ED, lab views on point-of-care cardiac troponin

Charna Albert

June 2021—Point-of-care cardiac troponin testing got a fresh look last December when an emergency medicine physician and a clinical chemist came together to talk about the use of both conventional POC troponin assays in a high-sensitivity era and high-sensitivity POC troponin testing when it becomes available.

“When we talk about the emergency department and the need for point-of-care testing, it gets down to one key factor,” and that’s time, said Deborah Diercks, MD, professor and chair, Department of Emergency Medicine, UT Southwestern Medical Center, in a 2020 AACC virtual annual meeting session. Proponents of POC troponin testing argue that a rapid result will shorten length of patient stay. But in practice, “we don’t have robust data showing that length of stay actually declines,” she says.

Whether POC cardiac troponin results drive admission and disposition decisions is unclear, she says, because other tests go into the workup of a chest pain patient and each takes time. “So when we think about point-of-care testing, we have to consider what else we’re going to do to that patient.” If POC troponin does not change a patient’s trajectory or length of stay, “it probably doesn’t add as much value as we hope,” she says. “There’s fear in the high-sensitivity troponin era that because it detects so much myocardial injury, we can’t easily differentiate a patient who has myocardial injury from myocardial infarction without more information that may come further down in the patient’s evaluation.”

Dr. Wu

To Alan Wu, PhD, co-presenter in the session, if the POC device has conventional sensitivity, “that’s a no-brainer. We shouldn’t be using it.”

“You might get a fast answer, but it might not be the best answer. And you may still have to wait. So you get a 15-minute answer only to wait another two hours for the next specimen,” says Dr. Wu, chief of clinical chemistry and toxicology, San Francisco General Hospital, and professor of laboratory medicine, University of California San Francisco.

“We need to segregate our existing point-of-care devices,” he says, “which are not high sensitivity, from the ones that are going to come on the market soon—I hope—that will fulfill the requirement of high sensitivity.” Without high sensitivity, “we’re not getting early rule-out and the accelerated protocols that we can with the central laboratory.” The one-hour sample in, say, a zero-, one-, and three-hour rule-out protocol may not produce a positive result using a POC assay with conventional sensitivity. “But if you send it to the lab and use a high-sensitivity assay and it is able to rule out, then you have gained two additional hours. Because for point-of-care [testing], you have to wait three to rule out, whereas with the central lab, even though it takes 45 minutes longer to get the result, you can at least rule out on that specimen.”

“Until we have [POC] high-sensitivity troponin, FDA cleared, and we have documentation of its efficacy,” he says, “I’m not a proponent of doing it.”

UT Southwestern stopped running its POC troponin test after the central laboratory switched to high-sensitivity troponin two years ago, Dr. Diercks says. “We felt we would get more value from each test and much more

information per test by having a consistent assay using a consistent platform. And the platform we chose was high-sensitivity troponin. It wasn't a big deal for us to make that change because it came in the process of a well-defined algorithm on how we were going to implement new testing with high-sensitivity troponin."

Will POC and central lab testing be used in tandem when both have high sensitivity claims? Dr. Wu foresees that to be the dilemma. "What will be key is standardization between the two assays. Even if the numbers don't match, if we have two by two concordance, that's going to be good. But the problem is these assays won't have the same antibodies. They're not going to be picking up the same subunits. I can envision a time when one is positive and the other is negative, and that's going to add to confusion."

Still, standardization will not be an issue for the majority of patients, he says. With a high-sensitivity POC test, "even if you don't have standardization with the central lab, you'll be able to rule out 60 percent of patients within one to three hours. They'll never get a central lab result, and there is no issue with standardization. And we can deal with the additional 30 or 40 percent that do have prolonged decision-making by sending it to the lab, and perhaps needing a re-baseline from their initial sample."

Proving that implementation of a high-sensitivity POC device for troponin improves outcomes will be difficult, Dr. Wu says, because a patient's survival depends on so many other aspects of care—how fast the patient gets to the catheterization lab, for example. But it should be possible to document economic outcomes, he says, noting that serial collection time frames can affect lengths of stay.

"Economically, I don't think there's any question that high sensitivity can make a big difference, particularly in the rule-out."

Dr. Wu has evaluated the central laboratory high-sensitivity assays and says they're superior to the conventional assays in terms of assay interference. "That in itself would be a good reason to switch," he says. "We have a better assay than we did before." The FDA will demand the same quality from a POC assay, he adds: "The point-of-care devices will be held to the high standard we see in the central lab."

Many hospitals today use POC troponin testing because the central lab's turnaround time exceeds one hour. How has the TAT in Dr. Wu's laboratory been improved such that the initial high-sensitivity troponin result is available before the one-hour second high-sensitivity troponin has to be drawn?

"It's a struggle," Dr. Wu says, "and you have to try to change some of your processing to put this as higher priority over something else. That's difficult to do. Other people who have other needs are going to say, 'My patient and my lab test take priority.' So it's a juggling act."

He acknowledges the advantage he has of having spent much of his career in this field and carrying a little more weight at his institution than some others in his position might at their institutions. "So it requires, even if you're not an expert, believing that this is an important thing to do and being the driver for it. It's also important to find a key opinion leader or somebody in the ED who shares the need and can help drive the need for turnaround time within hospital administration. If you don't have an advocate within the ED, then this is not going to work."

Dr. Diercks credits the team approach at UT Southwestern for their success. "Cardiology, emergency medicine, and our laboratories have been engaged and worked together. It's been terrific. It has allowed us to be innovative and implement a high-sensitivity troponin pathway."

The ideal POC high-sensitivity troponin device would have to be a handheld device, Dr. Wu says. "A benchtop reader that has to be put in some central location, even within the emergency department, I classify as near the patient, rather than point of care." It could still be whole blood and produce good results, he says, "but you have to walk the sample to the place where testing is done, as opposed to having the device moved to the bed." Some EDs lend themselves to an ED laboratory located near patient beds. But in a large ED "that doesn't work, because if you have to walk a long distance to get a sample to the ED lab, you might as well send it to the central lab."

Dr. Diercks agrees: "A test that I have to send or take somewhere doesn't provide the time savings that a true

bedside test would."

The high-sensitivity POC devices likely will be inexpensive, Dr. Wu says, "so the cost for the instrument has to be taken out of the equation. It's the cost of the consumables, the calibrations, and the labor, and those are going to be higher for point-of-care [testing], at least analytically." Real cost savings, he says, may come from changes in emergency department flow.

And those savings come from opening up an ED bed, Dr. Diercks responds. In her ED, which relies on the high-sensitivity troponin performed in the clinical laboratory, "we check a test only once if it's below the limit of detection" and the patient is low risk by a stratification score like HEART. "Then we can stop testing that patient. That's only 25 to 30 percent of patients that we see in the emergency department. Everyone else will get serial tests. And in the era of serial testing, the cost savings on throughput just aren't as great. When you balance the decrease in time of patient stay in the ED" with the analytic and POC laboratory issues Dr. Wu raises, she says, "that makes me fall right in the middle. Maybe it will be cost-effective. We just don't have enough information to make a statement."

Does Dr. Diercks see clinical utility in a conventional POC troponin device being used outside the ED—in primary care practice, for example, or ambulances? She is hesitant to endorse such testing. "As an ED physician I always get a little nervous when we do tests outside of an acute care setting. It makes people wonder why we're doing the test and what we expect to get from the result. I've heard reasonable arguments from cardiologists that having a point-of-care device in their office would make a difference, in that they could assess myocardial injury," she says. "But for the acute chest pain patient—I'd hate for them to have a test anywhere but the emergency department, especially if they're coming in with acute chest pain."

Studies have assessed conventional sensitivity POC troponin testing during ambulance transport. One such study evaluated a prehospital modified HEART pathway (PMHP) paired with in-ambulance quantitative conventional sensitivity POC troponin measurement, with the objective of improving prehospital triage (Stopyra JP, et al. *PLoS One.* 2020;15[10]:e0239460). Prospective application of the pathway and POC cardiac troponin during transport achieved high specificity and negative predictive value for 30-day major adverse cardiac events, offering "proof of concept that paramedics are able to accurately risk stratify patients with possible ACS, beyond STEMI recognition, by using a PMHP with POC cTn," the authors write.

A clinical trial reported in 2015 randomized chest pain patients presenting by ambulance to usual care or conventional POC troponin testing in-ambulance (Ezekowitz JA, et al. *J Am Heart Assoc.* 2015; 4[12]:e002859). The patients who received POC troponin testing had a slightly shorter median time from first medical contact to discharge from the ED or admission to the hospital (8.8 versus 9.1 hours).

"So a decision and test-to-brain time frame for the treating physician went down," Dr. Diercks says, though there's "no real knowledge that that's improved outcomes."

"As we look at where patients can be best cared for in the U.S.," she says, "whether they need to go to a percutaneous coronary intervention-capable setting, or a cardiac care center of excellence, having a point-of-care device may help ambulance drivers and emergency medical systems triage patients to appropriate locations, if it was known they had an elevated marker."

Dr. Wu doesn't dispute the need to get results faster and in pre-emergency department settings. "But from a clinical lab perspective, it kind of scares me," he says. The POC device would have to withstand temperature, humidity, and mechanical stressors, and personnel would have to be trained. "In the emergency room I have absolute confidence that staff can deliver an excellent result time in and time out." But elsewhere, "the training becomes a little more problematic."

Quidel received a CE mark for the TriageTrue High Sensitivity Troponin I Test and launched it in Europe in early 2019. TriageTrue is the first POC assay on the market to meet the requirements for high-sensitivity troponin testing, Bill Ferenczy, senior vice president of the Quidel cardiometabolic business unit, said in an interview. Two

criteria constitute a high-sensitivity assay, he notes: having a less than 10 percent CV at the 99th percentile of normal and the ability to measure troponin in 50 percent or more of a normal, healthy population. A completely different cartridge design was needed to make the TriageTrue system work, he says, “but this allows users to perform the testing on the existing Triage MeterPro, a portable, 1.5-pound instrument that is already widely deployed worldwide.”

Ferenczy

Quidel introduced the high-sensitivity POC test in Europe first with the intention, he says, of receiving FDA clearance and introducing the product in the U.S. after high-sensitivity troponin testing becomes better established in the U.S.

Another reason for the early launch in Europe was to enable studies that would validate the performance of the test against established central laboratory assays, Ferenczy says. A study conducted as part of the Advantageous Predictors of Acute Coronary Syndromes Evaluation (APACE), an ongoing prospective multicenter study aimed at advancing early diagnosis of MI, compared the test’s diagnostic accuracy with that of the hs-cTnT-Elecsys and hs-cTnI-Architect and found it to be at least comparable (Boeddinghaus J, et al. *J Am Coll Cardiol.* 2020;75[10]:1111–1124). And a low single cutoff concentration of less than 3 ng/L at presentation identified nearly one-half of patients as low risk with a negative predictive value of 100 percent (95 percent CI: 99.4 percent to 100 percent).

The study’s authors developed a zero-/one-hour algorithm specific to the POC hs-cTnI-TriageTrue assay. That algorithm was found to have higher efficacy for direct triage toward rule-out or rule-in than the zero-/one-hour algorithms used with the central lab tests. Based on a single POC-hs-cTnI-TriageTrue concentration at presentation, 43 percent of patients were directly ruled out or ruled in for MI without the need for serial hs-cTnI sampling, a higher proportion than for the hs-cTnT-Elecsys (25 percent) and the hs-cTnI-Architect (22 percent).

At this point, Ferenczy says, there are no data to show that the TriageTrue improves medical outcomes or that it allows patients to be discharged more quickly. But now that the APACE study has demonstrated that the assay has diagnostic accuracy comparable to that of central lab analyzers, he says, “the second stage is to measure those impacts in hospitals that have implemented the test at the point of care.”

The clinical trial in the U.S. is underway, he says, adding, “It’s a significant one given the challenging requirements.” A launch in the U.S. would come in late 2022 or early 2023, Ferenczy says. “We fully expect other diagnostic companies, including Abbott and Siemens, to develop and pursue FDA clearance for high-sensitivity troponin on their point-of-care testing platforms and view this as validation of the market need for faster results.”

In the U.S., Quidel plans to target emergency departments in large hospitals, the laboratories of small hospitals, and the freestanding EDs and urgent care centers. “We’re going into places where we’re confident they can run the test the proper way,” Ferenczy says.

Large hospitals are leading the way with high-sensitivity troponin implementation, he notes, and testing at the bedside in their busy EDs can speed up diagnosis and patient disposition. The vast majority of hospitals in the U.S. are small and will be increasingly under pressure to move to high-sensitivity troponin, Ferenczy says.

“Many of them are already running contemporary troponin tests in the laboratory using Triage or similar point-of-care instruments. These approaches are simpler and more cost-effective in these low-volume settings. TriageTrue will offer these small hospitals and similar low-volume settings such as freestanding EDs and urgent care centers a

quick and easy transition to high-sensitivity troponin on a practical, cost-effective platform." And they're likely to do it in the lab, he says, "so they won't have the complexity of training nonlaboratory personnel and everything else related to point-of-care implementation."

Charna Albert is CAP TODAY associate contributing editor.