TOM ALLISON: Greetings. I'm Tom Allison, cardiovascular specialist at the Mayo Clinic. During today's roundtable, we'll be discussing lipoprotein (a), and I'm joined here by my colleague, Dr. Steve Kopecky, who specializes in this area. Welcome.

So Steve, here's our first question today. So can you tell-- what is lipoprotein (a), and why do we have it? What role does it play?

STEVE KOPECKY: Yeah, good question. Lipoprotein (a) is really a combination of a couple of standard molecules that we all know about. One is an LDL cholesterol-type molecule or low-density lipoprotein.

The second is an apolipoprotein (a), which is bound to the LDL-like molecule at the apoB receptor with a disulfide bond. Now, what does that mean? Well, it's a cholesterol-type molecule, basically is what it is.

TOM ALLISON: OK. And understand there are different sizes of these lipoprotein (a).

STEVE KOPECKY: Yes. There are different sizes. Because the apolipoprotein portion can have different kringles. Some are very big. Some are very small. The smaller ones seem to be the more atherogenic or the ones that cause more problems.

TOM ALLISON: Like the small dense LDL.

STEVE KOPECKY: Like the small dense LDL. Now, one of the things comes up is, why do we even have this molecule? It seems to be involved with clotting. It may promote some clotting, which may not be a good thing, and although years ago, if you had some trauma, it may help wound healing, may help clotting, may help in childbirth, that you have some-- you don't bleed as much. So there may be a reason that we actually have it in our bloodstream.

TOM ALLISON: Now, what evidence do we have that this causes heart disease or contributes to our risk of heart disease? And I presume we're talking about coronary artery disease, right?

STEVE KOPECKY: Yeah, or really any ischemic stroke also could be involved. And so first, you look and say, what is it about this molecule that may be causing some problems? Is there a reason? Well, if you look at the LDL particle, we know that that can actually promote atherosclerosis.

We also know that the apolipoprotein particle is similar to plasminogen. So it can promote clotting. It inhibits fibrinolysis. And the third thing is it's an inflammatory molecule. So it does three things-- causes the atherosclerosis, causes the plaque rupture with inflammation, then causes the clotting at the site of plaque rupture.

Now, if you look at some big observational studies, say the INTERHEART study, which looked at many nations and continents around the world, the evidence shows that if they had an elevated lipoprotein (a), they had increased risk of MI.

If you look at some Mendelian randomization studies, where they looked at large numbers of patients, subjects, if you have an elevated lipoprotein (a), you also had an increased risk of myocardial infarction and stroke.

TOM ALLISON: Now, am I correct that some recent trials have shown that the on-treatment level of LPA in a clinical trial actually correlates with the event risk?

STEVE KOPECKY: Yeah. If you look at some LDL cholesterol trials where they gave statins, got the LDL under control, that the best predictor at that point of recurrent events was actually the lipoprotein (a) level, not the LDL level.

TOM ALLISON: OK, interesting. So what is the cut point? I mean, at what level do we see the increased risk?

STEVE KOPECKY: Yeah.

TOM ALLISON: And I know there's a little controversy about what the cut point is.

STEVE KOPECKY: Yeah, because a lot of it's observational. And if you look at the world, you know, 80% of the world has a normal, with the normal being a less than 50, say. In the US, we have an average of about 20 milligrams per deciliter. If you look at certain ethnic groups, the Asians, Caucasians are very similar. African-Americans, looks like Arabs also have higher levels, maybe two or three times higher levels.

The question is, how much of that goes into risk? And that's not quite clear. Is an African-American's risk higher because they have a higher apo or LP little a or not. That really hasn't been worked out.

TOM ALLISON: OK. So 50, is that the number?

STEVE KOPECKY: Yeah. In general, the average number is 20 over 50 we start to call increased risk. That's what most guidelines have said. If you're going in nanomoles per liter, it's more like 100 or 125 is elevated risk.

TOM ALLISON: Yeah. Now, in the Prevention Clinic at Mayo, do you measure LPA on everybody or are there specific groups that you think it's more important?

STEVE KOPECKY: Yeah, people have said we should measure it in everybody. I don't think we're quite there yet, mainly because we don't have a treatment so much yet, but also because if the people that may benefit the most are the ones that come in with early atherosclerosis or they have a family history. They say, gee, my two-year older brother just had a heart attack at age 48. That may be a good time to check it.

Patients that have recurrent atherosclerotic events in spite of optimal treatment, that has been made a case to track those patients. And then patients that have FH, familial hypercholesterolemia. About one in five people have elevated lipoprotein (a). Maybe one in three patients with FH have elevated lipoprotein (a). It increases risk. So that's been standard we check.

And the last group is the aortic stenosis. Bicuspid aortic valve is probably the prototype of that, that there is evidence that elevated lipoprotein (a) with bicuspid aortic valve, they have more rapid progression of the aortic stenosis.

TOM ALLISON: Now, that's new, right?

STEVE KOPECKY: That's fairly new.

TOM ALLISON: That hasn't been part of the traditional.

STEVE KOPECKY: That has not been, but I think we're starting to think of that when we look at these patients with the bicuspid aortic valve.

TOM ALLISON: OK. So now you have the lipoprotein (a), and it's over 50, what do you do?

STEVE KOPECKY: Yeah. Well, first off, you make sure that when we're talking about over 50, we're taking about over 50 milligrams per deciliter.

TOM ALLISON: Yeah.

STEVE KOPECKY: And versus like 125 nanomoles per liter. The reason that's important to differentiate is the milligrams per deciliter is kind of the mass concentration. The nanomoles per liter is the particle concentration. And as you implied a minute ago, the particles are different size.

So we can't like convert one to the other like we can do LDL or something or HDL. It has to be a completely different measurement. And so there's a push right now to say let's have a single way of measuring the nanomoles per liter, which would take into account the size, the particle size.

TOM ALLISON: And that's 125.

STEVE KOPECKY: That would be like, 125, yeah. So if it's high, what do we do? Well, we know we can-- lifestyle is always very important. Always work on lifestyle, although 80%, 90% of your LPA level is genetically determined. It's a kind of a co-dominant inheritance, meaning you can get a gene from each parent and both will raise it more.

You can give things like niacin or hormone replacement therapy. We know that can lower it some, but it doesn't lower events. In fact, it may increase cardiovascular events. So it's not recommended. Statins don't affect it. The PCSK9s lower it maybe 25%, but they're not indicated for that.

And then there's things like lipoprotein apheresis, which can be helpful in a very small percentage of patients. So we have some treatments, the PCSK9, but it's not indicated for lowering it.

TOM ALLISON: Now, I understand, am I correct, there is a new drug under development, that I think was presented at the American Heart Association, that has a significant lowering, like 80% decrease, but it's not available.

STEVE KOPECKY: Right. It's still going through clinical studies in antisense oligonucleotide that actually lowers it significantly, as you said. We don't know the outcomes yet. It sounds like it's a good idea, but we've got to get the outcome studies to show that it really benefits patients.

TOM ALLISON: No dietary therapies.

STEVE KOPECKY: Yeah. Your lifestyle is important, but it doesn't really lower your lipoprotein (a). It lowers your risk, but that's separate from the LPA.

TOM ALLISON: OK. Steve, before we end, any other points we should make about this?

STEVE KOPECKY: Well, I think it's always good to look at the guidelines. And what do the guidelines say? The recent ACC/AHA lipid guidelines say you should consider a lipoprotein (a) over 50 milligrams per deciliter or 125 nanomoles per liter as a risk enhancer.

TOM ALLISON: Risk enhancer, yeah.

STEVE KOPECKY: So you're a little more aggressive in treating those patients. It may be the risk enhancer you use with different types of patients, primary or secondary prevention. And it's always something I think worth checking, especially if you have patients that have recurrent events or early events or a family history of early events, because it helps you be more aggressive in treating the patients.

TOM ALLISON: Do you ever bring in a patient's family and check it?

STEVE KOPECKY: Oh, yeah. Cascade screening.

TOM ALLISON: Like you're 40 years old, you have an MI. Should your brother, your kids get it checked?

STEVE KOPECKY: Yes. And we actually have a letter we give patients. Once we've checked them and it's elevated, we say, here, give this letter to your first-degree relatives. You don't have to talk to them. The letter explains everything. It says you've had this elevated lipoprotein (a). It can being associated with increased risk of heart disease. Take this letter to your primary care provider, and they can check it for you.

TOM ALLISON: Good. Good. Steve, thanks for this update and for your insights. And I want to thank everyone for joining us on the heart.org Medscape Cardiology. Thank you.