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# High-Sensitivity Troponin I Assays: A Breakthrough in AMI Diagnosis

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# High-Sensitivity Troponin I Assays: A Breakthrough in AMI Diagnosis

Thanks to high-sensitivity troponin I assays, new possibilities have emerged for quicker, more accurate diagnoses of myocardial infarction. We spoke to Peter Kavsak, PhD, FCACB, FACB, FCCS, Associate Professor of Pathology and Molecular Medicine at McMaster University in Hamilton, Ontario, Canada, about these high-sensitivity assays and their potential to significantly impact patient care and protocols.

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In an emergency setting, a rapid diagnosis is essential to allow patients with suspected acute myocardial infarction (AMI) to be treated faster and more successfully. For years, detection of cardiac troponin (cTn) has been the gold standard for the diagnosis in concerned patients presenting to the emergency room with chest pain. Technological advances have led to the development of next-generation troponin assays, which offer improved sensitivity and precision compared with conventional assays. This can lead to meaningful changes for patients, physicians, and hospitals, according to Peter Kavsak.

High-Sensitivity Troponin I is now available on the ADVIA Centaur System, Atellica IM Analyzer, Dimension EXL\* and Dimension Vista\* Systems

\*Not available for sale in the U.S. on the Dimension EXL and Dimension Vista Systems



Kavsak has made significant contributions in the area of cardiovascular biomarkers, in particular cardiac troponins. He was among the first to demonstrate the use of low cardiac troponins to identify patients at long-term risk of cardiovascular events and to study the use of high-sensitivity troponin assays primarily in the acute coronary syndrome setting.

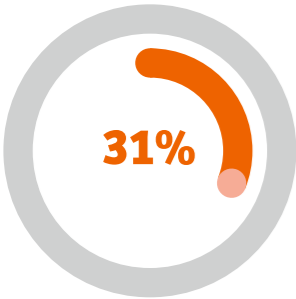
“Data suggesting the potential for new high-sensitivity cardiac troponin I testing to simplify and expedite rule-out protocols is of great interest,” says Kavsak. “A high-sensitivity assay is able to detect much lower levels of troponin and smaller changes to a patient’s troponin levels than traditional assays. This means that patients who are experiencing an AMI can be more quickly identified and treated, plus physicians can rule out the possibility of AMI more quickly in a large percentage of patients.”

High-sensitivity troponin assays have been used in countries outside of the US for several years.

Taking aim at a global killer

The greater sensitivity of the next-generation assays may well have multiple implications. Cardiovascular disease has been the leading cause of death worldwide for the last 15 years, according to the World Health Organization.[1] In 2015, an estimated 17.7 million people died from cardiovascular disease, including coronary heart disease / acute coronary syndrome (ACS) and stroke, accounting for 31 percent of all global deaths.[2]

Chest pain is a common symptom of ACS. In the U.S., chest pain is the second most common reason for presenting to the emergency room (ER).[3] According to Kavsak, the use of high-sensitivity troponin assays has the potential to change how patients with chest pain are triaged in the emergency department.



... of all global deaths are caused by cardiovascular disease.



Quicker diagnosis and treatment for patients

before: 3 – 6 h  
now: 1 – 3 h

Faster rule-in/rule-out

While there are a number of high-sensitivity assays on the market, each has unique performance characteristics that clinicians should be aware of when diagnosing a patient. For patients with suspected AMI, both professional laboratory<sup>1</sup> and clinical organizations<sup>2</sup> recommend that the cutoff to designate myocardial injury should be the 99<sup>th</sup> percentile derived from a healthy population (i.e., upper reference limit). Ideally laboratories should be able to measure this level with a coefficient of variation which reflects repeatability of measurement of at least 10 percent. To be classified as high-sensitivity assays, the majority of individuals will now have measurable levels of troponin (i.e., at least 50 percent of the healthy population will have troponin concentrations above the limit of detection of the assay).

“The research is ongoing, but these tests give greater confidence in patient results at the low end of the assay range,” Kavsak says. “Data suggests that very low levels of high-sensitivity troponin can rule out AMI with a single draw, thus eliminating the need for serial measurements.”[4]

The increase in accuracy and speed can provide multiple benefits: Patients may be diagnosed and treated quickly – in one to three hours vs. three to six. They receive earlier invasive therapy if needed, and for the majority of patients, improved assays may lead to ruling out AMI sooner.

“Patients having an AMI can be treated and admitted more quickly, and other patients can be discharged.”

Peter Kavsak, PhD  
Associate Professor of Pathology and Molecular Medicine at McMaster University in Hamilton, Ontario, Canada

Same protein, different reporting

A fellow of both the Canadian and American Academies of Clinical Biochemistry, Kavsak adds that it is imperative that clinicians understand how to appropriately interpret and respond to high-sensitivity troponin tests. “With high-sensitivity troponin assays, the same protein is measured, but the reporting is different – including shortened algorithms. It’s still troponin I. An elevation with a high-sensitivity troponin assay is an elevation of troponin. It is just presented differently.”

He explains, “The numbers will be different because these assays are validated and developed differently. We can now quantify concentrations that were previously undetectable. So, when going to high-sensitivity troponin assays, the recommendations from all professional societies to date have indicated that troponin results should be reported in whole numbers and nanograms per liter.[5] That will be a big change for some clinicians as standard assays are currently reported in nanograms per milliliter or micrograms per liter.”

Reporting high-sensitivity assay results in whole numbers can help avoid confusion and transcription mistakes. “For example, with a contemporary assay, you may have a result of 4 nanograms per milliliter, which is quite elevated; now with the high-sensitivity assay, it would be reported as 4,000 nanograms per liter. It’s important that clinicians know this distinction.”

The potential for errors can increase when very low levels are reported as nanograms per milliliter with multiple decimal places in the value. “To avoid a problem of having too many zeros, we’re advocating that people use whole numbers for these values,” says Kavsak. “It’s better to do that than to use a lot of zeros falling after the decimal point and have someone in the middle of the night miss seeing a zero and become confused and do something wrong clinically. It’s easier to communicate 7 ng/L as compared to 0.007 ng/mL.”

Accelerated pathways benefit patients

Managing patients with chest pain in the emergency room is a clinical challenge, and the primary role for troponin assays since their inception has been to diagnose patients with AMI. With improved sensitivity and specificity of troponin measurement, one benefit is increased diagnostic accuracy, which leads to accelerated clinical pathways.

“Because we are able to measure troponin in a variety of normal individuals at these very low concentrations, there is a lot of interest and work on accelerated pathways for patients with chest pain in the emergency department,” Kavsak says. “With contemporary assays, a patient might have to wait three to six hours or longer for the assay to detect abnormal levels of troponin. Because we are able to get accurate measurements of troponin at these very low levels, we are able to get shorter diagnostic pathways, within one to three hours using high-sensitivity troponin.”

Kavsak explains how this translates into peace of mind for patients and family members: “No one wants to be in an emergency room. They’re hectic places. The quicker clinicians can make a decision, the better for everyone,” Kavsak says. “Data shows the longer a stay in the ER is, the worse it is for patients.”

He adds: “Earlier decision protocols initiate quicker interventions for those who need medical intervention, and on the flip side, are useful to rule out when patients are not having an AMI.”



Challenges for adoption

High-sensitivity assays are more analytically sensitive. Kavsak explains, therefore, that “the other thing that will be apparent to clinicians caring for patients is that they will have, by and large, observed measurable troponin in a larger group of patients. A patient can have elevated troponin after running a marathon, for example.”

In the emergency setting, new cutoff values must be established and validated when using cutoffs below the 99<sup>th</sup> percentile, particularly in the U.S. when adopting new algorithms for rule-in/rule-out, analytical performance of high-sensitivity troponin assays is important. “Adoption of high-sensitivity troponin assays will require collaboration from a team – physicians, clinicians, laboratories, and hospitals,” says Kavsak.

According to Kavsak, the opportunities far outweigh the disadvantages. The introduction of high-sensitivity troponin assays to the market has resulted in new patient care approaches, including the adoption of shortened algorithms. Faster, reliable diagnostic options result in improved clinical confidence, shortened decision time, optimized allocation of resources, and most importantly better patient outcomes.[6]

He concludes: “Shorter protocols are really key to effective management of patients and healthcare resources. Shorter protocols are really only possible with high-sensitivity assays.” ●

Diana Smith is a writer specializing in medical topics. She is based in Liberty Hill, Texas, USA.

[1] Top 10 causes of death:

http://www.who.int/mediacentre/factsheets/fs310/en/ (date accessed 07/31/2017)

[2] Cardiovascular diseases (CVDs):

http://www.who.int/mediacentre/factsheets/fs317/en/ (date accessed 07/31/2017)

[3] Top 5 reasons for emergency room visits:

http://www.bidmc.org/YourHealth/Health-Notes/FirstAid/EmergencyCare/Top5ERvisits.aspx (date accessed 07/31/2017)

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<sup>1</sup> National Association of Clinical Biochemistry (Academy of the American Association for Clinical Chemistry) and the International Federation of Clinical Chemists  
<sup>2</sup> European Society of Cardiology and American College of Cardiology  
[4] Shah ASV, Anand A, Sandoval Y, et al. High-sensitivity cardiac troponin I at presentation in patients with suspected acute coronary syndrome: a cohort study. Lancet 2015; 386: 2481–8.  
[5] Apple FS, Collinson PO. IFCC Task Force on Clinical Applications of Cardiac Biomarkers. Clin Chem. 2012 Jan; 58(1):54-61.  
[6] Eggers KM, et al. European Heart Journal 2016:2417-2424  
The outcomes by Siemens’ customers described herein are based on results that were achieved in the customer’s unique setting. Since there is no “typical” hospital and many variables exist (e.g., hospital size, case mix, level of IT adoption) there can be no guarantee that other customers will achieve the same results.

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