

High-Sensitivity Troponin I Assays: Quicker Rule-Out,* Safer Rule-In

Successful introduction of high-sensitivity troponin assays in a hospital is a team effort – and it should not be delayed. With such assays, myocardial infarctions can be detected more accurately, and low-risk patients can be identified quicker. This will reduce the pressure on emergency rooms, while at the same time increase patient safety and patient satisfaction.

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Whether or not a patient has suffered from myocardial infarction (MI) is among the most common and clinically most relevant questions that emergency physicians have to answer. And it is a tricky one: "Nine out of every ten patients who come to the emergency department with chest pain do not have a heart attack," says Professor Nicholas Mills, Chair of Cardiology at the University of Edinburgh and Consultant Interventional Cardiologist at the Royal Infirmary of Edinburgh, Scotland. Neither clinical examination nor ECG can reliably identify a 'true' MI: "Therefore, we absolutely rely on cardiac troponin as a biomarker."

With troponin testing, a paradigm shift is underway. Rapid rule-out pathways that use high-sensitivity troponin assays instead of the far less sensitive contemporary assays have been included in the guidelines,* for example of the European Society of Cardiology.¹ Rightly so, says Mills: "From an emergency physician's perspective, the advantages are clear: Decisions can be taken quicker, and we can discharge patients who are identified as low risk more safely. This will take pressure from the emergency departments, and it will free up time for evaluating severely sick patients."

"No good argument not to switch"

In spite of its obvious advantages, the uptake of the new and better assays has been somewhat slow. A recent survey among 2,000 hospitals worldwide showed that an estimated 40 percent are already using high-sensitivity troponin. But Mills expects this number to increase quickly: "Different manufacturers have developed excellent high-sensitivity troponin I tests in recent years. I am convinced that, over the next few years, we will see much more widespread adoption of high-sensitivity tests. There is really no good argument not to switch."

In Scotland, most hospitals have made the switch already. In this context, Mills recently published an independent evaluation of the novel Siemens Healthineers Atellica IM High-Sensitivity Troponin I Assay as part of the larger High-STEACS trial. The Atellica Analyzer is one of four laboratory platforms from Siemens Healthineers, with

the new high-sensitivity troponin I assay being aligned across all of these platforms. It has been available in Europe since May 2017 and received FDA clearance in July 2018. For Mills' study, cardiac troponin was measured in 1,920 patients with suspected acute coronary syndrome.

"In summary, the assay produces excellent results," says Mills. "The limit of quantification is at just around 2 ng/L. This means, we are not talking about ruling in and ruling out myocardial infarction at the 99th percentile anymore. We can move to a different approach where we use the test to its full potential." This different approach is one in which rapid rule-out pathways are implemented that use different cut-off levels for an early rule-out and an early rule-in of myocardial infarctions. And this approach makes use of serial testing only in patients in-between these thresholds.

Two thirds of patients identified as suitable for discharge

The High-STEACS pathway is a good example of a two to three hour pathway, in which myocardial infarction is ruled out without further testing in patients when cardiac troponin I concentration is below 5 ng/L at presentation – provided they don't show signs of ischemia in the ECG. This rule applies to all patients except those who present early within two hours of symptom onset, in which case cardiac troponin is retested three hours after presentation. Patients with troponin concentrations above 5 ng/L, but below the 99th percentile, are retested at three hours after presentation.

According to Mills, most Scottish hospitals have been using the High-STEACS pathway for three years now: "When you adopt the high-sensitivity troponin I assay within a High-STEACS framework, it is very effective, and identifies two thirds of all patients in the emergency department as low risk and suitable for discharge." Using the High-STEACS pathway, as Mills points out, was significantly better than using the ESC recommended zero to three hour pathway with a 99th percentile cut-off: "When we use the Siemens Healthineers Atellica assay in this manner, we have fivefold fewer high-risk patients that we would miss using the 99th percentile alone." >

Urging hospitals across the globe not to delay the introduction of high-sensitivity troponin assays: Nicholas Mills, MD, Chair of Cardiology at the University of Edinburgh and Consultant Interventional Cardiologist at the Royal Infirmary in Edinburgh, Scotland (right) and Fred Apple, Co-Director Clinical & Forensic Toxicology Laboratory Hennepin Healthcare/Hennepin County Medical Center, Principal Investigator Cardiac Biomarkers Trials Laboratory (CBTL) Hennepin Healthcare Research Institute (HHRI), Professor, Laboratory Medicine & Pathology University of Minnesota, USA (left).

*High-sensitivity troponin assays have not been cleared by the U.S. FDA for rapid rule-out testing.

Hospitals can choose best pathway

Mills' study not only evaluated the High-STEACS pathway, but also a different rapid rule-out pathway, the ESC one hour pathway, in which the Siemens Healthineers assay worked similarly well. But Mills says that the ESC one hour pathway isn't really suitable for Scottish hospitals: "It has proven impossible for us to really deliver a one-hour turnaround in any of the hospitals that

we work with, and I also don't like the idea of taking another blood test before I know the outcome of the first test."

Having different options available is an advantage, though, because it gives hospitals that plan to implement early rule-out pathways the possibility to choose the pathway that best fits the local needs: "Independently from the pathway, using very low cardiac troponin concentrations to identify low-risk patients has major potential to improve safety and decision-making in the emergency department," says Mills.



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Speaking of collaboration ...

"I think collaboration is critical when introducing a new test, whatever test it is. Establishing a new clinical care pathway that involves laboratory and clinical practice needs to be a partnership. When we introduced high-sensitivity troponin testing in our hospital, we had a group with representatives from the laboratory, from cardiology, and from emergency medicine. This allowed us to develop shared knowledge and introduce high-sensitivity testing into clinical routine really smoothly. In the end, the critical factor is identifying champions within each speciality that pass forward the knowledge. Most importantly, the laboratory team needs to take an active role. Don't just release the test and then wait for the feedback!"

Successful switches: education and teamwork

So how to successfully switch to high-sensitivity troponin assays in a hospital that is still doing it the contemporary way? For Professor Fred Apple, Co-Director Clinical & Forensic Toxicology Laboratory Hennepin Healthcare/Hennepin County Medical Center, Principal Investigator Cardiac Biomarkers Trials Laboratory (CBTL) Hennepin Healthcare Research Institute (HHRI), Professor, Laboratory Medicine & Pathology University of Minnesota, USA, successful transformation projects in cardiac troponin testing are all about education – and about teamwork: Laboratorians, cardiologists, and staff in the emergency department need to work together closely. Specific recommendations on how to implement high-sensitivity troponin testing have been listed in the recent AACC/IFCC joint publication "Clinical Laboratory Practice Recommendations for Use of Cardiac Troponin in Acute Coronary Syndrome". This publication contains a number of clear recommendations to help laboratories as well as cardiology and emergency departments to move smoothly from the old world into the new one.

High-sensitivity troponin I: "No increase in number of patients tested positively"

Importantly, Apple says, certain preconceptions should be addressed proactively. One of these preconceptions is that high-sensitivity troponin assays lead to a steep increase in the number of patients that end up in the cath lab. This preconception, according to Apple, goes back to the introduction of the first high-sensitivity troponin T assay that indeed reported a steep increase in the number of patients tested positively. The reason, however, was that the older

“contemporary” troponin T assays had missed a considerable number of patients with troponin elevations. With the recently introduced high-sensitivity troponin I assays, the situation is totally different, says Apple: “The contemporary troponin I assay of Siemens Healthineers, for example, is a very good assay. Switching to the new high-sensitivity assay will clean up the ‘noise’ and allow an early rule-out, but we won’t see a dramatic increase in the number of patients that are tested positively.”

Professor Mills can confirm this by experience: “When we introduced high-sensitivity troponin I testing, we noticed no difference at all in our day to day workflows. Depending on how low the troponin threshold was with the contemporary assay, the number of patients that are identified with an abnormal result might increase by one in 25. But this is not the sort of thing that you notice on a day to day basis.” Furthermore, Mills emphasizes, with the high-sensitivity tests, clinicians can be sure that these patients genuinely have some other sort of myocardial injury: “So they will benefit from seeing a cardiologist, whether they need an angiogram or not.”

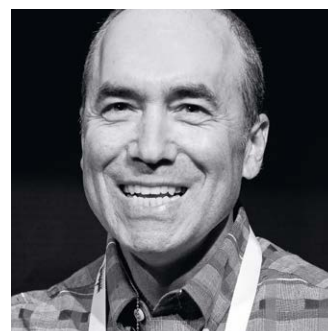
Gain in precision by sex-specific cut-offs

Another group of patients who will strongly benefit from switching to high-sensitivity troponin assays, according to Mills, is women. The reason is that high-sensitivity troponin I assays, unlike contemporary troponin assays, offer the possibility to define sex-specific cut-off values: “When we use a conventional single threshold assay, we are disadvantaging women. Adopting sex-specific criteria will increase the proportion of women identified with myocardial infarction and allow us to initiate proper treatment as early as possible.”

Given the wealth of data that exists on high-sensitivity troponin testing, Fred Apple urges hospitals all over the world not to delay introduction of the modern assays: “It makes complete sense for hospitals to embrace this new technology and get rid of the old assays quickly. Imagine you were a patient: When you show up in a hospital with chest pain, you expect an assay that is going to give you the best results.” ●

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Speaking of collaboration ...

“For applied scientists, laboratory physicians, and practicing physicians, working together is the key to success in today’s world. No one can do it alone; those days are definitely over. When I train my own laboratory medical residents and fellows, I recommend that they go out into the clinical settings and find like-minded people in the emergency medicine department and in the cardiology department – like-minded people who they can work with and who understand biomarkers. Don’t try to be the one who has all the answers and takes all the decisions. Work as part of a team. When implementing new biomarkers, we need uniform decisions among all involved disciplines in order to make the transition a success.”

¹ Also implemented in the expert consensus document of ESC, ACC, AHA and WHF: Fourth universal definition of myocardial infarction (2018)

Product availability may vary from country to country and is subject to varying regulatory requirements.

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