Part 1 – Lp(a) Discovery Neurology Perspectives Transcripts

Speaker 1 (00:06):

Welcome to the American Heart Association's Heart 360 Podcast. This podcast brings together diverse groups of clinical experts from around the world to share their expertise, insights, and models on how to implement guideline directed medical therapy to combat the number one cause of death cardiovascular disease. Each episode contains focused professional conversations for providers across the spectrum of care, targeted at improving patient outcomes through quality improvement. And now today's episode.

Speaker 2 (00:40):

Hello and welcome to today's episode of the LP Little a discovery podcast, perspectives from neurology and cardiology. My name is David Pena, a program consultant for the AHA and host for this podcast series. As a part of the LP little a discovery initiative, we seek to better understand system level practice patterns for patients tested for elevated LP little A, as well as develop national models for LP little a testing. Today we'd like to welcome a cardiologist and a neurologist from Duke University Health System to talk more about their clinical considerations for testing LP little A. We'd like to welcome Dr. Shah and Dr. El Husseini. Dr. Shah, would you please tell us more about yourself?

Speaker 3 (01:28):

Yeah, absolutely. First and foremost, David, thank you so much to you and the AHA for this invitation on this extremely important topic. And I couldn't be more honored to be here with my good friend and colleague, Dr. Nada El Husseini who I work very closely with. A little bit about me. I'm a preventive cardiologist here at the Duke University Medical Center and in the Duke Clinical Research Institute, I have both clinical practices as well as I'm very involved in clinical research, both from an implementation science standpoint and a clinical trial standpoint. I have a passion of all things cardiometabolic disease, specifically in dyslipidemias. I see patients from around the state and as well as the country who come with very complex dyslipidemic disorders. And a question I commonly get is what do I do about my elevated LPA or should I get an LPA test or I've read about LPA, what does that mean? And so I'm very glad we're having this discussion. I'm involved very much in our community in terms of community engagement and education around lipid management. And so this could not be a very more timely discussion.

Speaker 2 (02:43):

Absolutely. We're really glad to have you. Dr. El Husseini. I believe you're a neurologist. Would you please share with us a little bit more about you and your role?

Speaker 4 (02:53):

Sure. Thank you for having me today. Participate in this discussion with Dr. Shah. I'm a vascular neurologist at Duke. I am involved in the inpatient management of individuals having a stroke as well as outpatient management in the stroke prevention clinic. I also am involved in stroke outcome research. The most common two questions that come up from stroke patients end up being what can they do to recover from a stroke, but also why did they have a stroke in the first place and what they can do to prevent another stroke. I'm very keen into looking at traditional and non-traditional risk factors. The discussion about lipoprotein A has been evolving over the past several years. Dr. Shah and I have co-managed several patients and continue to collaborate when it comes to these questions about how to

best prevent a stroke in these patients. So it is a very timely topic and a very exciting research going on that hopefully will shed more light about how to best manage these patients.

Speaker 2 (04:24):

I think I can speak for everyone when I say it's very interesting to hear more about those patient cases where you co-manage folks with elevated LP little A. But before we get into that, would love Dr. Shah. If you could maybe explain why we are here today and the importance of this discussion.

Speaker 3 (04:45):

Absolutely. So as we highlighted, LPA is a growing topic, we're learning more about it on a daily basis. Our guidelines are starting to involve LPA testing and screening. If it's not for everyone, depending on which guidelines you're reading, it's certainly for people who are at high risk of atherosclerotic cardiovascular disease. And so LPA, why we're talking so much about it, it's because it is a very atherogenic lipoprotein. It really increases people's risk considerably if elevated and has family implications as well because LPA levels are very genetically mediated. So it's not only important because it can help identify those at the highest risk for a cardiovascular event, but it can also help screen family members who need to be on risk factor modifying either lifestyle strategies or treatments early to prevent event in the future. The other important thing that the people need to know about LPA is that we have a lot of therapies that are in clinical trials right now that can directly inhibit LPA at very high levels. We're looking at what the outcomes cardiovascular outcomes will be for those trials now. So stay tuned because there's certainly a lot of information that will likely come out here in the future. But that being said, if there is promise in some of these investigational therapies, then in our lifetime there may be a more therapeutic options for LPA as well. And so as we're testing to see what the benefit of those therapeutics are going to be, it's really important to start establishing a practice pattern of risk modification and identification in patients with elevated LPA

Speaker 2 (06:44):

As a neurologist, Dr. El Husseini, when would it be most appropriate to test and screen a patient for LP little A?

Speaker 4 (06:54):

So I think the answer to that has quite evolved over the past years. Many years ago, we used to test for it with the idea that maybe there will be medications like niacin that actually decreases lipoprotein A and may decrease stroke risk as well. The AIM high trial that was done in 2011 or published in 2011 did not show benefit in stroke reduction, but also it was not designed to evaluate the effect of niacin on stroke reduction in patients who had elevated lipoprotein A. So it was mostly designed to evaluate the effect of niacin as an additional agent to statin to increase HDL in patients who already have well-controlled LDL. And that particular study, surprisingly the numerical value of stroke. So patients who were treated with extended release NIA and actually had more strokes than those who were not. But after adjusted analysis, it doesn't seem like there was a major association.

Speaker 4 (08:19):

So after the study as neurologists, we were left with, yes, niacin can decrease the lipoprotein A level, but we don't have evidence that it helps in stroke prevention. And so we went for many years. And again, when I talk about the practice, I'm talking about myself and maybe my colleagues. I'm sure the practice may be variable in other places, but also there weren't any guidance on checking lipoprotein A in the

most recent secondary stroke prevention guidelines from the AHA that were published in 2021. So there are literally really no guidance on checking lipoprotein A in stroke patients specifically for secondary stroke prevention. That being said now with the renewed interest in lipoprotein A, the additional research I personally have been checking, again, lipoprotein a definitely in patients who have atherosclerotic stroke with no clear risk factors otherwise, or patients who have a stroke and atherosclerosis at a young age, those who have a strong family history of atherosclerotic cardiovascular disease at a young age as well.

Speaker 3 (09:48):

Yeah, and those are excellent, excellent points that you bring up. I think it's important to understand the history and how it's evolved, especially with this growing interest in lipoprotein A and a lot of it is dictated by so many genome-wide association studies, Mendelian randomization studies, large otherwise observational studies that are extremely well done that have over the years showed us that there is a direct and causal relationship of atherosclerotic not only disease but events with higher turnstiles of LP little A. And so it just goes to show that the more we see it through research, the more we can kind of refine our study questions and understand which populations will benefit the best in terms of being aggressive in testing for LP little A. And in the fact the data has gotten so good from what we see that in the European guidelines, they recommend at least once in a lifetime testing for LPA, just to identify those that are at the highest tertile and the highest risk.

Speaker 3 (11:04):

And we're starting to see that motion as we start seeing statements from national societies even in the US where LPA testing is recommended in generally and current guidelines, LPA is identified as a risk enhancer. So if you have someone who is at least intermediate or borderline risk, not unreasonable to test for LPA because it may redefine that patient's risk and may put that patient in a position that needs more modification of what can be modified such as LDL, cholesterol, hypertension or blood pressure, excuse me, weight glucose control and so forth. And so one thing that we do know is that this is certainly a very strong marker of risk across all patients.

Speaker 4 (11:59):

Yep. I think you make a wonderful point here. From a stroke standpoint, based on observational studies and cohort studies, lipoprotein A is independently associated with increased stroke risk ranging depending on the study anywhere between 22% increased risk to a twofold increased risk of stroke. So in terms of evaluating this risk, it is definitely important. And the approach in my opinion should be even if while waiting for the ongoing trials that are evaluating whether decreasing lipoprotein A will decrease stroke risk, it's definitely helpful to at least check it in patients and use it as you're mentioning if nothing else, as a risk amplifier and manage the other risk factors. And I think that renewed interest in lipoprotein a corresponded with the PCSK nine inhibitor trials that now we know that these medications do increase lipoprotein A by about 30%. They did decrease and the Fourier and the Odyssey outcomes, they did decrease strokes even though and Fourier 20% of that cohort had prior ischemic strokes and the odyssey outcomes about 5% had history of strokes, but still they did look at recurrent stroke as a pre-specified analysis. However, none of these studies did analysis by lab protein A for stroke risk per se. They did an analysis by lipoprotein a interaction with recurrent cardiovascular events, but stroke was not included in these analysis. So that being said, that tells us that at least PCSK nine inhibitors decrease lipoprotein A and decrease stroke risk. We just don't know yet if they should be used for the only indication of elevated lipoprotein A and decreasing stroke recurrence.

Speaker 3 (14:39):

Yeah, absolutely. And I'm sure there's going to be more to come in that realm with ongoing studies and clinical trials to help us define that subgroup a little bit better. And that's the beauty I feel like of just clinical medicine and how we really can redefine our practice and redefine our understanding. We're always learning based on what we discover. And I think it starts with conversations like this, where are the gaps? Where is there a lack of understanding that we need to clarify what are the disparities in care? And interestingly, despite all of this amazing evidence that's coming out, when you look across the country, testing for lipoprotein A is extraordinarily low. We did an analysis across multiple health systems here at Duke and we found that the testing rates were as low as like 0.4 to 0.6%, and that's actually been replicated in other studies that other groups have done. And so there's still a large lack of awareness or other system-based issues. I'm sure it's in terms of testing for LPA and the importance of it. And so hopefully as we learn more about it and we start having more and more clinical trial evidence of not only possible therapeutics that could be beneficial, but also just more understanding of how to implement strategies to improve testing or make testing easier for patients, I think that'll hopefully help the number of people we screen for Elevated lipoprotein. A

Speaker 2 (16:47):

For our listeners, you all mentioned screening patients from our listeners who may be cardiologist or neurologists in America, which patients would make the most sense to start testing now and with the patient populations they work with?

Speaker 3 (17:07):

Yeah, absolutely. That's a great question. So what I personally would start with the foundation of if there's anybody you are worried about in terms of their cardiovascular risk or if there's a patient that wants to learn more about their own personal cardiovascular risk, I think it's very reasonable to test any of those patients. For LP little A, I'm personally in agreement with the European guidelines and that everyone should have at least once in a lifetime testing for LPA. That being said, there are variations in the cost of the test. There are variations in the access to the test. And so if we really wanted to get specific and narrow the testing pool to a specific phenotype, I would say in general patients who have had a very strong family history of atherosclerotic cardiovascular disease, premature atherosclerotic cardiovascular disease, both in the family but also a personal history of premature atherosclerotic cardiovascular disease patients who are related to the first degree.

Speaker 3 (18:24):

So a parent to sibling, a child of someone with very high elevated LP little A levels patients with familial hypercholesterolemia, that's another patient that I would certainly want to test for lipoprotein A in. We know based on just population studies that approximately 20% in some studies a little bit higher of patients with FH have elevated LPA. So a very important group to test for LPA in another group to test for LPA in would be patients with persistently elevated LDL that is not really responding to treatment. Why is that? It could be because they have high LPA levels, because remember in the LPA core itself, about 40 to 50% of that core is LDL cholesterol. So sometimes assays that just test for LDL may not be able to distinguish between LDL that's attached to the LPA molecule and free LDL in itself. And so that's another group, a very persistently elevated LDL or a group that just cannot respond to treatment.

Speaker 3 (19:37):

And then if you have a person that otherwise has imaging evidence of pretty aggressive atherosclerotic disease but has not necessarily had an event yet, that's another group that I tend to test LP little A four and an example would be someone that's otherwise young and healthy but has an extremely high coronary artery calcium score. We're seeing more and more data to help us understand the interaction between coronary artery calcium and lipoprotein A. And I think there's going to be more to come in that field, but just another group of people I like to test in, and I'm sure there's many other phenotypes as well, not I'd love to kind of hear your thoughts from a neurology perspective.

Speaker 4 (20:17):

Sure. These are all great points. So in addition to this, from a neurology standpoint, I agree that individuals who have had a stroke, in my opinion, I also agree with the European recommendation to check it at least once in a lifetime. We do check for LDL cholesterol and hemoglobin A1C and everyone who's had a stroke, I think that checking for lipoprotein A would make sense as well. But outside of this, again, that possible recommendation to check it in, everyone with a stroke, those who may benefit the most may be those who also have atherosclerosis at a young age. So for example, individuals who may be seeking stroke prevention because they were discovered to have carotid stenosis, carotid atherosclerotic disease, and that can help with determining, we do have an LDL goal for these patients that is already less than 70, but those who also may not have control with a statin, as you mentioned, they may have a subset of these individuals have elevated lipoprotein A and that's why they are not achieving their LDL goal with a statin.

Speaker 4 (21:49):

Those who have a stroke at a young age, those who have cryptogenic stroke, where you've done all the traditional risk factor evaluation and still can't find why a patient has had a stroke. Also, definitely those who have, again, a borderline A-S-C-V-D risk that they have a TIA possibly they have a little bit of atherosclerosis, and that can aid in the discussion of risk modification therapies. What LDL goals should we get for these patients so that can help determining that goal. And those who have a family history of stroke or heart disease at a young age also should be screened.

Speaker 3 (22:46):

Yeah, absolutely. Those are amazing insights and if you follow the current American College of Cardiology, American Heart Association and multi society guidelines, they recommend screening LPA and those at our intermediate to borderline risk just to assess what the effect on risk enhancement is. Because LPA is a risk enhancer, so it could, like we talked about earlier, increase someone's risk. So if you think about it, out of all the people we mentioned, that is a wide net. And so certainly in my opinion, I think we should be screening a little bit more when you look at national data and what the screening rates are currently at, because there may be a lot of people out there that will benefit. I mean, from what we know currently across the population in general global population, it is estimated that it's somewhere in the realm of 20% of people have elevated LPA and some studies have shown higher prevalence numbers.

Speaker 3 (23:57):

And I think as we test and screen more, we may redefine what that actual number is. But I mean, that's a big chunk of the population and my personal practice knowing that how much of a risk LPA confers in terms of developing atherosclerotic disease. I treat patients with elevated LPA levels as I would a patient who has established atherosclerotic disease, even if they don't have had an event yet, so they've not

had a stroke, they've not had an mi, I treat them as if they have atherosclerotic disease. So what that means is I drive their LDL as low as I possibly can to really help modify their risk. There is rising evidence of the benefit of aspirin in these patients, assuming their bleeding risk is low. I think there's more to be clarified in that space, but from what I've seen so far, there's been some pretty interesting evidence that there may be benefit here.

Speaker 3 (24:56):

And so a patient with elevated LPA may be eligible for aspirin therapy. And then of course if you have a patient with an elevated LPA, I tend to do cascade screening. I recommend screening for all first degree family members for that patient. And so those are just a few things that you can do today if you know your LPA value is elevated. The point here is that it's very actionable because that's a common question I get is, well, I can't do anything about an elevated level, but I would argue that you absolutely can't, and that's another reason to maybe screen more because we can do things.

Speaker 4 (25:39):

Absolutely. I actually have a follow up question about how you would, if you think it would help to screen in specific high risk populations based on the known risk, for example, in those who have kidney disease, we know that lipoprotein A increases and menopause increases in those who have chronic kidney disease increases in those who have liver disease, and also it is higher in certain populations with African descent or South Asian descent. Do you recommend in particular screening in these higher risk populations that have usually higher lipoprotein a?

Speaker 3 (26:29):

Yeah, no, that's a great question. I do. I do typically keep that in mind. I look at the overall patient risk and look at their comorbidities as you suggested, and I certainly screen them because as far as we know, the higher the LPA, the higher the risk. And so it's good for, especially if we don't have a test at all in that patient, I tend to screen them, especially if I do worry about the risk of an event prognostically what a high level means, let's say in someone who may genetically have high levels or has a comorbid condition that could somewhat mediate the levels. Hard to know. We don't have much literature to really guide us. I think the safer thing to do always is that if you have an elevated level is to be aggressive in risk factor modification, and so that's been kind of my general practice to the date.

Speaker 2 (27:32):

Thank you all both so much for being here today and talking about this important subject for sharing your insights and everything regarding care considerations and perspectives on lipoprotein little a. We are going to continue this discussion in part two of this podcast and we'll talk more about what the future holds. We'll dive deeper into cascade screening, and we will talk about what differing practice patterns may look like. To learn more about lipoprotein little a, listen to the LP little A Discovery Series podcast and watch presentations@heart.org slash lp. Little a discovery. Thank you all so much.

Speaker 1 (28:18):

Thank you for listening to Today's Heart 360 episode. Today's content discussed current barriers and care and how these barriers have been addressed in the communities featured. These views do not necessarily reflect the American Heart Association. American Stroke Association's official position. The association does not endorse any product or device. For more quality improvement information and resources, visit www.heart.org/quality.