Lipoprotein A - A Cardiovascular Risk Factor Commonly Ignored

Announcer: Welcome to the Mayo Clinic cardiovascular continuing medical education podcast. Join us each week to discuss the most pressing topics in cardiology and gain valuable insights that can be directly applied to your practice.

Dr. Kopecky: Hello, I'm Stephen L. Kopecky, M.D., a preventive cardiologist at Mayo Clinic in Rochester, Minnesota. A great pleasure to be speaking with Vlad C. Vasile, M.D., Ph.D., today who is both, has an appointment, in the Department of Cardiovascular Diseases in preventive cardiology and in our cardiovascular lab. So welcome, Dr. Vasile.

Dr. Vasile: Thank you very much, Dr. Kopecky. It's a pleasure for me to be here as well.

Dr. Kopecky: So we'll be talking today about a molecule, an entity that's getting a lot of press — lipoprotein (a). And you've studied this quite a bit, Vlad. Why, why is, what is LPA and why is it not good for us?

Dr. Vasile: Dr. Kopecky, lipoprotein (a) is a circulating protein that associates with a cholesterol complex. It does comprise two particles. One is an LDL particle, LDL-like particle or bad cholesterol-like particle. And the other one is apolipoprotein A or simply called APOA, which wraps around the first particle. So this is really the structure of lipoprotein (a). It is associated with increased atherosclerotic cardiovascular events in an independent manner, independent of the traditional risk factors such as LDL, hypertension, smoking or diabetes. It has also been associated with valvular heart disease such as aortic stenosis. Studies have shown that approximately one in five people have elevated lipoprotein (a). And these elevations have a strong genetic component. And unfortunately to date, we don't have any specific drugs that reduce levels or, reduce levels and at the same time influence outcomes.

Dr. Kopecky: So it, if I understand you then, the lipoprotein (a) will actually form plaque because it has an LDL molecule. It is a proinflammatory molecule also? Is that correct?

Dr. Vasile: That is correct.

Dr. Kopecky: And is it a pro-clotting molecule?

Dr. Vasile: One of the components of the lipoprotein (a), is very similar with some clotting factors and therefore we believe that it also has clotting properties.

Dr. Kopecky: So it's not good as you explained; it causes the plaque, it ruptures the plaque and it clots at the rupture. So that I can certainly understand it's not so good. So do we have any drugs to treat lipoprotein (a)?

Dr. Vasile: Currently we do not have any drugs that reduce the lipoprotein (a) and influence outcomes or reduce the bad outcomes. We do have some drugs that reduce the level of lipoprotein (a), such as niacin. Niacin is an older drug that was used many years ago to reduce cholesterol. It has been associated with a lot of side effects. So generally speaking, we needed to

pretreat these patients before we started them or niacin or every time they took niacin they needed to be pretreated. Additionally, some studies have shown that even if you reduce the lipoprotein (a) by niacin, you don't influence outcomes. Therefore, we believe that at this point, we don't have sufficient evidence to use niacin in clinical practice to reduce lipoprotein (a). Other, more novel drugs such as PCSK9 inhibitors also reduce the lipoprotein (a). However, we don't have data as far as outcomes. So again, these have not made their way into the guidelines, at least as of yet.

Dr. Kopecky: And then the third antilipid drug we use, statins. What do they do, they raise it, they lower it, they effect it at all? We know the statins don't really change the outcomes, though.

Dr. Vasile: That is correct and I'm not aware of, you know, there are some changes that I see with initiation of statins in patients with elevated lipoprotein (a). But our approach in treating elevated lipoprotein (a) is not really etiologic. We do not address the lipoprotein (a). We don't attempt to decrease or change the lipid profile with statins. Rather, we address the patient from a very comprehensive perspective, very aggressively trying to reduce all the risk factors for coronary artery disease: We treat blood pressure, cholesterol, all those things. In addition to that, I recommend all, the majority of the patients with elevated lipoprotein (a) to start a statin and also a baby aspirin, again, in an attempt to reduce the overall cardiovascular risk.

Dr. Kopecky: And then what about lifestyle, you know, diet, activity? Do we know that benefits them and do you recommend to patients?

Dr. Vasile: I absolutely recommend it to all of the patients that have elevated lipoprotein (a), again, as an overall and comprehensive approach to reducing the coronary artery disease risk.

Dr. Kopecky: Very good. Now, why do some people have high levels of LPA and others do not; is it genetically transmitted?

Dr. Vasile: We believe that elevation in lipoprotein (a) has a very strong genetic component. And therefore, every time I have a patient in the clinic that has elevated lipoprotein (a), I always recommend that all first-degree relatives be screened for lipoprotein (a), because there is a very strong genetic component.

Dr. Kopecky: And what do we know about the genetics? Is it a dominant gene or how does it work?

Dr. Vasile: It is an autosomal dominant gene. But generally we don't test for that particular gene.

Dr. Kopecky: So if you know the LPA level, you don't need to check the genetics.

Dr. Vasile: We don't need to check the genetics because it wouldn't influence what we do from the perspective of recommendations and interventions.

Dr. Kopecky: Ok. Very good. Now, you mentioned if you have a patient in clinic with a high LPA, what's the reason we would check an LPA in a patient, anyway?

Dr. Vasile: This is a very good question because the topic is quite controversial. The current US guidelines are not very specific in this regard. If you look at the ACC guidelines, they endorse lipoprotein (a) testing in patients with familial hypercholesterolemia, with a 2a level of confidence. But if you look at other US societal guidelines, they extend these recommendations. If you're peeking at our colleague, our cardiology colleagues in Europe, they recommend a universal testing of lipoprotein (a) as a one-time lifetime testing in everybody. In my practice I tend to test or follow the European Society of Cardiology guidelines and test pretty much everybody once for lipoprotein (a), because I think this is a condition that is often missed. In addition to this screening approach, I also test lipoprotein (a) for patients that have or are suspicious of familial hypercholesterolemia, or patients that have atherosclerotic disease, or patients that had a personal history or a family history of premature coronary artery disease.

Dr. Kopecky: When you do find a patient that has early ASCVD and you find they have a high LPA, what do you, do you give the patient a letter to give the family, or do you call the family in, or how do you manage that?

Dr. Vasile: I generally call the patient and start some sort of interventions. One thing that is important know about lipoprotein (a) is that the level is important. There is a dose-response effect, meaning that the higher the level of lipoprotein (a), the higher the risk. And this has been recapitulated in many studies. And so depending on the level of lipoprotein (a), I may be more aggressive with my recommendations. In addition to the lifestyle changes, I may recommend a moderate or a higher intensity statin. And so I want to discuss with the patient all these things over the phone rather than simply communicating, because it's not just a simple result of a blood test. It has many implications for the patient and for their first-degree relatives. So I prefer to call the patient and have a conversation on the phone.

Dr. Kopecky: Very good, Dr. Vasile. Now is, if you have two patients, A and B that aren't related, and they both have a high LPA, is their risk the same or is there a difference in LPA and different people?

Dr. Vasile: There are certain studies that suggest that we should also look at the particle size for lipoprotein (a) because there may be differences in risk depending on the size of these particles. However, I think these studies need more refinement. We actually need more studies to draw a definitive conclusion from that perspective. And at least at Mayo Clinic, currently, we do not offer this as a routine testing.

Dr. Kopecky: Very good. Well, this is a fascinating discussion, Dr. Vasile, about lipoprotein (a) and it's great to hear you say that you check it very frequently in people with early ASCVD or in families that may have it. Helps you with valve disease, aortic stenosis. And it's a molecule it sounds like we'll hear more and more about as drugs may come along to treat it, since we have no treatment now. Any final words, Dr. Vasile?

Dr. Vasile: No, I think one recommendation that I would give to all my cardiology colleagues who are taking care of patients in the preventive clinic, for example, is do not miss screening for lipoprotein (a). I see this over and over. I see patients in the clinic and I see patients in the

hospital setting that have elevated lipoprotein (a) and this has been missed for many years. Another thing that I think it is important for us cardiologists not to forget, is that once you've identified an elevation in lipoprotein (a), we should be very aggressive about screening all first-degree relatives. Because again, this is a thing that is, can be easily missed, and in this way we can miss patients.

Dr. Kopecky: Even if we can't treat it, it's good to know their risks, and if the risk has increased they are other things they can do. Well. Fascinating discussion, Dr. Vasile. Thanks for joining us today.

Dr. Vasile: Thank you very much, Dr. Kopecky. I appreciate being here.

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