7 pointers for POC cardiac troponin measurement

Amy Carpenter

January 2024—Seven recommendations for the use of cardiac troponin measurement at the point of care were published last year and reported in a session at the Association for Diagnostics and Laboratory Medicine annual meeting, shortly after the recommendations appeared in print (Collinson P, et al. *Clin Chem Lab Med.* 2023;61[6]:989–998).

The guidelines and recommendations are those of the International Federation of Clinical Chemistry and Laboratory Medicine's Committee on Clinical Applications of Cardiac Biomarkers (C-CB). Of the 11 authors, four are from the U.S.: Amy Saenger, PhD, and Fred Apple, PhD, of the Departments of Laboratory Medicine and Pathology at Hennepin Healthcare/HCMC in Minneapolis and the University of Minnesota, and Allan Jaffe, MD, and Brad Karon, MD, PhD, of the Department of Laboratory Medicine and Pathology at Mayo Clinic. (Dr. Jaffe is also in Mayo's Department of Cardiology, and Dr. Karon is dean of the Mayo Clinic School of Health Sciences.)

"Repeat testing is reported to be beneficial, depending on the assays and the strategy, at the one-hour or two-hour mark after that first sample was taken," said Louise Cullen, MBBS (Hon), PhD, emergency medicine staff specialist and clinical trialist, University of Queensland and Royal Brisbane and Women's Hospital in Australia, in presenting the cardiac troponin measurement recommendations last summer. "With central labs, we're not getting those results back in our hands by the 60-minute mark from the first test" before having to decide if the patient needs a second.

Many patients have repeat venipunctures for a second test they may not have needed, "because we haven't been able to access the result from the initial sample," she said. "That is incredibly important from an ED perspective."

Dr. Cullen is not a coauthor; she presented for coauthor and chemical pathologist Paul Collinson, MB, BChir, MD, of the clinical blood services and cardiology departments at St. George's University Hospitals NHS Foundation Trust, London. Dr. Cullen said she envisions that EDs within five to 10 years will move to point-of-care testing exclusively for the 90 percent of tests needed to investigate patients to get them in and out of EDs faster.

"There are a handful of specialized tests that I appreciate we'll never be able to get on a point-of-care platform," she said, "but the majority of my decision-making can be made with fairly simple and straightforward tests, and it won't be high-sensitivity cardiac troponin alone because I can't discharge someone usually just on that alone." Hemoglobin and renal function test results are important too.

It's time now, she argues, to push the integration of POC testing into the ED, "because we've got the critical demand." She understands those who say an hour isn't much time given what has to happen between sample collection and the report of the result.

"But an hour for me means I've seen three other patients and I have to come back and reorient myself to those patient results and that patient story to be able to make a disposition decision. And it's definitely impeding our flow at the moment."

The IFCC C-CB report published last year provides recommendations for appropriate use and information on analytical performance and gaps in clinical studies related to the use of POC cardiac troponin testing.

High-sensitivity cardiac troponin POC methods are the focus, "as only these are suitable for the rapid triage algorithms" discussed in the article, the authors write. Their discussion is limited to portable and benchtop instruments.

Their first recommendation says clinical studies of cardiac troponin POC testing should be structured. "In

multicenter interventional studies," the authors say, "patient pathways should be harmonized to ensure coherent approaches to clinical decision making, informed by POC results."

What's important, Dr. Cullen said, is "harmonizing the patient pathways for clinical decision-making." This is not just about one result, she said, but how to harmonize them within the system.

Recommendation No. 2 says clinical validation studies of high-sensitivity cardiac troponin measurement by POC testing require the analysis to be performed by non-laboratory trained personnel, ideally those who will use such methods, on whole blood, in the clinical environment where routine use is being contemplated.

This recommendation, Dr. Cullen said, recognizes "preanalytical errors and other things that we need to embrace when we're thinking about giving us real-life, real-world information."

"The analytical evaluation and monitoring of point-of-care testing in cardiac biomarkers should be at the same standards of the central lab assay. That should be a given," she continued. "We cannot expect substandard care for patients when we are using point-of-care platforms."

Studies have been published on the clinical validation of high-sensitivity troponin measurement by POC testing in serum and plasma, though "we're in the early stages of looking at the clinical implications," Dr. Cullen said (Pickering JW, et al. *JAMA Cardiol.* 2018;3[11]:1108–1112; SÖrensen NA, et al. *Clin Chem.* 2019;65[12]:1592–1601; Boeddinghaus J, et al. *J Am Coll Cardiol.* 2020;75[10]:1111–1124).

In a more recent study, Dr. Cullen and coauthors investigated a single high-sensitivity POC whole blood cardiac troponin I measurement (Atellica VTLi, Siemens) to rule out patients at low risk for acute myocardial infarction (Apple FS, et al. *Circulation.* 2022;146[25]:1918–1929). The assay was able to identify a substantial number of patients at very low risk for MI and who may be discharged rapidly and safely, they reported. Citing this study, the IFCC C-CB authors say in the guideline that it meets the appropriate clinical validation of high-sensitivity cardiac troponin measurement by POC testing—"demonstration of clinical equivalence with laboratory-based hs cardiac troponin measurement when tested in the real world environment."

Third, the authors recommend that cardiac troponin POC testing include an evaluation of the factors that affect POC testing devices in general.

The sample matrix, for example, is important. Some of the published studies of POC testing devices have used serum and plasma samples, Dr. Cullen said, "which is just not the sample type we are going to be using" in the ED. Among the other factors are the blood sampling method, hemolysis detection, operational complexity, quality assurance, the operating and regulatory environments, and IT requirements. "A world of things," Dr. Cullen said.

The fourth recommendation—that the evaluation of cardiac biomarker POC testing should address analytical issues specific to the analysis of cardiac troponin assays—comes back again to sample matrix studies, for example. "If we've looked at plasma or serum, how does that compare to whole blood and capillary specimens?" Dr. Cullen said. The blood sampling method, too, and the impact of ED hemolysis rates on the results given to clinicians must be considered. Hemolysis detection "may be a particular problem with cardiac troponin assays using whole blood," the authors write.

Recommendation No. 5 calls for a quality assurance system that will ensure appropriate training and use of POC high-sensitivity cardiac troponin measurement. "It should include quality control targeted at the decision levels used in routine patient management," the recommendation says, "as well as operator competency and real-time assessment of analytical performance."

"The QA is incredibly important and the one thing I worry about when we think about moving POC assays into the hands of clinicians," Dr. Cullen said, stressing the need for a robust system and appropriate training.

Quality control is targeted at the decision levels, she said. "We're not using the 99th percentiles in routine use in the ED. We're using values that are significantly lower, close to the assay's limit of detection, and it's important to

ensure we have confidence in those results."

The authors note that QC testing using third-party materials below and slightly above the 99th percentile may be challenging for some high-sensitivity cardiac troponin assays using plasma or whole blood as the matrix as there may be limitations with the third-party material.

The frequency with which QC material should be measured is a matter for debate, they say. Testing should be done to verify the performance of every different lot as acceptance testing, they write, "but the frequency thereafter can be debated." POC tests include internal quality checks and if the cartridges are robust in a range of conditions, testing could be done monthly. If the quality system in place includes paired laboratory testing, the authors add, "it could be argued that larger intervals could be used."

The authors recommend, in No. 6, that the POC system include regular automatic system checks, but if these are not done, then a weekly maintenance procedure should be done to verify instrument performance.

"As a clinician, I fear this element," Dr. Cullen said. "When we talk about point-of-care systems working collaboratively in clinical spaces, this needs to be a collaboration between the laboratory experts and the clinicians." ED physicians should not go it alone, she said, "because there are so many elements we don't know about, that we don't do well, and if not attended to appropriately and properly, will potentially lead to patient safety issues."

Last, the authors say that when several cardiac troponin assays are used within one institution, the laboratory information system should use different labels—for example, POC cardiac troponin and cardiac troponin, for requesting and reporting results, and the relevant decision cut-off values must be communicated for each assay. Diagnoses using serial samplings must be based on only one assay, they write, and a strategy is needed for divergent between-assay results.

"We need to flag that they're different," Dr. Cullen said, "and ensure people understand the differences in the sex-specific 99th percentiles and that the rapid rule-out algorithms and the delta concentrations used in serial monitoring may significantly differ. You don't want staff taking what they know and do in the ED up to the wards, for example, with a completely different assay."

The IFCC C-CB authors write: "Often the cause of a cardiac troponin increase above the sex-specific or overall 99th percentile upper reference limit from admitted patients is not clear and the delta value becomes a crucial piece in the diagnostic puzzle to differentiate acute from chronic myocardial injury. If the first blood sample were only analyzed by POC, the information concerning changing cardiac troponin concentrations will be invalid unless the same assay is used for the second sample measurement."

Dr. Cullen described the demands on the ED as "ever increasing," and said her concern is mainly increasing capacity in her ED rather than reducing costs.

No new EDs are being built in her institution, and even if they were, "we don't have the workforce" to staff them, she said. Efficiency is therefore the aim.

POC testing for cardiac troponin has received significant pushback, she noted. One common concern is that performing POC testing before the clinical assessment will lead to the cardiac troponin results driving the decision-making.

"I'd argue that's already happening," she said, "because to try to create efficiencies we are often using protocolized systems," in which cardiac troponin is ordered before a clinician sees the patient.

Amy Carpenter is CAP TODAY *senior editor.*