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Evaluating the Updated ACC/AHA Cholesterol Guidelines

Dr. Sorrentino:
Welcome to Heart Matters on ReachMD. I'm Dr. Matthew Sorrentino, and joining me to discuss the latest in lipid management and improve our understanding of the lipid guidelines is Dr. Erin Michos, who's an Associate Professor of Medicine and the Director of Women's Cardiovascular Health, as well as the Associate Director of Preventive Cardiology at Johns Hopkins Medicine. Dr. Michos, welcome to the program.

Dr. Michos:
Thank you for having me here today.

Dr. Sorrentino:
The ACC/AHA released new cholesterol guidelines in 2013, with an update in 2018. The 2013 guidelines moved away from specific LDL cholesterol goals, but the 2018 update kind of reintroduced some specific goals, such as an LDL target of 70 mg/dL or less in our very high-risk patients. Can you help us understand why these changes were recommended and the rationale for the 70 mg/dL LDL target for our very high-risk patients?

Dr. Michos:
Yeah, so, in these latest update guidelines we focus both on absolute risk and levels. So, absolute risk does matter. That individual is at greater risk for cardiovascular disease, derived greater benefit, both absolute and relative benefit, with a more intensive lipid-lowering therapy. So there is still maintenance, for both primary and secondary prevention in the guidelines, for doing some kind of risk assessment. Even in secondary prevention, the new guidelines have delineated between high risk and at very high risk for cardiovascular disease, and they have different strengths of recommendations for this. So in the guidelines, for those who have – secondary prevention, who are not at very high risk for individuals under the age of 75 again, we're still using a statin as a Class 1 indication – a high-intensity statin to lower LDL by more than 50%. And then there was a little weaker recommendation – 2B recommendation, but that if on the high-intensity statin, or the maximally tolerated statin, the LDL is still above 70 that you could add ezetimibe, may be reasonable with a class 2B indication. But they gave a stronger recommendation for secondary prevention for very high risk, because we know that there's a difference between patients that maybe had stable angina and got a statin ten years ago and have been doing fine, versus the patients who have been in your CCU, with an acute coronary syndrome these are the ones who are even greater risk of recurrent events, so you want to treat more intensively. So the guidelines delineate this group of very high risk as those who've had a recent acute coronary syndrome event within the past 12 months or a history of a myocardial infarction, ischemic stroke, symptomatic peripheral arterial disease along with some high-risk conditions, which are so common in these patients, like an older age or having diabetes, hypertension, CKD or smoking. So it is in this very high-risk group that again, you want to use your high-intensity statin at first, to reduce your LDL by more than 50%. And then they gave a stronger indication, a 2A indication for adding ezetimibe to the statin if the LDL is above the threshold of 70. And then, additionally, in this high-risk group, they said if you're on a maximally tolerated statin and ezetimibe, and the LDL is still above a threshold of 70, they gave, a 2A indication as reasonable to addPCSK9 inhibitors in this group. Now keep in mind the U.S. guidelines are a little different than the European guidelines, in that they did consider cost. These lipid guidelines came out in 2018, and this was a little bit before we had the cost reduction with the PCSK9 inhibitors. Where the European guidelines didn't include cost in their recommendations, and as for their very high-risk individuals they had recommended an even lower LDL more than, less than 55 mm/dL would be the target in those really high-risk groups. So both absolute risk matters, as well as levels matter in these latest guidelines.

Dr. Sorrentino:

Many times we see some of these high-risk patients that are not on the maximal dose of statin. We see a lot of patients on atorvastatin, 40 mg, for example, or rosuvastatin 20 mg. Would you recommend pushing the statin to the highest dose first, or if you need a 20-30 mg/dL fall in LDL, should we be going right to a different agent like ezetimibe?

Dr. Michos:
Yeah, so it depends why they're not on the high-intensity statin. Whether they actually had a intolerance. Sometimes side effects muscle statin-associated muscle symptoms are greater on the higher intensity statins or whether it's just inertia that they were never initiated or it was never tried. I do believe in the LDL hypothesis that if we can lower LDL through up-regulation of the LDL receptor we'll have meaningful results, so I frequently add ezetimibe to a statin. It might not be high-intensity if the patient does not wish to go up to the highest dose, or had intolerance with the highest dose. But many patients were never tried or never offered a high-intensity statin and I think that's a missed opportunity. Certainly, we have data supporting that. But the good news, this is beyond the guidelines, because the guidelines came out in 2018, but I'm really excited that we have new tools in our tool kit that can further lower LDL so I think that's why the levels do matter, perhaps more than just the drugs. Obviously, you wanna use drugs that have proven outcome benefit. The FDA approved, earlier this year bempedoic acid can be used as an adjunct to diet and maximally tolerated statin for patients who had ASCVD or heterozygous familial hypercholesterolemia if they need further LDL lowering. Now, of course, the outcome trial for bempedoic acid is ongoing, but I'm certainly encouraged by any drugs that can lower LDL. And this drug may be particularly of interest because it is oral and it doesn't precipitate in skeletal muscles, so it might be particularly useful for those patients who are so common in our practice, that are reporting statin-associated muscle symptoms. But probably the one I'm the most excited about on the horizon is the new PCSK9 inhibitor through the small, interfering RNA inclisiran I'm very excited that just dosing this twice a year every six months, that you can reduce LDL by 50%. I mean, that's pretty remarkable just one more time a year than your flu shot, and you can lower your LDL by 50%. And so I think this is undergoing evaluation and outcome trials as well, but I think this may be really important in the future, particularly younger adults who maybe have FH to improve adherence because we know that, unfortunately, adherence with statin therapy tends to wane over time.

Dr. Sorrentino:
For those just tuning in, you're listening to Heart Matters on ReachMD. I'm Dr. Matthew Sorrentino, and here with me to discuss the management of our high-risk patients and treat their lipids is Dr. Erin Michos. Dr. Michos, I'd like to just shift a little bit to primary prevention. I think we all know that some of our secondary prevention, high-risk patients, we need to be very aggressive on, but are any of our primary prevention patients be considered very high risk, and would they also be candidates for PCSK9s and bempedoic acid and some of these newer agents?

Dr. Michos:
That's a great question. So of course our primary prevention guidelines are risk-based. For everybody, of course, we endorse a healthy lifestyle. The best way to prevent cardiovascular disease is to follow a healthy lifestyle throughout the lifespan. Now the primary prevention guidelines still recommend that for adults age 40-75 without diabetes and without cardiovascular disease to start with a 10-year risk assessment using the pooled cohort equations. And then, once you estimate 10-year risk, you can bend patients into these four groups low risk patients: less than 5% 10-year risk, lifestyle might be enough; high-risk patients with a 10-year risk above 20%, lifestyle plus drug therapy, high-intensity statins; and then there's this large group in the middle, these borderline, the 5-7.5%, 10-year risk and the intermediate, 7.5-20% 10-year risk group, where there may be some more uncertainty. So particularly for this borderline intermediate-risk group, the guidelines introduce what they call "risk-enhancing factors." So these are factors that are already clinically you should hopefully already know about your patients. The guidelines acknowledge that after you estimate 10-year risk, and after you consider these risk-enhancing factors, there can still be uncertainty about a patient's risk, or patient's indecision about the net benefit of statins for them. And so, in these cases where there is risk indecision, you can get a coronary artery calcium score. You're actually measuring atherosclerosis, and we know that individuals with a zero score it's not zero risk, but a zero score is associated with a low risk over ten years, like a 0.1% per year risk. And so these individuals may wish to defer statin therapy if they so desire, but really any non-zero score crosses above the 7.5% 10-year threshold of events in ten years, and so the guidelines does favor statins for anybody with a non-zero score. But there is a graded fashion, of course, with the higher the score, the more risk. So you got back to the question about should we use non-statin add-ons to statins in primary prevention. And so this wasn't addressed in the guidelines, so I'll be clear that I'm sort of now going into sort of my opinion and what other experts say but weren't in the guidelines. But indeed subclinical atherosclerosis is sort of this intermediate phenotype between primary and secondary prevention. So what do I do in my clinical practice? Well, if somebody has a lot of disease, as manifests by an elevated coronary calcium score, I actually do aim for an LDL less than 70 in these individuals by adding a ezetimibe to a statin. This is a little bit of an emerging area, but in some of these patients, particularly who have a poorly controlled LDL, and a lot of subclinical disease, I've used that to try to get pre-authorization approval for PCSK9 by arguing that their extensive, you know subclinical vascular disease might qualify them for PCSK9 inhibitors, and that has worked in some cases. So I've used PCSK9 selectively in these individuals, usually more often in individuals who have a diagnosis of FH for primary prevention.

And then bempedoic acid has only come out this year. The label for bempedoic acid is for secondary prevention and heterozygous FH. But that being said, I actually think the space for bempedoic acid might have the most role, because it's oral, it's exactly this primary prevention group who maybe can't tolerate statins because of statin-associated muscle symptoms, which we know we don't have that problem with bempedoic acid. So I actually am interested in using bempedoic acid in the primary prevention population, but that's outside of the FDA label.

Dr. Sorrentino:
As a final quick question, I've noticed that the guidelines do specifically give an age cutoff of 75 years in our primary prevention patients. Should we consider stopping lipid-lowering therapy at that age, or reduce the dose in patients over age 75?

Dr. Michos:
So, you know, aging is very heterogenous, and I wouldn't make the decision just based on age. I would look at their overall life expectancy and their quality of life. I generally recommend keeping patients on a statin if they're already on a statin. There is observational data, from France that have shown that older adults who stop their statin after age 75 actually have an increased risk of events, so there is a suggestion that withdrawal of statins in older adults may be associated with adverse effects. I take each patient as an individual, as part of shared decision-making, I wouldn't make the decision just based on any absolute age cut point. But it is true that the guidelines did kind of differentiate the intensity. For secondary prevention, above 75 they still gave a class 2A indication of initiating and continuing moderate or high-intensity statins. And then for primary prevention, the guidelines actually gave a lot of options. They said if someone is above 75 but had a lot of comorbidities that was reasonable to stop statins. They also said it was reasonable to continue statins. And then they even give a third option which is something that sometimes I use, is that they said that you could, for those age 75 to 80 get a coronary calcium score. So even the guidelines give a lot of options, including the potential option was 2B indication a little bit weaker than in the younger adults, but that you even could use coronary calcium in this age group too, to guide shared decision making.

Dr. Sorrentino:
Well, with those final thoughts in mind, I want to thank my guest, Dr. Erin Michos, for joining me to share her insights on how to utilize the cholesterol guidelines and manage our patients' lipid levels. Dr. Michos, it was great having you on the program today.

Dr. Michos:
Thank you so much for having me. I enjoyed talking with you.

Dr. Sorrentino:
I'm Dr. Matthew Sorrentino. To access this and other episodes in our series, visit reachmd.com/programs/heartmatters, where you can be part of the knowledge, and thank you for listening.