in the future?’” Dr. Lazo says. “The answer was yes. That is exactly what we found.”

The researchers used Cox proportional hazards models and the Kaplan-Meier survival analysis method to examine the association between baseline hs-cTnT and the risk of incident diabetes after adjustment for traditional risk factors associated with diabetes. The study found that after that adjustment, participants with baseline hs-cTnT levels ≥ 9 ng/L had a significantly increased risk for diabetes compared with those with lower hs-cTnT levels. Dr. Lazo says the risk factor was 1.25, which she characterizes as moderately strong.

“Our study suggests,” says Dr. Whelton, “that hs-cTnT may incorporate some underlying pathophysiologic overlap between CVD and diabetes that is not captured or incorporated by other, more traditional risk factors. It may identify patients at a higher risk for both of these chronic disease states and potentially facilitate the use of resources to treat this high-risk group.”

The study also demonstrated that high-sensitivity troponin T still may have unforeseen and unexplored diagnostic boundaries. “Our work clearly supports the notion that hs-cTnT has the potential to be a marker for something other than CVD and that there may be an expanded value of testing it,” Dr. Lazo says. “Clinicians who see patients without overt diabetes but with strong risk factors, such as high BMI, and an elevated level of hs-cTnT can now advise them that they are not only at risk for CVD but also for diabetes.”

Because hs-cTnT is not approved as a screening assay, the discovery of high levels would likely be outside a clinical search for diabetes. “I don’t think these results alone will change clinical practice,” Dr. Whelton says, “but those who do find out their troponin levels are elevated would certainly benefit from knowing they are at increased risk for both CVD and diabetes.” For those patients, he says, clinicians may want to advise earlier, more intensive risk factor modification in the form of exercise and dietary and lifestyle changes.

Although more studies are needed on the possible use of hs-cTnT in diabetes prediction or screening, Dr. Whelton hopes that when troponin levels are measured for already approved purposes, clinicians will take into account the expanded picture they provide for disease states other than CVD. “The goal is always to improve risk prediction, patient care, and patient outcomes, including a reduction of CVD and diabetes,” he says. “Anytime we can share these kinds of findings, it is gratifying.”

The study has made a strong contribution to the body of knowledge surrounding the biomarker and its potential uses, in Dr. Lazo’s view, as well as the relationship between CVD and diabetes. “This opens the door to more inquiry,” she says. “People using these markers have been focused only on CVD outcomes. Now we know hs-cTnT has greater applications and forces us again to consider common routes of these two diseases that we have not yet clarified. Perhaps other disease states will emerge from the same roots and we will begin to similarly predict other diseases.”

“It takes a fair amount of time for research to be translated into changes in clinical practice,” Dr. Lazo admits, “but I can foresee that in a few years this work may help to justify expanded hs-cTnT testing for many individuals.”
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