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The Risk of Lipoprotein(a) in ASCVD

You're listening to ReachMD. This medical industry feature, titled "The Risk of Lipoprotein(a) in ASCVD" is sponsored by Amgen. This program is intended for physicians.

Here's your host, Dr. Pam Taub.

Dr. Taub:
Cardiovascular risk is influenced by several factors. One factor in specific is dyslipidemia in which we tend to focus on elevated LDL cholesterol levels. In addition, we also focus on modifying lifestyle factors such as physical inactivity, tobacco use, blood pressure, and unhealthy diet. But, over the last decade, we have come to recognize an independent, genetically determined risk factor for atherosclerotic cardiovascular disease called lipoprotein(a), also known as Lp(a). In this episode, we will discuss why it's important to recognize elevated levels of lipoprotein(a) as an additional cardiovascular risk factor and important contributor to residual risk in our patients with atherosclerotic cardiovascular disease.

I'm Pam Taub, I'm a Cardiologist and Professor of Medicine at UC San Diego and I'm joined by my friend and colleague, Dr. Bob Rosenson.

Dr. Rosenson:
Well Pam, I serve as Director of Metabolism and Lipids at the Mount Sinai Health System and I'm also Professor of Medicine at Mount Sinai Heart at the Icahn School of Medicine in New York.

Dr. Taub:
To start us off, Bob, can you give us a high-level overview of lipoprotein(a)?

Dr. Rosenson:
Yes, Pam. Lipoprotein(a) is an LDL like particle, and it's comprised of apolipoprotein B100, a shared protein with other atherogenic lipoproteins and an apolipoprotein(a). The apolipoprotein(a) or Apo(a) protein distinguishes Lp(a) from LDL. It's important to recognize that Apo(a) is heterogeneous and are multiple isoforms that account for some of the differences in cardiovascular risk as well as some of the racial and ethnic differences in Lp(a) levels. In addition, Lp(a) is a major transporter of oxidized phospholipids. And oxidized phospholipids drive a pro-inflammatory response that further accentuates the cardiovascular risk associated with lipoprotein(a).

We recognize that lipoprotein(a) is primarily genetically determined, and it is non-responsive to conventional lifestyle changes such as a low saturated fat diet, weight loss, and exercise. However, as you mentioned in your introduction, improving all the risk factors that contribute to cardiovascular disease mandate adoption of a healthy lifestyle, as well as treatment of those risk factors according to national guidelines.

I want to ask you Pam, which patient populations are more susceptible to having elevated levels of lipoprotein(a)?

Dr. Taub:
Well, elevated lipoprotein(a) concentrations are more prevalent in African and South Asian individuals. But by using the cutoff of 50 mg/dL, it's estimated that approximately 1.4 billion people globally have elevated levels of lipoprotein(a). I find this number pretty astounding and it's something that we need to be aware of because 1 in 5 people have elevated lipoprotein(a) levels. And lipoprotein(a) is measured using a simple blood test. There are two different assays; one that measures lipoprotein(a) in nmol/L and another that measures it in mg/dL.

With that background in mind, what do the current guidelines and scientific statements say about lipoprotein(a) levels and cardiovascular risk, Bob?

Dr. Rosenson:
Well, lipoprotein(a) levels are measured differently, and different professional societies recognize those differences. And keeping the historical literature in mind, both measures are often referred to. The mass concentration in mg/dL and the molar concentration in nmol/L. When you're reading the literature, it's important to keep in mind there are no direct conversion factors between the two currently used methods. And so, one just has to be aware of those cutoff values.

Across the American College of Cardiology, American Heart Association guidelines, the National Lipid Association statements, the European Society of Cardiology/European Atherosclerosis guidelines, and HEART UK, the range of elevated lipoprotein(a) is considered to be between 100 to 430 units of nmol/L and 50 to 180 units of mg/dL. For those of you joining online, there's a detailed slide to show the differences.

All of the societies agree that the key indications for lipoprotein(a) measurement should be largely in individuals with a family history of early onset atherosclerotic cardiovascular disease and those with a personal history of atherosclerotic cardiovascular disease. It's interesting to note that the 2021 AHA scientific statement recognizes that elevated lipoprotein(a) is genetically determined, causally associated with cardiovascular disease, and it's a prevalent risk factor for atherosclerotic cardiovascular disease, and it impacts on clinical decision-making and risk management.

Now, how often should clinicians be measuring lipoprotein(a) in their patients? Pam, what do you do in your practice?

Dr. Taub:
In my practice, I follow the European Society of Cardiology and European Atherosclerosis Society guidelines that specifically recommend that lipoprotein(a) measurements should be considered at least once in each adult person's lifetime to identify those who may have a lifetime risk of atherosclerotic cardiovascular disease that's similar to patients with heterozygous familial hypercholesterolemia. So, every patient that sees me will get a lipoprotein(a) checked.

Lipoprotein(a) is typically not measured in most patients before they have or even after they have an atherosclerotic cardiovascular event, and it's important that we start thinking about measuring lipoprotein(a) in all of our patients because what we're seeing is this is an evolving area and determining lipoprotein(a) levels can be important in terms of management.

The NLA and American Heart Association recommend that we test lipoprotein(a) for those with a family history of atherosclerotic cardiovascular disease. So that includes a broad range of individuals. I do believe the European guidelines are more advanced and I hope the updated American guidelines will also recommend checking lipoprotein(a) at least once in each adult person's lifetime.

For those who are tuning in, you're listening to ReachMD. I'm Dr. Pam Taub and I'm speaking today with Dr. Bob Rosenson about lipoprotein(a), also known as LP(a) and why it's important to recognize elevated lipoprotein(a) as an additional cardiovascular risk factor and as an important contributor to residual risk in our patients with atherosclerotic cardiovascular disease.

Bob, now that we've taken a look at elevated lipoprotein(a), let's delve into how lipoprotein(a) impacts cardiovascular risk in general and residual risk. Can you share some recent data from major cardiovascular outcome trials on elevated lipoprotein(a)? And can you talk about why it's an additional risk factor to consider in our patients who have atherosclerotic cardiovascular disease including acute coronary syndrome?

Dr. Rosenson:
So, Pam, there have been multiple studies in patients with stable cardiovascular disease that have shown that a high lipoprotein(a) on the background of statin therapy is associated with increased residual risk. Subsequently, there have been two large studies that evaluated baseline lipoprotein(a) levels for their association with cardiovascular disease. Studying individuals with stable coronary disease and other forms of atherosclerotic cardiovascular disease, the FOURIER trial, and another study in post-ACS population the ODYSSEY OUTCOME study.

In a prespecified analysis of the FOURIER trial from 2019, in the ASCVD placebo population, when lipoprotein(a) levels were measured at baseline, the third and fourth quartile of lipoprotein(a) levels were associated with an increased risk of cardiovascular events, including myocardial infarction.

In a post-hoc analysis of the ODYSSEY OUTCOMES from 2020 that an ACS placebo population when Lp(a) levels were measured at baseline, higher Lp(a) levels were associated with an increased risk of future cardiovascular events.

I just wanna make one comment about measurement of lipoprotein(a) levels, post-ACS, post-myocardial infarction. Although lipoprotein(a) is genetically determined, its synthesis can increase under circumstances of inflammation, interleukin-6 drives the liver production of lipoprotein(a).

When it comes to the risk of myocardial infarction, Pam, what do we know about the role of elevated lipoprotein(a) levels?

Dr. Taub:
Elevated lipoprotein(a) is associated with a higher risk of cardiovascular disease, particularly myocardial infarction, as shown by epidemiological studies, meta-analysis, mendelian randomization, and genome-wide association studies, as well as analyses of clinical trials that Bob just highlighted.

An analysis from a large epidemiological study showed that elevated lipoprotein(a) levels may be associated with an increased risk of myocardial infarction. The risk of coronary heart disease, particularly myocardial infarction is linearly associated with increasing levels of lipoprotein(a). There is almost a three-fold increase in risk of myocardial infarction comparing the reference group with less than 5 mg/dL of lipoprotein(a) to the group that has a lipoprotein(a) level that is greater than 117 mg/dL.

Well, Bob, we've covered a lot of ground today, but before we close, are there any take-away messages that you'd like to share with our audience?

Dr. Rosenson:
Well, Pam, lipoprotein(a) is proatherogenic, proinflammatory, and prothrombotic, and it represents in an independent, genetically inherited risk factor for atherosclerotic cardiovascular disease. We're learning more and more about lipoprotein(a) associated residual risk. But the evidence suggests there's a causal relationship between high LP(a) levels and increased risk of atherosclerotic cardiovascular events, including myocardial infarction and stroke, calcific valvular aortic stenosis, and peripheral arterial disease. Guidelines and scientific statements recommend that we should be measuring lipoprotein(a) in patients with atherosclerotic cardiovascular disease. It's important to recognize that LP(a) levels are an emerging cardiovascular risk factor and a source of residual risk in patients with atherosclerotic cardiovascular disease.

Dr. Taub:
Well, that was a great summary Bob as we come to the end of today's program. I hope the audience will share in our enthusiasm and passion for lipid management and also recognize that lipoprotein(a) is an additional cardiovascular risk factor in our patients with atherosclerotic cardiovascular disease. It was great speaking with you today.

Dr. Rosenson:
Well, great working with you, Pam. And, you know, we're both engaged in lipoprotein(a), research trying to help our patients who suffer from this genetically determined lipoprotein. We look forward to future work in this area.

Announcer:
This program was sponsored by Amgen. Dr. Pam Taub and Dr. Robert Rosenson have been compensated by Amgen for participating in this program. If you missed any part of this discussion, visit reachmd.com/industry feature, where you can Be Part of the Knowledge.

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