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Q&A: Nonfasting Sample for the Determination of Routine Lipid Profile: Is It an Idea Whose Time Has Come?

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Guest: Dr. Samia Mora is a cardiologist and cardiovascular epidemiologist with appointments in Cardiovascular Medicine, Preventive Medicine, and Women's Health at the Brigham and Women's Hospital and the Harvard Medical School.

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

For many years, the determination of a routine lipid profile has been routinely in the clinical laboratory using a blood specimen that's collected in the fasting state. There are a number of reasons for this requirement, including postprandial changes in lipid protein composition, particularly the increases in triglyceride concentrations. In addition, many clinical trials and epidemiological studies on which treatment goals are based used fasting samples for lipid measurements. However, because most of each person's lifetime is spent in the postprandial state, the wisdom of collecting a fasting sample to determine future risk of cardiovascular disease has been challenged. The March 2016 issue of *Clinical Chemistry* published a Q&A session where a group of experts in this field shared their thoughts on nonfasting samples for the determination of routine lipid profile, asking if this is an idea whose time is come.

We're joined by one of those experts in this podcast. She is Dr. Samia Mora, a cardiologist and cardiovascular epidemiologist with joint appointments in the divisions of Cardiovascular Medicine, Preventive Medicine and Women's Health at the Brigham and Women's Hospital where she is an Associate Physician and an Associate Professor of Medicine at Harvard Medical School.

Dr. Mora, patients are usually told to fast before a blood sample is taken. What is the evidence that fasting samples are better than nonfasting samples for a clinical use for lipid measurements?

Dr. Samia Mora: Well, it's an interesting question because there's been more and more data showing that nonfasting lipids for risk prediction, for cardiovascular events, as well as even for treatment decisions may be just as good as fasting samples. So the whole assumption that we need to fast prior to lipid testing seems really derived from smaller physiologic

studies that show that there's some variability especially in the triglycerides with food or with even a high fat load or high sugar intake.

However, we find now that for predicting risk, which is what most clinicians and most patients get their lipids either ordered or done for risk prediction of cardiovascular events so that they can estimate what's their risk of having cardiovascular event, for that reason in turns out that nonfasting is just as good if not better than fasting. The other reason is really for treatment decisions when a clinician and a patient are looking at their lipids and they're trying to see, well, should they adjust the dose medication.

And again, even for that, more and more we're realizing that the differences are so small between the fasting and nonfasting results. Again, just with the exception sometimes for triglycerides, where there could be some variation for some patients. But for the general part, most people really have very small changes in their lipids with the fasting or nonfasting state.

Bob Barrett: What are the main advantages of using nonfasting samples?

Dr. Samia Mora: Well, you know, nonfasting is just much more practical. It's easier for the patient, easier for the doctor or a healthcare provider. Often patients come to their clinic visits and they don't know that they're going to get their lipids done or if they did, they were, let's say, feeling a little bit hungry or weakened and they wanted to eat something, and they come to the clinic visit and they may not know that they should have fasted. And so, by the time then the patient returns or has actually returned for another test several weeks or days may have passed and then it's now the responsibility of the healthcare system for the healthcare provider to follow up on that result, see that the patient really gets it, call the patient or send them a letter communicating the results or if they didn't come, encouraging them to come and get their test done.

So just from a practical situation, it's really cumbersome to get some lab fasting for lipids or for any measurements, and then there are some people who, you know, it's very difficult for them to fast. For example, patients who are diabetic, it may be very difficult for them to fast, and children, it's very difficult to ask a child to really fast. And then, for the lab's standpoint, the lab is then getting these patients often coming all in the morning, first thing in the morning like around eight a.m. to get all these blood tests, and later in the day there is less volume. So again, it's kind of like an upfront loading of volume for the labs so also for the lab it's also difficult for lab workflow purposes. It's much easier to get them nonfasting.

So unless there's a really good reason to do them fasting, from a practical perspective, nonfasting is really much, much more convenient for everyone. So it could really solve a lot of problems. And again, like I said earlier, the data for showing for risk prediction, for cardiovascular events, is really even better for nonfasting compared with fasting lipids or at least the same for risk predictions. Therefore, there is really no strong reason to suggest that they should be fasting, and it's much more practical and easier on everyone to just do them nonfasting.

Bob Barrett: Well let's talk about the situations where fasting samples are really required. What are those situations?

Dr. Samia Mora: That's a good point. Well, there are some thoughts about when patients should really get them fasting but it's not really clear. I guess the question then becomes as to what's the purpose of getting the lab test in the first place. So if the purpose is for predicting somebody's risk for cardiovascular events, let's say from using the 2013 ACC/AHA guidelines for risk prediction, or using a European equation for risk prediction, well, in those cases, you really don't need to be fasting because usually, you're putting into the risk equation the total cholesterol and the HDL cholesterol, and these really have very minimal changes with food and they predict risk just as well whether they're fasting or nonfasting.

Some people say, "Well, maybe if the triglycerides are high, that in a nonfasting, let's say the patient comes in nonfasting, you measure their triglycerides and they turned out to be high." Some people may think we should repeat those or some guidelines that suggest that the nonfasting triglycerides is more than, say, 450 or more than 500 milligram per deciliter, that in those situations maybe we should repeat it and see if there are reasons why the triglycerides were high driven let's say by a diet or driven by other things like, say, alcohol; is it a reversible thing or does a patient have another genetic underlying cause for hypertriglyceridemia?

But honestly, the fact is that for most situations, we really don't need the fasting measurements at all and we can manage patients just as well with the nonfasting samples. The conundrum, you know, becomes how do you interpret them, or how do you interpret the nonfasting triglyceride level or how do you -- as I said, earlier triglycerides are really the only one of the lipids that has some substantial change like up to say 20% or 25% in some individuals compared when you're comparing fasting with nonfasting versus all of the other lipids like the LDL cholesterol, the HDL cholesterol, total cholesterol, apoB, apoA-1, those

really have very minimal changes in the order of less than 5%.

Bob Barrett: Let me ask this. What if you're testing for something other than lipid, say, glucose for example, wouldn't it then be easier to just have a fasting sample?

Dr. Samia Mora: Well that's an interesting point too. You know, should you get a fasting. I mean fasting is more standardized. So for example if one wants to apply a criteria for diabetes, you can say, "Well, let's check a fasting glucose." But however, for diabetes you also have nonfasting criteria so we know that if a nonfasting glucose is elevated it just has to be a higher level of nonfasting that would then meet the criteria for diabetes. And even for diabetes more and more people are turning anyways towards other diagnostic biomarkers such as hemoglobin A1c or some of the other biomarkers that reflect you know like a glucose average over a period of a few weeks. So in those cases really you don't need to be fasting.

Again, in that case as well, you can do it both ways and in fact the diabetic patients are the ones who would, you know, it's the hardest for them to fast anyway so also practically, it would be easy. So again, we just need to have an understanding of whether the sample was done fasting or nonfasting so that we know what criteria they could be used for the glucose or for the triglycerides. But in terms of the predictive value or in terms of the management, you know, again that can be done either way.

Bob Barrett: Finally, doctor, let's go back to the question of nonfasting triglycerides. How should a clinician interpret nonfasting triglycerides?

Dr. Samia Mora: Yeah. Well, a lot of clinicians come to me and say, "Well how should we for sure your data -- " because we have data from Women's Health study and other data from Copenhagen General Population Study and also City Heart Study and many other studies showing that nonfasting triglycerides and nonfasting lipids are just as good if not better than fasting measures but then the question is as a clinician, "well, what cut point do you take?"

Like I said earlier, for things like triglycerides which do fluctuate with food and with time since the food intake, for these things, we actually did a study in the Women's Health Study a large population of about 28,000 women and then we had about 6,000 plus women who were nonfasting, and we followed them for events for up to 17-year follow-up. And what we noticed there was that the cut point for nonfasting triglycerides of 175 milligram per deciliter, which

ends up being about 1.98 millimole per liter or approximately 2 millimole per liter, I should remember that. Well that's the cut point that turned out for the nonfasting triglycerides do have the best sensitivity and specificity for cardiovascular events. And interestingly, that cut point of 175 milligram per deciliter or 1.98 millimole per liter, is also what the European Atherosclerosis Society had recommended in the past for the cut point for nonfasting triglycerides, and also, very similar to what an Athens expert panel had recommended -- no that's lower than the cut point currently recommended by the American Heart Association guidelines.

The American Heart Association guidelines currently suggest that a cut point in the nonfasting state of more than 200 milligrams per deciliter would be considered high. But what we found in our study again, using a large number of women followed for many years, was that a cut point of 175 milligram per deciliter was for the triglyceride was able to capture more accurately the women who went on to have cardiovascular events, suggesting that if you're a clinician seeing a patient and you do a nonfasting lipid panel, as really now the data suggesting we really should be doing, well in those cases, when you get the nonfasting triglycerides, just keep in mind the cut point of 175 milligram per deciliter or 1.98 millimole per liter and not to use the fasting cut point which is lower.

For example, for the fasting, the guidelines recommend 150 milligram per deciliter as a cut point so that's 25 milligram per deciliter lower than the nonfasting threshold for considering the triglycerides elevated. So again it's just very simple. It's just we can use the triglycerides as well in the nonfasting state and we know their predictive value.

For cardiovascular events, it's even greater from the studies that have been done because we think most people are in the nonfasting state most of the time and so having a measure of their nonfasting lipids is likely a better predictor of their overall lipid protein metabolism state than doing it in the fasting state.

So, for a clinician seeing a patient, I encourage them to order the nonfasting lipid panel. Their predictive value is just as good if not better than for a fasting. It's easier for everyone, for both the clinician and for the patient, and for the lab, and for everyone overall. And now we also recognize that even for the triglycerides, which is the only lipid that really changes potentially with food intake and even for that one, we have now a good cut point that we can use practically to screen individuals who may be considered to be having high triglyceride level. We just

have to use -- remember that the threshold is slightly different than if they are fasting.

Bob Barrett: That was Dr. Samia Mora from the divisions of Cardiovascular Medicine, Preventive Medicine, and Women's Health at the Brigham and Women's Hospital and the Harvard Medical School. She has been our guest in this podcast from *Clinical Chemistry* on nonfasting samples for the determination of routine lipid profiles. I'm Bob Barrett. Thanks for listening!