Transcript Details
This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: https://reachmd.com/programs/heart-matters/a-look-at-lipoproteina-key-screening-treatment-strategies/14992/

ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

A Look at Lipoprotein(a): Key Screening & Treatment Strategies

Dr. Cheeley:
According to the CDC, patients with familial hypercholesterolemia, or FH, or who show signs of coronary heart disease are at an increased chance of having heart attack, stroke, and aortic stenosis due to high levels of lipoprotein (a). So how can me manage lipoprotein (a) in our patients?

You're listening to *Heart Matters* on ReachMD. I'm Dr. Mary Katherine Cheeley, and I'm speaking with my fellow ReachMD host Dr. Alan Brown. He's the Director of the Division of Cardiology as well as the lipid clinic at Advocate Lutheran General Hospital and a past President of the National Lipid Association. He's also the lead guitarist in a band, which I think is pretty cool. Today we will be discussing lipoprotein (a).

Dr. Brown, thanks for joining me.

Dr. Brown:
Yeah, thanks a lot, Mary Katherine. It's great to see you again.

Dr. Cheeley:
Agreed. So give us a little bit of a primer. Tell me what is some background on lipoprotein (a)? And how do you say it?

Dr. Brown:
We say LP(a), but lipoprotein (a) is probably more correct. And this is a lipid particle that we've been aware of for quite some time. We knew that this particle existed, that patients who had high levels had a significantly increased risk of developing atherosclerotic cardiovascular disease, but even to this day, we're not a hundred percent sure how the particle is cleared from the body. We've tried a lot of different medicines to adjust it in the past including estrogen and high doses of niacin, which have their own issues giving them to patients, but no real prospective randomized trial had been done to show whether it should be a target of therapy until a couple of new classes of medications which are now available have been developed that actually predictably lower the levels of LP(a).

Dr. Cheeley:
What patients do you look for LP(a) or check LP(a) in?

Dr. Brown:
Well, that is a great question. It's been a little bit of a controversy recently based on the zealots about LP(a) versus some of the more conservative folks. We know that it's an autosomal-dominant trait, so we definitely think about it in families that have a high incidence of premature atherosclerosis. We also look for it in patients who have unexplained progressive atherosclerosis whose lipids and other risk factors might not be that severe, but yet they tend to be progressing with coronary disease closing down their bypass graphs and having other cardiovascular events, and some folks think it's appropriate to test on everybody because it's highly prevalent. About 20 percent of the population has elevated LP(a). And in particular, in the modern era where we're starting to have therapies that can affect it, it

makes sense that in particular if those therapies turn out to reduce cardiovascular events, it would be reasonable to test on everybody. And then if you have a patient who you know has elevated LP(a), cascade screening of the family would be appropriate.

Dr. Cheeley:
So patients who have a less than anticipated response to their lipid-lowering therapy?

Dr. Brown:
Particularly the statins because, LP(a) doesn't go down with statins. In fact, it may go up slightly. There was a recent very nice article showing that that doesn't necessarily increase risk. You still get a reduction in risk on the statins, but sometimes the LP(a) can be measured as part of the LDL fraction, and therefore, you would see the LDL not going down when you added a statin, and that is sometimes related to elevated LP(a), so that's a very good point.

Dr. Cheeley:
As a pharmacist, I immediately jump to "Well, they're not taking their drug," but that's not necessarily the case. We have patients who religiously pick up their medicines. I know that they're taking it, and they still just only get maybe 20, 25 percent from a high-intensity statin that we would anticipate a 50 percent reduction, and so we check LP(a), and lo and behold it's 300.

Dr. Brown:
Yeah. You're going to see that particularly in the people with really high LP(a)s. There can be other reasons why patients are refractory to statins, but that's a really good idea is to think about it in a patient that doesn't seem to respond.

Dr. Cheeley:
Are there any patient populations or ethnic groups that you tend to see higher LP(a) levels at baseline?

Dr. Brown:
Yes. You do see higher baseline LP(a)s in African Americans, for example, and whether the cut points should be the same in terms of risk, that is also a debate. Maybe not. Maybe the numbers are a little bit higher, but that's something that we're going to have to get our arms around as we think about having an approach once the therapeutic agents and if the therapeutic agents turn out to show benefit.

Dr. Cheeley:
Does that impute kind of a higher risk stratification for those folks or—because you mentioned a higher cut point—does 50 become a hundred, or is truly a hundred just as risk-prevalent in white folks as in black folks?

Dr. Brown:
And you can correct me if I'm wrong, but my recollection is the risk is slightly different based on the same cut points, so that's why the normal cut points are going to have to be a little bit different based on ethnicity.

Dr. Cheeley:
Yeah. I think it's really cool that we're still learning so much about these things. Even in the last 10 or 15 years, I feel like our body of evidence and what we know about lipid management has grown exponentially in the last decade, which is really cool because when I started it was "Oh, give him statin. Give him ezetimibe," and we were kind of done at that point.

Dr. Brown:
Every month we learned something new. And LP(a) is a great topic where we absolutely are learning stuff new.

We don't see 20 percent of the population with rampant atherosclerosis even though 20 percent of them have elevated LP(a), and so I think we are finding that there are certain risk factors associated with LP(a) or certain markers of risk that help us stratify who with elevated LP(a) we have to worry the most about. For example, those people with hsCRPs over 2, they have a linear association with LP(a) and risk. The higher the LP(a), the higher their risk. But the people with HsCRPs below 2 seem to have a pretty flat risk even with elevated LP(a). And calcium scoring, which intuitively makes a lot of sense to all of us, that also has a very good correlation with the risk when associated with LP(a), so a person with high LP(a) with a zero calcium score at least over the short term has a significantly lower risk than someone who has evidence of calcification, and the higher the calcium score the greater the correlation with risk with LP(a).

So these are things that we're going to have to look to as we try to decide who should we be treating.

Dr. Cheeley:
For those just joining us, you're listening to *Heart Matters* on ReachMD. I'm Dr. Mary Katherine Cheeley, and I'm speaking with Dr. Alan Brown about patients with lipoprotein (a).

All right. I'm going to ask you a super controversial question. Where do you fall on the measurement and the units of LP(a)? What camp do you live in?

Dr. Brown:
Yeah. Actually, I don't think that's real controversial. I think most people believe now that nmol/L is the way to measure it, and the reason is that tends to give you a better feel for the number of particles whereas just getting mg/dL doesn't correlate as well with risk. As you know, the NLA published a document on this, but it seems like there seems to be pretty broad international consensus that nmol/L is a better assessment of risk than mg/Dl. But it's really an important point because patients will often get their blood tests at multiple times for reasons unclear, and they might go to one lab and get a result in mg/dL, and then they go to another lab and get a result in nmol/L and they think suddenly their LP(a) has tripled, and I get a lot of consults for that, so I think it's really important to standardize how we measure it especially as we get into an era where there may well be therapeutics to intervene on elevated LP(a). And it seems pretty consistently agreed that we will move to nmol/L.

Dr. Cheeley:
So you mentioned that you have patients that go to multiple labs. Should we follow LP(a) over time?

Dr. Brown:
Well, I think in the era where we don't have a therapy for them, I don't know that following it makes much sense. It's pretty static over the course of your lifetime, and it is determined by a single gene. LP(A) is the name of the gene that produces apo(a), and so it really doesn't change much.

However, some people are looking at it, for example, when they put a patient on a PCSK9 inhibitor knowing that there might be about a 20 percent drop, and I'm not sure what you'd do differently if you didn't see a change, but it's a little bit reassuring if the patient does drop. That isn't consistent, but the majority of patients will get a modest reduction in their LP(a). It's still not an indication for a PCSK9 inhibitor, but for those patients that have elevated LDL and elevated LP(a), I will occasionally get a follow-up LP(a) on them just to see if they were one of the responders. We have at least circumstantial evidence that the people who drop their LP(a) as well as their LDL on a PCSK9 inhibitor tend to have better outcomes. It's not a prospective randomized data set, but observationally, it looks like they're at higher risk, and they also get more benefit if they drop their LP(a) as well as their LDL on a PCSK9 inhibitor.

Dr. Cheeley:
So we've already talked a little bit about treatment options, but can you talk us through these ethereal drugs in development that we've been talking about or other therapeutics like we might have? So we've already taken estrogen and niacin off the table. We know that those are not options for us. But what else do we have to treat LP(a) currently or coming in the future?

Dr. Brown:
Again, no randomized prospective outcomes trial for treating LP(a), but we do have randomized prospective outcomes trials for treating LDL that show benefit, and they show what looks like an enhanced benefit in those people who have high LP(a) and whose LP(a) drops on the therapy. There are also several drugs in development that specifically target LP(a). Most of them antisense or siRNA drugs, and they can drop LP(a) anywhere from 80–98 percent and they are currently in secondary prevention trials looking at high-risk individuals with elevated LP(a) as we discussed. And we're probably talking somewhere between three and five years before we see the results of those would be my guess, but very exciting because as a target of therapy, LP(a) makes sense. It has biological plausibility because it's highly oxidized. It very readily promotes atherosclerosis, and then it has the apo(a) amino acid sequence similar to plasminogen, so it also competes with plasminogen going to plasmin and causing increased risk of thrombosis, so that double whammy of increased clotting and increased atherosclerosis is what we think makes sense why LP(a) is a particle that's not good for you, so it also makes sense when you have the biological plausibility that lowering it as a target of therapy should translate into better outcomes.

That isn't always the case. I mean, we felt that way about homocysteine, and we targeted homocysteine and weren't able to show an outcome benefit. And then we do already have LP(a) apheresis.

So in those patients who have progressive events— again not prospective randomized double-blind studies, but where patients serve as their own control—those with very high LP(a)s who had lots of events when they get put on apheresis, we see a significant reduction in the number of events per year. So for those refractory patients that despite all our efforts in getting their LDL very low, they still continue to have events, we shouldn't forget about apheresis as a very effective treatment for LP(a).

Dr. Cheeley:
That's a great point. Well, this has been a fascinating look at LP(a). I would love to thank my guest, Dr. Alan Brown, for sharing his insights.

This was to fun chatting with you. Thanks for coming.

Dr. Brown:
Thank you, Mary Katherine. It's great to be on this side of microphone.

Dr. Cheeley:
For ReachMD, I'm Dr. Mary Katherine Cheeley. To access this and other episodes in our series, visit ReachMD.com/HeartMatters where you can Be Part of the Knowledge. Thanks for listening.