A Multicenter Assessment of the Sensitivity and Specificity for a Single High-Sensitivity Cardiac Troponin Test at Emergency Department Presentation for Hospital Admission

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Guest: Dr. Peter Kavsak is a professor in the Department of Pathology and Molecular Medicine at McMaster University in Hamilton, Ontario, Canada.

Randye Kaye: Hello, and welcome to this edition of "JALM Talk," from the *Journal of Applied Laboratory Medicine*, a publication of the American Association for Clinical Chemistry. I'm your host, Randye Kaye.

Randye Kaye: The onset of high sensitivity troponin assays has revolutionized the management of patients in hospital emergency rooms who present with symptoms of acute myocardial infarction. While conventional troponin assays required multiple serial blood samples over several hours to reliably identify at risk patients, high sensitivity troponin has allowed for faster rule in and rule out strategies for these patients. High sensitivity troponin might even allow for a single troponin test at the patient's presentation to manage their care.

However, the reliability of this approach depends on the presentation timeline of the patient relative to his or her symptoms, as well as the analytical precision of troponin measurement at low concentrations. Clinical assessments that incorporate troponin test results with other factors may increase the reliability of rapid rule out approaches. An original research article published in the September 2019 issue of the *Journal of Applied Laboratory Medicine* describes the validation of a clinical chemistry score which incorporates high sensitivity troponin with other laboratory results of glucose and estimated glomerular filtration rate as an alternative assessment strategy for emergency room patients with possible myocardial infarction.

The first author of this study is Dr. Peter Kavsak. Dr. Kavsak is a professor in the Department of Pathology and Molecular Medicine at McMaster University in Hamilton, Ontario, Canada. He provides service as a clinical chemist within the Hamilton Regional Laboratory Medicine Program and is primarily based at the Juravinski Hospital and Cancer Centre with special clinical and academic focus and interests in cardiac and cancer-related laboratory tests. Dr. Kavsak is our guest for this podcast. Welcome Dr. Kavsak. Can you describe the clinical chemistry score and explain the

rationale for using it rather than relying on the troponin result alone?

Dr. Peter Kavsak: Yes. It's actually quite intuitive and the fact is that when people come with potential chest pain to the ED obviously they're worried about being in acute coronary syndrome and they're worried about a heart attack. But as we know, there are more than just perhaps troponin that's important in assessing risk for patient who presents with acute coronary syndrome. So, to provide a more holistic approach to assessing a patient, what we came up with is a kind of a quick way to assess an individual for risk stratification, not only obviously the cornerstone is troponin, but we thought that other things that we've known for quite a while over the last, you know, 10, 20 years when we knew the important for risk stratification such as kidney function and metabolic status such as high glucose and so forth.

So, what we looked at, is that could we actually improve the performance of troponin alone? A troponin by itself to rule out any one for risk stratification is, we'll give it a Grade A. So, what we're trying to do is get to the A plus, and what we looked at is by adding in glucose and creatinine to assess kidney function, especially estimate glomerular filtration rate, what we are able to do is just slightly improve the performance of troponin alone for risk stratification, those patients at low risk versus high risk. And in that manner, what we're actually pretty excited is that this may be useful to do with the presentation blood sample in the Emergency Department to make a quick decision for a certain number of patients.

Randye Kaye: All right, thank you. Well, let's talk a bit about the clinical evidence. Is there yet any clinical evidence that supports the use of the clinical chemistry score?

Dr. Peter Kavsak: Yes. So, last year in August 2018 we published a multi-center study in the *Canadian Medical Association Journal* where we actually assessed the clinical chemistry score in four international emergency department population study populations. That was in Canada, Germany, Australia, and New Zealand. And what we found in the combined cohort or combined pool of those populations, we found in over 4,200 individuals, about 727 patients within this first 30 days of presentation to the Emergency Department experienced a myocardial infarction or unfortunate death in that period of time and what we are able to do with the clinic chemistry score, for example when using in combination with high-sensitivity troponin I, we were able to identify all patients that would have a myocardial infarction or unfortunate death within the 30 days and thereby we are able to identify 10% of the population that did not have any cardiovascular events in that period of time. So, that was zero. So, we

didn't miss anyone and if we compare that to troponin alone out of 727 individuals, upwards of 25 events were missed.

So, the point is that troponin works amazingly well by itself for risk stratification, those at low risk versus high risk and so forth. But to push it above the edge, the sensitivity and the really high negative rate to value what we found is that the combination of glucose and eGFR as part of the clinical chemistry score actually provided the highest sensitivity and negative predictive value as compared to troponin I. That's the clinical evidence that was published in the international studies to date.

Randye Kaye: Great, wonderful. Now, can you summarize the findings that you described in this current JALM article and explain how this adds to that existing literature?

Dr. Peter Kavsak: Yes. So, a lot of times people are worried to rule in and rule out myocardial infarction. That is definitely the case when someone comes with chest pain; Emergency Department physicians really want to quickly decide if this is a heart attack or not. But that doesn't necessarily mean that the patients can be sent home. All that means is that they're not suffering myocardial infarction heart attack, which is definitely very important information to know for the physician. But can they actually send the patient home?

So, what we did in this particular publication manuscript is we assessed a period of time in two cities, both in Hamilton and Calgary. Hamilton currently measures a high sensitivity troponin I. Calgary in Alberta, Canada, measures high sensitivity troponin T. And what we decided to do is look over a period of six months using the clinical chemistry score, could we identify patients that were discharged home from the Emergency Department?

So, we're not actually addressing whether or not they had an MI or not. But more importantly, what we wanted to assess is that if the clinical chemistry score could identify patients that would be eligible for hospital admission versus hospital discharge but hospital discharge home. This is the key difference between the *Journal of Applied Laboratory Medicine* publication versus other ones. We wanted to see what could be the impact on emergency department workflow if using the clinical chemistry score. So, in essence retrospective study combined cohort would be over 35,000 patients, 25,000 or so in Calgary, 10,000 or so in Hamilton, and what we observed is that with the low risk as determined by clinical chemistry score, we could achieve a sensitivity of upwards of about 98% which almost indicates that we could possibly send patients home with a clinical chemistry score less than one. This would be compared to

below 93% sensitivity if we were using troponin T and actually a lot lower sensitivity after using troponin I.

On the converse side, there's -- when we actually applied a clinical chemistry score and say, should we perhaps rule in. We also identified patients that would actually be a high specificity. So, what we're doing with the clinical chemistry score is quickly not only identifying patients at low risk versus high risk, the current publication actually extends that information to say potentially we might be able to do better and offer now discharge patients home or do immediate admissions to the hospital.

Randye Kaye: All right, thank you. That's certainly an important distinction. What would you say is the primary message that you would like the readers or listeners here to take away from this study?

Dr. Kavsak: First of, when sites or when hospitals adopt high sensitivity troponin testing, they will be able to achieve early, more efficient management of patient outcome, the patients who present at the Emergency Department. I think overall that, I mean, that's not what this study shows, but overall the wealth of evidence says that high sensitivity enables earlier decision making in Emergency Department enables earlier ordering sets instead of, you know, 03, 02, 01.

So, there's all these things that can occur, where hospitals can take advantage of well, more importantly, physicians who practice in hospitals that have high sensitivity troponin testing can do in emergency settings. What this study actually quickly adds to that data set is the fact that we can now perhaps reliably use the clinical chemistry score to identify low risk and high risk. And is this little bit important, especially for the laboratory professionals, is the fact that if the cutoffs that we use in the clinical chemistry score are all measurable concentrations of high sensitivity troponin I. What this is important for is the fact that now, laboratories can actually appropriately monitor their high-sensitivity troponin I assays by obtaining quality control near these cut points that are used in the clinical chemistry score.

So, this is a little bit different than using the limited detection or undetectable to rule out or rule in patients for myocardial infarction. We're using high-sensitivity troponin. It is very difficult for a laboratory to monitor something that is undetectable, that's basically the signal is below the lower limit. So, how is a lab to monitor that? The clinical chemistry score actually provides a way that with the cutoffs are all measurable concentrations, now laboratories can obtain quality control or construct their own quality control at those concentration cutoffs, and now can monitor

troponin in a manner that can be used to rule in and rule out and more importantly, if there is a problem with the assay drifts and so forth or there's an issue that's identified with quality control in an area, the laboratory can preventively stop or correct that action so further patients' classification could be mitigated, as opposed not measuring quality control in that area.

So, I think this is just another way that high-sensitivity troponin can be used in order to risk-stratify patients who come with chest pain to the ED. It may be this data, retrospective data, demonstrates that it could be used for early discharge home, but I think it is important to say that all these data to date really build toward a need and perhaps for a prospective study to definitely demonstrate the utility of the clinical chemistry score as compared to troponin level when deciding patient management in the ED.

And so there is still some more work to do but I think at the end of the day, this data actually provides another step forward in how high-sensitivity troponin can be used for early decision making in the emergency department.

Randye Kaye: All right. Thank you very much. Thank you so much for your time and for joining us today, doctor.

Dr. Peter Kavsak: Thank you very much for the opportunity to discuss.

Randye Kaye: That was Dr. Peter Kavsak from McMaster University describing his original research article from the September 2019 issue of JALM, "A Multicenter Assessment of the Sensitivity and Specificity for a Single High-Sensitivity Cardiac Troponin Test at Emergency Department Presentation for Hospital Admission." Thanks for tuning in to this episode of "JALM Talk." See you next time and don't forget to submit something for us to talk about.