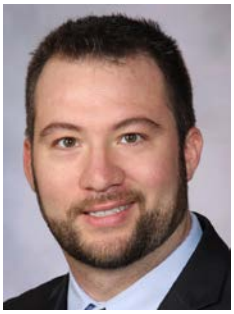

Article:
J. Meeusen, A. Lueke, A. Jaffe, and A. Saenger.
Validation of a Proposed Novel Equation for Estimating LDL Cholesterol
Clin Chem 2014;60:1519-1523.
http://www.clinchem.org/content/60/12/1519.abstract

Guest:
Dr. Jeff Meeusen is Co-Director of Cardiovascular Laboratory Medicine at the Mayo Clinic in Rochester, Minnesota.

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

Aggressive strategies to lower Low Density Lipoprotein cholesterol in circulation are recommended for prevention of cardiovascular events. Most often laboratories report LDL-cholesterol based on an equation using measured values of total cholesterol, HDL-cholesterol and triglycerides, the so called Friedewald calculation named after the first author who published that work in *Clinical Chemistry* back in 1972.

A newly derived equation for LDL-cholesterol estimation was recently published that reportedly addressed limitations in the commonly used Friedewald equation. A study from the Mayo Clinic published in the December 2014 issue of *Clinical Chemistry* compared these two equations to a gold standard ultracentrifugation method for measuring LDL-cholesterol using over 23,000 patient samples.

Dr. Jeff Meeusen is Co-Director of Cardiovascular Laboratory Medicine at the Mayo Clinic in Rochester, Minnesota, and was the principal investigator for this study. He is our guest in today's podcast. Dr. Meeusen, why did you decide to evaluate the issue of a new equation for determining LDL-cholesterol?

Dr. Jeff Meeusen: Well it's generally accepted that the Friedewald calculation has difficulties in certain situations particularly when triglycerides are elevated. And the Johns Hopkins team that proposed this novel calculation showed that it does have improved accuracy compared with a Friedewald method and since -- at Mayo Clinic we had access to a substantial dataset that included LDL-cholesterol that was measured by the gold standard preparative ultracentrifugation method, we decided we were in an ideal situation to independently verify this novel method.

Bob Barrett: How were the two methods of estimating LDL-cholesterol derived? The Friedewald equation was first published in

Clinical Chemistry over 40 years ago, certainly there have been dramatic changes in the way laboratories measure cholesterol itself?

Dr. Jeff Meeusen: Well actually, measuring cholesterol is fairly straightforward in that the enigmatic method that was in existence 40 years ago hasn't changed dramatically in the years since. However, the more difficult task is determining the contribution to the total cholesterol from each of the lipoprotein particles, and the one we're most concerned with, particularly in this project, is the low-density lipoprotein or LDL.

So the gold standard method for distinguishing amongst the various lipoprotein particles is preparative ultracentrifugation and as you said the Friedewald calculation was published in 1972, and at that time they derived the equation based on a group of about 400 patients and those patients had LDL cholesterol measured by the preparative ultracentrifugation method, and they were able to determine that the very low density lipoprotein cholesterol could be reasonably estimated by dividing the triglyceride level by a factor of five.

This novel calculation which was derived at Johns Hopkins uses an adjustable factor instead of a static factor of five, it changes the factor as a function of both triglycerides and non-HDL cholesterol, and they derive their adjustable factor from a dataset of more than a million patients. However, the measured LDL-cholesterol in that group used a method called gradient vertical spin or the VAT method.

Bob Barrett: Well, Jeff, what were your findings? Was one equation clearly better than the other?

Dr. Jeff Meeusen: Our findings largely agreed with the published data. The novel calculation was incrementally but significantly better at estimating LDL-cholesterol when compared to the Friedewald equation. However, neither equation performed perfectly. So at lower values of LDL-cholesterol the novel equation classified fewer patients has having LDL-cholesterol less than 70 mg/dL as compared with Friedewald equation. However, there was some concern that this may have been due to the populations studied being somewhat different between their group and ours.

Bob Barrett: And were there differences between the populations?

Dr. Jeff Meeusen: Yes. So both data sets were based on clinically ordered lipid profiles; however, our cohort had much lower HDL-cholesterol and higher total cholesterol as well as triglycerides indicating our patients that was likely including a higher percentage of dyslipidemic individuals.

Bob Barrett: The 2013 American Heart Association and the American College of Cardiology Guidelines on treatment of blood cholesterol no longer recommends treating to a specific target value. Does this new guideline influence the choice of one or the other of the equations?

Dr. Jeff Meeusen: Well, it does, in that the new guideline recommends achieving a percent change from an individual's baseline, so to that end you want to make sure that you are comparing apples to apples and that you are using the same method both at baseline and any subsequent follow up visits.

However, the minor differences between the two estimations are really unlikely to influence treatment decisions in a large group of patients, and for that reason primarily we didn't advocate for one or the other equations, despite the fact that the novel equation is a bit better.

Bob Barrett: Well finally doctor, for the past several years procedures are available for laboratories to directly measure LDL-cholesterol without the need of ultracentrifugation. While that's not part of your study, is there a possibility those methods of calculated LDL-cholesterol are things of the past?

Dr. Jeff Meeusen: Well, that's a good question. There are a variety of detergent based direct LDL methods that are on the market. As far as calculated LDL becoming a thing of the past, calculations are free and you need to measure total cholesterol triglycerides and HDL-cholesterol anyway, so it's hard to beat the cost-effectiveness of a calculated cholesterol.

I will say that my group has an interest in these new direct assays and we have other projects and publications in the works.

Bob Barrett: Dr. Jeff Meeusen is Co-Director of Cardiovascular Laboratory Medicine at the Mayo Clinic in Rochester, Minnesota. He has been our guest in today's podcast on Equations for Calculating LDL-Cholesterol in Serum.

I am Bob Barrett. Thanks for listening!