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The Need to Develop Clinical Guidance for the Use of High-Sensitivity Cardiac Troponin in Pediatric and Neonatal Patients

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Guest: Dr. Allan Jaffe from the Mayo Clinic in Rochester, Minnesota.

Bob Barrett: This is a podcast from *Clinical Chemistry,* sponsored by the Department of Laboratory Medicine at Boston Children's Hospital. I'm Bob Barrett.

The clinical application and interpretation of cardiac troponin results, particularly using high sensitivity assays, can be complex and challenge clinicians in many clinical scenarios. An important population with unique circumstances for which the role of troponin testing remains controversial, is the neonatal and pediatric population. To help address this issue, the IFCC Committee on Clinical Applications of Cardiac Biomarkers published an opinion piece in the July 2022 issue of *Clinical Chemistry* with the title, "The Need to Develop Clinical Guidance for the Use of High-Sensitivity Cardiac Troponin in Pediatric and Neonatal Patients."

We are pleased to have one of the authors of that opinion paper with us in this podcast. Dr. Allan Jaffe is Professor of Medicine in the Department of Cardiovascular Medicine and Professor of Laboratory Medicine and Pathology and the Wayne and Kathryn Preisel Professorship of Cardiovascular Disease Research at the Mayo Clinic in Rochester, Minnesota, and a known authority on biomarkers of cardiac injury.

So first of all Dr. Jaffe, what stimulated your interest in the use of high-sensitivity cardiac troponin in children in the emergency department? Isn't it unusual to request troponin concentrations in children?

Allan Jaffe: Well, you know, those of us who've been in the field for a long time have always included children. And way back when we first developed the original assay, we did some preliminary studies in kids at [Washington University] when I was there. But over the years, because children are much less often at that ischemic heart disease, and that's what troponin was or is predominately used for, it hasn't been used very much in that group. And so over time, the pediatric community has become less and less involved with that area. But as we started to see that there are large numbers of potential indications with both primary and secondary prevention of

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cardiovascular disease, it was clear that we would move back into the pediatric area.

And one of the residents who was here said, "Well, I don't think we use it very intelligently." And so, he decided to look across the Mayo enterprise that included both Mayo Rochester, Mayo Jacksonville, and Mayo Scottsdale, as well as the Mayo Health System, which is a consortium of nearly 30 sort of community hospitals, and to see what was being done in the ED with pediatric patients. And it again fits, sort of, with the idea that as we understand the increased use of cardiac troponin and how powerful it can be, and eventually we will want to apply it to children and adolescents. And as our study suggested, the people it's being used most in it are not infants or neonates, it's teenagers who are closer and closer to adults and therefore more likely to have adult-like symptoms like chest pain.

Bob Barrett: Well, let's talk about that study. What were some of your findings?

Allan Jaffe: Well, it was sort of daunting. Of the probably nearly 30,000 pediatric visits, only about 380-some, was a troponin even drawn. So very, very little use of cardiac troponin and when it was used, it was used mostly in adolescents as indicated, so that it wasn't something people rely on. If one got one sample in the adult population, we almost always get a second to look for a changing pattern. That was done in only about a third of these patients, about 100. So, very little use. Indications were just very confusing. It was hard to tell what people were doing and why they were doing what they were doing there. The one group where it seemed to make a little bit of sense were in some patients who had chest pain, and some patients who had auto accidents and trauma. They caused cardiac contusion, can be diagnosed with troponin, and obviously can be a life-threatening circumstance.

So with the exception of those two, it wasn't clear who pediatric specialists, and in fairness mostly ED specialists, drew troponins on, and it also wasn't clear what they used them for. As best we can tell, it doesn't look like the troponin values, even when they were markedly elevated, had very much effect on clinical care.

There were, I think, of the 386, there were 6 patients who were diagnosed as having pericarditis, but none of them had elevated troponins. And even in the patients who had trauma, although a fair number were admitted, presumably not because of the troponin, but because of their other clinical circumstance. But even with very high values that would make you worry about a cardiac contusion, these values seem to be ignored.

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So what we found was, there isn't much use. When there is use, it doesn't appear to be consistent or focused, and it doesn't also appear to enter into the clinical decision-making that pediatricians or ED physicians seeing children or infants use to make clinical decisions. And it seems to me, and worries me, that that could be a real problem because some of these signals may be real. On the other hand, in fairness, we didn't have follow-up information because follow-up of this group, which was spread across the United States, would have been very difficult and there wasn't consistent follow-up within our medical records to allow it. Maybe all those patients did really well and a clinical judgment is all one needs, and that troponin shouldn't be used in these circumstances.

When you add sort of all that up, you say, "Well, seems to me that we need more information to be sure that, a) that if that's true, that it's not useful, that we document that and make sure of that. But if it is useful, we then define those areas where it might be useful and provide some guidance about how to use it optimally."

So we came to the conclusion that the field was confused, inconsistent, at least in our experience, and that what was needed was more work. Because of that, we wrote an editorial published in *Clinical Chemistry*, basically saying that's what we need to do and challenging the field to develop better standards.

Bob Barrett: You're obviously concerned about these findings. Why is that? Why is this so concerning?

Allan Jaffe: Well, you know, in the adult population, when you see an elevated troponin there often are adverse consequences, both short and long-term. They identify people who are at cardiovascular risk. Now, the risk is different in the critically ill. But for example, if you have a myocardial contusion, you can have QT prolongation and sudden cardiac death. And if indeed that's something that troponin could help to diagnose, the idea that even when the values were very high, they were being ignored, really does raise at least some concern. Even a loss of one child is a terrible disaster, to say nothing of the fact that this might become a much more common phenomenon or maybe even more common than were aware of. And if indeed troponin would be helpful, just let's take the example of the patients with possible contusion, this might well be a very important and good use.

In addition, we are starting to see, and this came up through the COVID era really, of people believing that they had, would have myocarditis after a COVID vaccination, and this was greater in young people. Well if young people come in and we're using troponin to make that diagnosis, what is really

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used, but we don't have the metrics in our hands around, what are the positives and false positives and false negatives, and what diagnoses are optimized by doing that, we're going to end up misdiagnosing people.

And for example, therefore misconstruing what might be a common problem or might be a very uncommon problem, we could be exaggerating. So, it seems to us that there were a whole lot of reasons why putting some better information together would be helpful.

Bob Barrett: Well, you've uncovered the problem. What's the answer? What can be done to deal with this?

Allan Jaffe: Well, the first thing we need to do is to find some pediatric laboratorians, people interested in pediatric laboratory medicine to make sure that the normal value studies that we all rely on to make decisions are done ideally. There are some in the literature from Australia, Peter Hickman and his group, and there is a group in Toronto called the CALIPER group that has done studies and they're really surprising to me.

They suggest that values are a little higher at the time of birth, and then go down and really are near adult values by the age of three or four. Now, that doesn't make total sense to me because most of what we see in the adult population suggests that values go up with age. But maybe that's correct. But boy it would be good to have large studies that really could confirm that. And then we need to put together groups of individuals who are interested in pediatric emergency medicine, pediatric cardiology, and laboratory medicine, to begin to collect systematically, samples in a variety of different settings. It probably will be very different for neonates, and yet different for young children, and then still more different for adolescents, because they have different diseases that they are prone to get and different reasons why troponin might be helpful or confusing in those settings.

So, what we need to do is mobilize groups that are interested in this, find funding, and then begin to study intensively how to deal with this problem so that if indeed there are real issues and troponin can help, we know how. And if troponin can't help, we can then confirm to the field that what they're doing now, which is basically ignoring it, is really the right thing to do.

Bob Barrett: Well, finally Dr. Jaffe, have you been able to identify a group to take this on?

Allan Jaffe: Well, we don't have formal organizations that have come to us as yet, but we're starting to find individuals who have enthusiasm to do this. As a matter of fact, one of the people

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who had a fairly immediate interest in this was Nader Rifai, the [Editor-in-Chief] of *Clinical Chemistry*, who is a pediatric laboratory medicine person with real knowledge in cardiovascular disease, who immediately said this is an important need. Once that happens, when you start getting people who really are knowledgeable and who are the nexus of their fields, the likelihood of putting together groups becomes much better.

So, no, the groups aren't formed. If people are interested, I'd be glad to serve as a clearinghouse to identify those people and move them on. I'm an adult cardiologist. I don't do pediatric cardiology and I haven't even stayed at a Holiday Inn to pretend I was a pediatric cardiologist. So my suggestion for my role would be to try and get those groups together. If I can help them find funding, I'd be glad to do that, and then let them go and generate what we need in the field to help neonates, children, and adolescents.

Bob Barrett: That was Dr. Allan Jaffe, Professor of Medicine in the Department of Cardiovascular Medicine and Professor of Laboratory Medicine and Pathology at the Mayo Clinic in Rochester, Minnesota. He joined us in this podcast on "The Need to Develop Clinical Guidance for the Use of High-Sensitivity Cardiac Troponin in Pediatric and Neonatal Patients." His opinion piece, co-authored with other members of the IFCC Committee on Clinical Applications of Cardiac Bio-Markers on that topic, appears in the July 2022 issue of *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.

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