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Assessing the Impact of LDL-C Reduction on Atherosclerotic Plaque & Distinguishing Imaging Modalities

Announcer:

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Here's your host, Dr. Hegele.

Dr. Hegele:
This is ReachMD, and I'm your host, Dr. Rob Hegele. I'm a Professor of Medicine and Biochemistry at Western University. I'm also the director of the London Regional Genomic Center at Robarts Research Institute in London, Ontario, Canada. Joining me today, to discuss atherosclerotic plaque is Professor Stephen Nicholls, a Professor of Cardiology and Director of Cardiology at the Monash Victorian Heart Institute at Monash University in Melbourne, Australia.

Professor Nicholls, welcome to the program.

Dr. Nicholls:
Thanks, it's good to be here.

Dr. Hegele:
So Stephen, how does coronary atherosclerosis progress? And what is the impact of vulnerable plaque?

Dr. Nicholls:
Well, we know that atherosclerosis is a chronic condition. It gradually and progressively accumulates in the walls of arteries over decades. Plaques can remain asymptomatic for many years or ultimately become obstructive enough to cause stable angina. However, we also know that there are some plaques that become vulnerable and rupture, break down at the fibrous cap, elicits acute thrombosis, and that may lead to an acute coronary syndrome, and so we've really understood now very well the ranges of the pathology across the disease continuum, so we know how a plaque first develops early in life.

Very much goes into the layer of thickening. We understand the accumulation of foam cells the formation of the fibrous cap. We understand how the artery wall remodels. We understand that you can develop this progressive luminal obstruction, but we also understand that, for the majority of patients who have an acute coronary syndrome, there'll be some sort of breakdown of the cap, whether is frank rupture, which is the classic lesion we see, whether it's plaque erosion, when they only have a breakdown of the endothelial cell layer itself, typically underlying these lesions is a plaque that contains a lot of inflammatory and lipid material. It may

contain a necrotic core as well. And so, we've learned a lot about how the plaques that cause events are different from the plaques that don't cause events.

Dr. Hegele:
Right. So, plaques are diverse, and there are the quantitative aspects of the plaque, the plaque size, but there's also qualitative aspects of the plaque. And it's these qualitative aspects that make a plaque more vulnerable.

So, what are the key features of a vulnerable plaque?

Dr. Nicholls:
Well, we've been really fortunate that it's not just the pathology studies that have been able to help us here, but there's a number of imaging modalities now, that enable us to look within the plaque and we've been able to use those techniques in patients with acute ischemic syndromes.

And that's really helped this field as well. So we know that, for example, optical coherence tomography, or OCT, is a light-based technique. It enables imaging with much higher resolution than a lot of other modalities. And so we can really see those vulnerable plaque features.

We know that our vulnerable plaque is going to contain a thin fibrous cap, typically with a cap thickness less than 65 microns. It tends to contain a large lipid core. We can see inflammatory cells, we can see new vessels grow within the plaque, and we can see cholesterol crystals, knowing that cholesterol can exist both within foam cells, but also in a crystalized form that we know goes hand-in-hand with plaque vulnerability.

Dr. Hegele:
Mm-kay, so as an endocrinologist now trying to summarize it for myself. So you've got stable plaque – so stable plaques have got a small lipid core. They've got a thick, stable fibrous cap, and they've got a higher population of smooth muscle cells, which are sort of stabilizing players in the whole pathology. And that contrasts, then, with the vulnerable plaque. So the vulnerable plaque, then, is really the opposite. It's got fat, large lipid core, and a little, thin, fibrous cap, and then it's got an increase in the population of macrophages, which are then kind of more destabilizing cells in the whole pathology.

So, you talked about imaging modalities. What are the imaging modalities specifically that can be used to look at changes in plaque burden, and changes in plaque composition?

For example you know, we've heard of things like OCT, or IVUS, or angiography. So, what are these different imaging modalities?

Dr. Nicholls:
Well, and we start with angiography. Angiography enables us to look at the degree of luminal obstruction in the coronary vasculature. It doesn't look at plaque itself, but it really looks at the consequences. Been a really important tool in the clinic, to be able to diagnose obstructive disease, and triage patients to revascularization.

OCT – or optical coherent tomography –that uses a light transducer on the tip of an intravascular imaging catheter. What comes along with that is high resolution imaging, so you can detect all of those vulnerable plaque features. We can measure the thickness of the fibrous cap. We can measure the size of the lipid core. We can see a number of those other features.

And so that becomes a really important tool because we can look at that, and we can look at it in cross-sections, and we can look at it across the length of the vessel, and it gives us really high sensitivity to detect those features which we've come to understand more likely to be present in a vulnerable compared with a stable plaque.

Dr. Hegele:
Right, so about OCT in particular then – it allows us to look at, sort of compositional aspects. Also allows us to visualize plaque rupture and thrombus.

But importantly, what it does is it provides us with some metrics, some actual quantitative thresholds or red lines. For example, for the fibrous cap thickness, or FCT, which then is defined as the signal-rich region between the lumen and the signal-poor necrotic lipid core. So there, the cut point is 65 microns. So anything less than 65 microns suggests a thin cap, and the thin fibrous cap is associated with a vulnerable plaque.

And then, for the lipid component – the lipid arc, it's defined as the widest arc demarcating a signal-poor region within diffuse borders, and so a wide lipid arc, greater than 90 degrees suggests increased lipid content, which is less stable.

And then, you could even then look at the lipid pool, or the core, which is then defined further as diffuse, signal-poor lipid regions, or signal-poor regions, which underly a signal-rich cap. So, but the critical thing is that we could put numbers on these, and then this allows us, in science, when you have things to measure, then you can actually follow things scientifically, and this allows us to, look at the qualitative aspects of the plaque with those metrics.

So that's OCT. IVUS, looks at something different. It looks at the extent and the distribution of the plaque, and it allows for even temporal assessment of changes in plaque burden.

Dr. Nicholls:
So IVUS, or intravascular ultrasound is again an intravascular imaging modality. This time the transducer on the tip of the catheter is an ultrasound transducer, and not a light transducer. That produces fundamental imaging differences. You still get cross-sectional images of the lumen and the coronary artery wall. Slightly less resolution – about 100 microns with IVUS, probably 10-20 microns with OCT. So you don't see with the same type of sensitivity, those features within the plaque, but what you do gain is you gain that penetration.

You see the outer vessel wall border and enables for us to be able to measure the burden of atheroma within the artery wall. We cannot only measure that as a plaque area in one single cross-section, but we can actually look at a whole series of cross-sectional images throughout a length of vessel and that permits us to quantify the volume of atheroma. We can do that in a matched artery segment, at different points in time, and that will allow us to understand both the clinical factors that associate with the natural history of disease progression, but also to ask the question, within clinical trials can therapies change plaque burden over time.

Dr. Hegele:
So on that theme what actual changes in atherosclerotic burden have been observed with LDL cholesterol lowering say, with statin therapy?

Dr. Nicholls:
Well, we've been fortunate. There've been a lot of clinical trials over the years. LDL cholesterol lowering has been shown to decrease atherosclerotic burden. There have been many clinical trials that have used serial IVUS imaging to assess the impact of LDL cholesterol lowering on atherosclerotic plaque burden. And what has been very consistent in observation in those studies, has been a direct relationship between LDL cholesterol lowering and a reduction in atheroma volume.

Dr. Hegele:
So we talked about plaque burden, but what's the effect of LDL cholesterol lowering therapy on plaque vulnerability?

Dr. Nicholls:
Well, I think the first thing is that using OCT imaging, we've been able to perform observational studies that showed us firstly that patients with higher LDL cholesterol levels tend to be more likely to have those vulnerable plaque features.

Patients treated with higher intensity statin therapy tend to be less likely to have those vulnerable plaque features. They tend to have thicker fibrous caps, and a smaller lipid arc. And important in both of these trials, that the degree of LDL cholesterol lowering associated with the degree of thickening of the fibrous cap – so if you think about it, we've now got really nice evidence that more intensive lipid lowering lowers LDL cholesterol levels in the blood, that the degree of stabilization is directly proportional to the degree of lipid lowering. So, it really provides a nice biological rationale, that connects intensive lipid lowering.

Dr. Hegele:
Yeah. Absolutely. Well, I think we're reaching the end. We're gonna round it out, and just to summarize the ground that we've covered, in the preceding few minutes.

So first of all, we distinguished plaque imaging modalities and particularly talking about OCT and IVUS, which can help visualize plaque features and help assess the effective lipid lowering therapies. OCT detects vulnerable plaque characteristics, whereas IVUS assesses plaque burden. We've also looked at the effect of intensive lipid lowering on plaque stabilization. So it's really clear that achieving lower LDL cholesterol levels has been associated with smaller lipid arc, increased fibrous cap thickness, lower percentage of vulnerable plaques. And so, then this leads to opportunities. There's multiple actionable opportunities across the continuum of care for acute coronary syndrome patients, to optimize LDL cholesterol levels and to improve features of plaque stability. Stephen, do you have any final thoughts? Anything you'd like to add before we wrap up the podcast?

Dr. Nicholls:
Well, you know, I think that what we've seen with all of these studies is the importance of intensive lipid lowering. More and more, we're seeing that that's requiring combination therapy for many of our patients, just like we treat hypertension and diabetes. Dyslipidemia is likely to require combination therapy for many patients, and you see the benefits in these trials. They directly connect lower LDL cholesterol levels in the blood to biological benefits in the artery wall.

Dr. Hegele:
Awesome. Thank you. So I think that's a great way to round out our discussion on atherosclerotic plaque and assessing the impact of LDL cholesterol lowering, and distinguishing imaging modalities. So, I really, really wanna thank my guest, Professor Stephen Nicholls, for helping us to better understand plaque composition and imaging.

Professor Nicholls, it was great speaking with you today.

Dr. Nicholls:
Thanks Rob!

Announcer:
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References:

1. Sandfort V, er al. Circ Cardiovasc Imaging. 2015;8:e003316.
2. Virmani R, et al. Thromb Vasc Biol. 2000;20:1262-1275.
3. Stefanidis C, et al. J Am Heart Assoc. 2017;6:e005543.
4. MacNeill BD, et al. Arterioscler Thromb Vasc Biol. 2003;23:1333-1342.
5. Tardif JC, et al. Circ Cardiovasc Imaging. 2011;4:319-333.
6. MacNeill BD, et al. Arterioscler Thromb Vasc Biol. 2003;23:1333-1342.
7. Shah NR, et al. MOJ Anat Physiol. 2015;1:11-14.
8. Stefanidis C, et al. J Am Heart Assoc. 2017;6:e005543.
9. Baumann AAW, et al. Ther Adv Chronic Dis. 2020;11:1-23.
10. Hoshino M, et al. J Am Heart Assoc. 2019;8:e011820.
11. Papaioannou TG, et al. J pres Med. 2019;9:1-14.
12. Dweck MR, et al. Nat Rev Cardiol. 2016;13:533-548.
13. Puri R, et al. Eur Heart J. 2013:34:1818-1825.
14. Kataoka Y, et al. Atherosclerosis. 2015;242:490-495.
15. Tardif J-C, et al. Circ Cardiovasc Imaging. 2011;4:319-333.
16. Daida H, et al. J Atheroscler Thromb, 2019;26:592-600.
17. Nicholls SJ, et al. JAMA. 2007;297:499-508.
18. Gili S, et al. Eur Heart J. 2018;19:524-531.
19. Kataoka Y, et al. Atherosclerosis. 2015;242:490-495.

20. Amsterdam EA, et al. J Am Coll Cardiol. 2014;64:e139-228.
21. Grundy SM, et al. J Am Coll Cardiol. 2019;73:e285-350.