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How Well Do Laboratories Adhere to Recommended Guidelines for Cardiac Biomarkers Management in Europe? The CArdiac MARker Guideline Uptake in Europe (CAMARGUE) Study of the European Federation of Laboratory Medicine Task Group on Cardiac Markers

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Guest: Dr. Paul Collinson is Professor of Cardiovascular Biomarkers and Honorary Consultant Cardiologist at St. George's University Hospital's National Health Service Foundation Trust and St. George's University of London.

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.

"How Well Do Laboratories Adhere to Recommended Guidelines for Cardiac Biomarker Management in Europe?" That is the question, and it's a question that serves as the title for a paper appearing in the August 2021 issue of *Clinical Chemistry*. That paper's objective is to benchmark clinical Laboratory practice compared with current clinical guidelines on cardiac biomarkers.

The lead author for that report and our guest in this podcast is Dr. Paul Collinson. He is Professor of Cardiovascular Biomarkers and Honorary Consultant Cardiologist at St. George's University Hospital's National Health Service Foundation Trust and St. George's University of London. He introduced testing for cardiac troponin and B-type natriuretic peptide into routine clinical use in the United Kingdom.

So Dr. Collinson, this paper is the latest in a series. When did all this start, and why did you want to take this program of conducting such surveys in the first place?

Paul Collinson: Well, we have to go back to the good old days when troponin was first introduced, which was in the late '90s and of course it had to displace our good friends CK and its MB isoenzyme CK-MB. So what we have was a progressive series of developments, people are getting used to these new assays; the assays were getting better. Then there were a whole sort of series of new guidelines that came along, but the one thing that struck me throughout all the years when this was happening is whenever I was giving talks or attending seminars on troponin, people kept asking the same questions over and over.

So one thing that occurred to me was that we should maybe be looking into this and the European Federation of Laboratory Medicine put together a task force with the

objective of looking at the evolution of the assays and we really understood these surveys to find out what was going on and see if we could highlight areas where people really were floundering where they really needed some additional education and help. And that's really how it all began.

Bob Barrett: What was the main focus in this most recent survey and how did it differ from previous iterations?

Paul Collinson: Well, the real thing that's happened of late, much less for the US, but certainly in Europe, is of course, that the high sensitivity troponin assays have become very well-established into routine clinical practice, they're certainly recommended in all the European Guidelines. You've had a bit of a little local difficulty over across the water in getting them introduced through the FDA, but they are arriving then there too.

So this is the real thing. It's that the high-sensitivity assays arrived and how are people using them, how are they finding them to be used in routine clinical practice, and particularly how they've implemented them. And we thought this would be particularly interesting to find out certainly in terms of potential future lessons learned.

Bob Barrett: So doctor, what were the main messages coming out of this survey this time around?

Paul Collinson: Well, the real thing that is there is that troponin is now established, it is the cardiac biomarker that everybody uses. The only people who said they weren't using it said it was purely for financial reasons. I find that a bit of a surprise given the fact that cost has fallen so dramatically. When I first introduced troponin testing, it cost $50 a test. And now of course, it effectively costs about $3. I probably shouldn't say that, everybody will be sending me your assays or your requests. I'm sure that that's not what's charged locally in the US, but never mind.

The real thing is that everybody now has access to a high-sensitivity assay. All the manufacturers who didn't have one originally are now introducing one. So, it's there, it's in routine clinical use. Traditional cardiac enzymes are really gone. Nobody, this time around said they was included AST and LDH in their Cardiac Panel, but the surprising thing was that CK-MB is still hanging in there and about 50% of people said they were still offering it. This was a bit of a surprise to me.

And when we were able to look in, when, because there were options in the survey for people to give a little bit of individual sort of clarification as to why they were hanging on CK-MB. And the thing that came over, they all wrote, "it's because

our clinicians want it" and this surprised me, because I didn't realize that the cardiological community and the ED physicians are really such a conservative bunch. I'd have thought they'd have been, they are being at the forefront of implementing these new assays but not necessarily so.

Bob Barrett: Well, looking at the current survey, what surprised you the most?

Paul Collinson: I was -- the thing that surprised me the most is that it's 20 years since myocardial infarction was proposed to be redefined in terms of the troponin standard and when it hit the sort of the big time with the universal definition, myocardial infarction about 12 years ago now, but still there are people out there, and it's not a small number, who are not using the universal definition recommended cutoffs. They are not using the 99th percentile, they're using a higher cutoff, and this surprised me a lot because you think well, well, why aren't you doing adhering to the guidelines? But this is something, which I've come across in another context recently.

The second surprise was that people are not pursuing a sort of uniform sampling strategy. The European Society of Cardiology Guidelines recommended essentially a zero, three hour coming on from 06, there are these rapid diagnostic algorithms. But there really isn't a great deal of consensus on when people take the samples.

The good thing is that doing the serial sampling, which is what is required by the universal definition, but the lack of any sort of consistency on when they do take the samples is quite a surprise. I'd have thought that people would have settled down onto something which would be aimed at expediting diagnosis, but not really.

The other thing that was quite interesting was that although the rapid diagnostic algorithms, which have been proposed by the European Society of Cardiology, that's measurement on admission and then measurement 1 to 2 hours post-admission. These aren't really being taken up very widely at the moment, and this was again the bit of a surprise because there's always great pressure on the emergency department. People want to get people out of hospital earlier, but people are not using these rapid serial measurements and this squares with some other information from another project I've been working on. And people find these really quite difficult to implement.

And I think it's the problem of not so much the zero-time sample, but by the time a one-hour sample is taken, the result is not back from zero times. So people tend to wait until they have both results back.

So this may be the problem there and that, I think, is something that people will have to work on the whether some of the new technologies which are coming out with point-of-care might be able to address that. And perhaps the other, and really quite worrying finding, was a lack of coordination and dialogue between the clinicians and the users of the service. And the laboratory side of it, that doesn't seem to be sort of coordinated strategy and quite often they said well, do you have -- one of the questions was do you have a protocol, and everybody said yes they did. When we asked it was it written down, there was a sort of well, yes, we've got it written down in our laboratory, or it's a verbally agreed protocol and to misquote the late great Samuel Goldwyn, I didn't think a spoken protocol is worth the paper it's written on; or these days, perhaps the electrons it's captured upon.

Bob Barrett: Well, finally Dr. Collinson, do you think there were particular lessons to be learned from these results, especially here in the US where we're just embarking on the introduction of high-sensitivity troponin testing?

Paul Collinson: I think that they definitely are. The real thing which I have been struck with is the absolute essential nature of dialogue between the laboratory and the clinical users. And that the clinicians themselves realized that this is potentially of great benefit to them because the sensitivity allows very rapid rule out, it allows rapid and safe rule out. I know it's more problematic with some of the assays because the FDA is quite stringent in what it defines as limit of quantitation. But I think that this is the real thing: talk to your clinicians, explain how the assays work. I bet you if you survey the Emergency Department and said to them which troponin do we use, you might get that right about 50% between T and I. If you ask them what method they used, that you've met by a blank. So, this is the important thing. They got to be educating and in dialogue, so education-dialogue, education-dialogue, education-dialogue, rinse and repeat, and never assume that because you've said it once, people remember it.

Bob Barrett: That was Dr. Paul Collinson from St. George's University of London. He has been our guest in this podcast on "How Well Do Laboratories Adhere to Recommended Guidelines for Cardiac Biomarker Management." He is a lead author of a paper describing results of a survey on that topic that appears in the August 2021 issue of *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.