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Zareen Farukhi and Samia Mora.
Nonfasting Lipids for All Patients?
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Guest: Dr. Zareen Farukhi from Brigham and Women's Hospital and Harvard Medical School in Boston.

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.

Change often takes time. In the medical community, one of the most notable shifts in scientific thought and clinical practice has been the gradual acceptance of utilizing nonfasting specimens for lipid testing and routine screening of cardiovascular disease risk.

An Opinion piece reviewing the status of such testing and key guidelines and consensus recommendations on nonfasting lipid testing appears in the January 2021 issue of *Clinical Chemistry*. Its authors are Dr. Zareen Farukhi and Dr. Samia Mora, both from the Brigham and Women's Hospital and Harvard Medical School in Boston. Dr. Farukhi is our guest in this podcast.

Doctor, you and Dr. Mora have described considerable evidence for the use of nonfasting samples for lipid profiles as first-line screening tests and detailed the progression of acceptance by several guidelines over the last decade. What do you think are some of the reasons that it has taken this much time for widespread acceptance?

Zareen Farukhi: Well, apart from the fact that change is hard, it seems that one of the major reasons for the slow uptake of nonfasting panels into clinical practice has been the concern about misclassifying patients into a lower risk category when assessing their LDL cholesterol using the Friedewald equation.

The Friedewald equation has been used for decades to calculate LDL cholesterol and uses an individual's triglyceride level divided by 5 to approximate their VLDL cholesterol. This is then subtracted from the total cholesterol minus HDL cholesterol to give the calculated LDL cholesterol value.

Now, it's well known that triglycerides increase a number of hours after eating. So a higher triglyceride level will result in a lower calculated LDL. However, we and others have shown that the difference in nonfasting lipids compared to

fasting ones when we measure routine lipids are relatively small with no significant difference in HDL cholesterol and only around 8 Mg/dL or 0.21 mmol/L lower LDL cholesterol, total cholesterol, and non HDL cholesterol in nonfasting samples.

Since this concept of misclassifications though has been a significant concern, investigators have looked at the degree of misclassification that could occur in nonfasting samples in a study called the ASCOT-LLA study. They found no significant misclassification that would adversely affect the decision for initiation of statin therapy and there was high concordance, about 95%, between fasting and nonfasting lipids. These are measured in the same individuals. So really there seems to be no reason to be worried about misclassification using nonfasting patents.

Another point though that clinicians who are really quite concerned about calculated LDL accuracy is that we can now use the Martin-Hopkins equation, which is a modification of the Friedewald equation and this has been shown to have improved accuracy when using nonfasting samples in particular.

Bob Barrett: So what are the benefits of obtaining nonfasting samples compared to fasting ones?

Zareen Farukhi: Well, there are several benefits; one common-sense benefit, if you will, is that nonfasting profiles are much more reflective of our natural physiologic state. Except for a few hours in the morning, most of us spend the majority of our lives in a nonfasting state. We now know also from numerous large prospective studies that nonfasting lipids are as good or even better than fasting samples for a general screening of CVD risk.

There was an evidence-based review of published literature from over 300,000 individuals and that found no diminution of lipid relationships with predicting incident events for nonfasting lipids. In addition, the ASCOT-LLA study which we just talked about also measured fasting and nonfasting lipids in the same individuals about four weeks apart with no intervention or advice given between the two visits, and they found that the association of baseline lipids with CVD events was similar irrespective of fasting status.

There have also been genetic studies that suggest capturing lipids in a nonfasting state, especially nonfasting triglycerides, have even stronger risk association with CVD and mortality. So in certain patients including those with metabolic syndrome, diabetes mellitus, or specific genetic abnormalities, fasting could mask these abnormalities of

triglyceride metabolism, which is captured by the nonfasting measurements.

And then finally from a systems perspective, nonfasting tests are much more convenient both for healthcare providers, but also for patients as well. And even though we don't really have a study assessing this, they're probably more cost-effective and in patients with diabetes they are also safer with much less likelihood of hypoglycemic episodes induced by fasting itself because of the test requirement. This is something that is kind of underappreciated at this point, but apparently is as prevalent as 25% of all people with diabetes fasting for studies.

Bob Barrett: I would imagine, too, that just scheduling a test would be easier because you could do it in the afternoon.

Zareen Farukhi: Absolutely. In fact many patients, just after their office visit, they will go down to the lab or up to the lab wherever it is, and really do appreciate how convenient that is.

Bob Barrett: Well that being said, do you have any specific dietary advice that you provide before blood samples are collected nonfasting?

Zareen Farukhi: Well, there have been some concerns that patients consuming a very fatty meal before testing will really increase the triglycerides so much so that the test will no longer be valid, but numerous studies have actually looked at this increase in the plasma triglycerides after what we would say is habitual food intake, and that's much less than what would be for a scientific fat tolerance test.

So for most patients, this is not really a concern but in certain populations, if you are worried as a clinician just advising your patients to have a lighter meal or to avoid fast food meal before their blood draw would be enough advice.

Bob Barrett: Now, there are many non-lipid laboratory tests that require that the patient fast prior to collecting a sample, we have fasting plasma glucose for example. Wouldn't it just be easier to have patients fast so that the specimens can be used for other testing?

Zareen Farukhi: Well, if someone needs a fasting sample or is going to be fasting anyway and their clinician also wants to check their lipids then we certainly wouldn't recommend them getting a second nonfasting test. So, yes, if they're going to be fasting anyway for other reasons then obtaining a fasting test is fine, but if it's just a routine lipid screening without any other reason to fast, then we would still recommend the nonfasting testing.

Bob Barrett: You've mentioned both in your article and right here that blood triglyceride concentrations are most affected by recent food intake. How should healthcare providers interpret these results and should there be a disclaimer on the laboratory report that the sample was taken in a nonfasting state?

Zareen Farukhi: That's a very important question since we know that elevated triglycerides and triglyceride-rich lipoproteins are independent CVD risk factors and also go up after eating. Fortunately though, their cut point for abnormal nonfasting triglyceride levels has been studied. Most guidelines including the latest US and European guidelines define elevated nonfasting triglycerides as greater than or equal to 175 Mg/dL, which is greater than or equal to 2 mmol/L.

Also, the 2018 and 2019 AHA/ACC guidelines consider nonfasting triglycerides over a 175 Mg/dL or 2 mmol/L as a risk enhancing factor that could prompt initiation of statin therapy or intensification of a patient's statin regimen.

In terms of notifying providers whether the lipid panel was obtained fasting or nonfasting, most laboratory reports provide this information on the report itself, and this makes it actually much easier for providers as well as patients when they get a copy of the results.

Bob Barrett: Well finally Dr. Farukhi, is nonfasting sampling for everyone getting tested, or are there still some people where you still recommend getting fasting specimens?

Zareen Farukhi: Well in general, anytime we're concerned about markedly elevated triglycerides, then fasting panels would still be the test of choice. For example, fasting panels are still useful in patients prior to starting a treatment that may itself result in high triglycerides or modify existing significant hypertriglyceridemia. They are also useful in patients with genetic lipid disorders being followed for hypertriglyceridemia in lipid clinics.

Currently, there is no consensus between the guidelines as to the triglyceride cut point that would prompt providers to order a repeat fasting panel. For example, the ACC/AHA guidelines require fasting for triglycerides greater than or equal to 400 Mg/dL, which is equivalent to greater than or equal to 4.5 mmol/L; whereas the European Atherosclerosis Society and the European Federation for Laboratory Medicine suggests obtaining fasting panels for triglycerides greater than 440 Mg/dL, that's greater than 5 mmol/L.

But based on the Danish experience, about 10% of all nonfasting panels will be repeated as fasting panels due to hypertriglyceridemia.

Bob Barrett: That was Dr. Zareen Farukhi from the Brigham and Women's Hospital and Harvard Medical School in Boston. Her Opinion piece with Dr. Samia Mora on the use of nonfasting specimens for lipid testing appears in the January 2021 issue of *Clinical Chemistry*. I am Bob Barrett. Thanks for listening.