Clinical Chemistry

Estimated Atherosclerotic Cardiovascular Disease Risk Score: An Automated Decision Aid for Statin Therapy

Article:
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Clin Chem 2022;68(10): 1302–10. https://doi.org/10.1093/clinchem/hvac120

Guests: Dr. Alan Remaley is from the National Heart, Lung, and Blood Institute and the Department of Laboratory Medicine at the National Institutes of Health Clinical Center in Bethesda, Maryland. Dr. Anna Wolska is also with the National Heart, Lung, and Blood Institute.

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.

Most diagnostic laboratory tests are typically reported along with a reference interval based on a healthy population. However, lipid results are usually reported with a desirable range. The complex relationship between various lipid concentrations and other factors such as age, sex, and race, limits the straightforward interpretation of lipid test results in terms of estimating atherosclerotic cardiovascular disease risk.

A paper appearing in the October 2022 issue of *Clinical Chemistry* examined a risk equation based on data generated by, or available to, most laboratories, namely total cholesterol, high density lipoprotein cholesterol, triglycerides, and age. This estimated atherosclerotic cardiovascular disease risk score is proposed as a decision aid in a manner analogous to that of estimated glomerular filtration rate, or eGFR, that has been useful in transforming serum creatinine concentrations into a more easily understandable and clinically meaningful parameter of renal function.

We are pleased to have two of the authors of that paper with us as guests in this podcast. Dr. Alan Remaley is a Senior Investigator at the National Heart, Lung, and Blood Institute and is also a senior staff member of the Department of Laboratory Medicine at the National Institutes of Health Clinical Center in Bethesda, Maryland where he leads the Special Chemistry section. He is joined by his colleague Dr. Anna Wolska, a staff scientist for the National Heart, Lung, and Blood Institute. Dr. Wolska, let's start with you. Why is it important to screen for atherosclerotic cardiovascular disease risk in patients?

Anna Wolska: Assessment of atherosclerotic cardiovascular disease risk is a key step in the clinical management of cardiovascular disease prevention. Cardiovascular diseases, which include

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atherosclerotic conditions such as coronary heart disease, cerebrovascular disease, or peripheral artery disease, is the most common cause of mortality among adults worldwide. The best treatment for CVD, cardiovascular diseases, is the prevention of events by modifying risk factors thanks to the accurate atherosclerotic cardiovascular disease risk assessment.

The last US Multi-Society Guideline on lipid management, for primary prevention recommends that such risk be calculated on everyone between age 40 and 75 to determine the necessity of treatment with statins.

Bob Barrett: Can you describe how your estimated ASCVD risk calculator, just published in *Clinical Chemistry,* works?

Alan Remaley: Yes, but if we can take a step back, I just want to like to say that the ASCVD risk calculator is embedded in the guidelines and it's relatively easy to do it on your phone or computer, but the genesis of the idea is that many times people do not follow the guidelines. And so, part of our responsibility in the laboratory is making sure that the results that we generate are interpreted and present them in such a way that maximizes their values. And so, that was the original idea.

The way the risk calculator works is that the risk score is dependent upon seven factors: age, sex, race, total cholesterol, HDL, smoking status, systolic blood pressure, and it's very hard to put all those numbers in your head and have a gestalt. So, there is a formal calculator, but if you don't use the calculation, many times people are surprised at the risk because age and sex are very important determinants and people don't realize that the risk.

The way our calculator works is we take the components of the risk calculator that are available to the clinical laboratory. The clinical laboratory generates the lipid results, the total cholesterol, and HDL. Most laboratory information systems have age, sex, and race. And so, we came up with an abbreviated score that generates your risk, and then we have a simple algorithm where either the physician or the patient, because patients many times see laboratory reports, you add your risk if you know if your blood pressure is elevated or from blood pressure meds or you're a cigarette smoker.

It has a sensitivity and specificity over 90% in identifying people that have a 10-year risk score at 7.5 and those are the people that one would consider for statin treatment. It enables both the physician and the patient to see whether they are likely to be eligible for statins and then one can then use the full risk calculator to confirm it. This is sort of a decision aid that would help both clinicians and physicians to interpret their laboratory report.

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Bob Barrett: What is the advantage of this new approach compared to the currently available ASCVD 10-year risk calculator?

Anna Wolska: The advantage of our estimated atherosclerotic cardiovascular disease risk score is that it can be paired with fasting lipid tests in the lab at no additional cost to quickly and automatically identify patients who could benefit from advanced cardiovascular diseases risk ratings. We propose that this new automated lipid risk score to be integrated as a primary prevention tool for screened patients at risk for cardiovascular diseases and as a decision aid for statin therapy.

Adding such a lipid risk score to a lab would provide great benefits for physicians since it is designed to automate screening and treatment decisions. As Dr. Remaley said, we also believe that it would strengthen patients' education by fostering discussions about lipids and cardiovascular health since it would be reported along with the patient's lipid panel test results.

Bob Barrett: In your paper, you emphasized the use of samples taken from fasting individuals. As you know, there's been a number of papers published over the past few years that suggests that non-fasting samples are suitable for lipid studies. Would that be the case for your new equation as well?

Alan Remaley: Yes. It's likely the original pooled cohort risk equations, which is a 10-year risk calculator that we are trying to have our score match, was also developed on fasting samples and as you stated, the new guidelines say it's no longer necessary to fast at least initially, but I think that is one element that probably needs further investigation what the impact is on fasting versus non-fasting.

Bob Barrett: They should tell my doctor that because I have one next week and I've got to fast for it.

Alan Remaley: Fasting does not change most lipids but it does change triglycerides. The original reason for fasting is that the LDL cholesterol, which is still central in guidelines, was calculated by the Friedewald equation and it's known that patients with high triglycerides adversely affects that calculation. There are new ways to calculate it that actually were developed by us and others that are now starting to catch on that are less affected by non-fasting, but to what degree our calculation is effective is something that we need to investigate in the future.

Bob Barrett: Well, finally, doctors, is your method of estimated ASCVD lipid risk score ready for routine use by most clinical laboratories

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and can it easily be added to lab information systems much the way that eGFR calculation is now commonly performed?

Alan Remaley: Yes, those that are familiar with the laboratory will probably recognize that we kind of use the same nomenclature as the eGFR. That's why we use the estimated—little "e"--ASCVD risk score and that was actually also part of the inspiration behind this. Using eGFR is of great value because people misinterpret, don't fully comprehend the logarithmic relationship between renal function and classic creatinine and it's much the same way with these risk scores.

So yes, we designed the parameters for our eASCVD risk score so that they depend on age, sex, race, and the lipids. Yes, one could integrate that in most laboratory information systems, but one issue that has recently come up with the eGFR and other kind of risk calculators is this issue of race, which is somewhat an artificial construct.

I think that the original intentions of using race were well understood but it has unintended, sometimes negative consequences so with the estimated GFR, we're now moving away from using race and when we designed our equation, we were using the original pooled cohort risk equations, which had men, women, African-Americans, and non-Hispanic Whites.

That's another issue going forward with our equation, whether using race, and sometimes race, the assignment is not correct and some lab information systems may not have it but most of them will have a sex or race in their lipids. But that's something going forward in the future we would like to look at and see to what degree race is important in the equations. But we're trying to model the existing equations for cardiovascular risk that still use age, sex, and race.

Bob Barrett: What about your score? Is it ready for primetime now?

Alan Remaley: One can certainly implement it. I think that, for example, non-HDL cholesterol is a simple calculation and non-HDL cholesterol has many advantages over LDL cholesterol and it's a free calculation. For many years now, the recommendation was for laboratories to report non-HDL cholesterol. I think that there are things in the future that may be better, such as ApoB, and we've been discussing the utility of ApoB for many years now.

And so, the reason that I bring up non-HDL and ApoB, it's been clear enough for many years and non-HDL, but unfortunately, many laboratories still aren't reporting non-HDL. There's still a concern about whether, to what degree, ApoB will add value. One can implement this; it may be happening, but I think that we'll have to have probably

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feedback from guidelines and other laboratories looking at other populations before being widely implemented. I think it's a step forward, but many times things that make sense take a long time till they get implemented.

Anna Wolska: Our goal with our risk was to enhance and simplify it. For that, we created this estimated lipid risk score but we have to remember that the reality is that the atherosclerotic cardiovascular disease risk score prediction, it's hard to have it perfect but we do work hard, and others will work really hard to hopefully have it improved to allow for better targeting of preventive therapies.

Bob Barrett: That was Dr. Anna Wolska from the National Heart, Lung, and Blood Institute of the National Institutes of Health in Bethesda, Maryland. She was joined by her colleague, Dr. Alan Remaley also from the National Heart, Lung, and Blood Institute of the National Institutes of Health. They've been our guests in this podcast on a newly proposed estimated atherosclerotic cardiovascular disease risk score. Their paper on that topic appears in the October 2022 issue of *Clinical Chemistry*. I'm Bob Barrett. Thanks for listening.

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