Ivor Cummins	00:37	I'm here in the Royal College of General Practitioners at the PHC UK Conference and I got to catch up again with Dr. Aseem Malhotra. Great to see you there.
Dr. Aseem Malhotra	00:45	It was good to see you, mate.
Ivor	00:46	Absolutely. And you were in Australia recently and you messaged me about a doctor over there who's doing a lot of calcium scanning and some really interesting stuff - you are learning from him.
Aseem	00:56	Yeah, absolutely. So I was on a speaking tour of Australia, and my top was really about too much medicine and statin, etc. One of my… somebody I become very friendly with who I met, last time I went to Australia is a cardiologist called Dr. Ross Walker. He's been a cardiologist for many years, at least three decades. So very experienced cardiologist, and very well known, very well respected, and he uses calcium scores a lot. In fact, he has treated and utilized calcium scores in tens of thousands of patients. So he's probably as far as I know, certainly the person I know more than anybody else is a clinical cardiologist has used them. And I think that's really interesting and useful to see what experience impact that's had on his knowledge and what he shared with me.
	01:45	I'm fully behind. Like with anything in medicine, of course, it's about using the right test in the right patient. But certainly, when it comes to assessing cardiovascular risk, this is the best tool we've got. It's a best way [Inaudible 00:02:02] calculator tells you whether you've got diseases as you know, Ivor, and it also tells you about the risk, and also what we can do serially. And I've started using this on my patients is to see about rate of progression of disease as well and risk. And I think that is definitely a useful, potentially very useful role for patients. For me personally, one thing I found very interesting about calcium scores is the use of calcium scores in patients who may be deemed a particular high risk from a [Inaudible 00:02:37] score or have high cholesterol, and are not particularly keen on going cholesterol and drugs, or statins, for example.
	02:44	So I'll just give you one example. And this has been repeated a few times is I've seen a number of patients with familial familial hypercholesterolemia, who first diagnosed in their late 50s. And, as you know, familial hypercholesterolemia is a genetic condition which has a very strong association with the development of premature heart disease. But that doesn't

mean everybody with FH is going to get heart disease. And these patients, you know, ladies in their late 50s, come to see me first diagnosis of cholesterols. You know, we're talking about total cholesterol of 20. LDL is of over 10, 15, I mean, very high LDL cholesterol, but otherwise extremely fit - normal blood pressure, no instant markers of insulin resistance, no more glucose, slim, active. And they have come see me because they've been told unless they go on a statin or cholesterol and drug in quotes, one of the doctors on, they wouldn't be around for much longer. Almost giving them a kind of death sentence like terminal cancer. Of course, you and I know that's not a very ethical or kind of scientific way of having a discussion with patients necessarily. But one thing that's been very useful in each of these patients is use of calcium score, and sometimes even a CT coronary angiogram, all of them have come back as zero. So clearly, logically, if cholesterol was a risk factor for them, for them personally, they would have at least some, if not extensive, coronary disease by the late 50s. And the fact they've got nothing is clear indication, it's not a problem for them, and therefore they can be reassured they do not need to lower their cholesterol.

Ivor 04:16 Yeah, no, that is another excellent juice for the scan. And actually, I'm getting a lot of people coming out of the woodwork now. If a gentleman of 62 with a LDL of I think around 340 American units and you're 9, a total cholesterol of 12, or 500 for an American units. And he got a scan and he got a zero score. And also a family of familial hypercholesterolemia who have been on drugs but they are in their 60s, and two at least of three siblings have zero score, zero heart disease registered. Now they are on lipid lowering drugs. But the reality is they still got enormous cholesterol. So it just shows that cholesterol is very much an association that may indicate a problem or it may not be a problem. And you need to look deeper to find out which it is.

Aseem 05:06 Absolutely right. And I think this is about the evolution of the science so we can identify the right patients for the right treatment. Unfortunately, our healthcare system is being run by more profit making industries and how doctors make decisions rather than actual good science, you know, and treating individual patients. So, I think the calcium score is a very useful tool for that. I think the other thing as well, I know Ivor you've looked at this in a lot of depth, and you know, we've shared information in all of this. And obviously, I see the patients in it, it's very useful to have various bits of information that can inform patients. But one of the things that's interesting

as well is how the progression of calcium score and the zero calcium scores can also predict risk of events. And I think you told me

that, if it's more than 15% in three years, then the increased risk of events is much, much higher than if it's less than 15% in terms of increase of calcium score.

Ivor 05:59 Yeah, the serial calcification, I mean, there's now some noise in the data, but the [Inaudible 00:06:03] study I showed you was really good. And it was 17 times more likely to have a heart attack if you were progressing rapidly, rather than slowly. Very fair study. In fact, it was 50% event rate modeled for people who are progressing rapidly and 3% for the same high scores at the start, but not progressing. But I think the best I can say about that is Professor Budoff, who's the world's leader in imaging, in general, he has a huge paper covering progression. And generally, regardless of the starting score, fast progression is six to eight times more risky, even for people who have a same starting score. So serial is powerful. And I think Dr. Walker was discussing that with you as well.

Aseem 06:45 Yeah. And I think this is again an area which I don't have a lot of expertise in specifically, but one thing that he pointed out to me, which was interesting, as well. As I know, as many people know, and cardiologist knows that, it's plaque rupture. That's the problem when it comes to cardiovascular events in terms of heart attacks and cardiovascular mortality. Of course, if you've got significant stenosis over time, it may well give you symptoms. Okay? But the real issue in terms of death and heart attacks is plaque rupture. And that often happens in plaque and non significant and may not be particularly calcified. You know, it's a softer blocks that are prone to rupture.

07:21 So one of the interesting things that Ross also highlighted to me as well is that even if you get increasing calcium score, if the overall plaque volume reduces, that's a result because hypothetically speaking certainly, a more calcified plaque is also a more stable one. And I've seen that when I've been doing angioplasties when I was in the Cath lab and we'd see people that, you know, the plaques, the most difficult and most challenging to stent, you know, to stick a metal coil to stretch the artery to improve the lumen diameter, improve blood flow, are the ones that are the most calcified.

07:55 So actually, the paradox a little bit, is a calcified plaque is probably less likely to rupture. But I think more calcium also indicates more soft plaque.

Ivor 08:05 That's precisely it, and I still, years, many years later, still get this argument about soft plaque but the people simply don't understand it. So more calcium means proportionately more soft plaque on the surface.

Aseem 08:19 Exactly!

Ivor 08:20 So that's why it's a very accurate measure of risk. Just because it's softer plaque or the kind of join or interface between calcified plaque and soft plaque is often a weak point. Just because that's where the rupture happens, doesn't take away in any way from the fact that higher calcium means higher calcified plaque and higher soft plaque proportionately.

Aseem 08:42 Exactly, exactly.

Ivor 08:43 Yeah. Perfect. And we actually… oh, you're aware we did with Don O'neal [Inaudible 00:08:48] of Serial Killers, we did a documentary.

Aseem 08:50 [Inaudible 00:08:51]

Ivor 08:54 He's a nice guy. He's a funny guy. You'd like him. We did a documentary which we already released for free, and I link it again on this podcast, a half hour documentary with Irish sporting heroes who are the top heroes in 1991 in Ireland. And we scanned 45 men in their 50s. Most of them slim, in great shape in their 50s, very impressive, big man. And we scanned them all. And all of them were deemed to be healthy by their doctors and all their blood markers looked fine - there was nothing suspected. And 20% of them had from 150 up to 3200 scores, so had to immediate follow up with doctors and cardiologists in some cases. So it just showed those 20% of super high risk guys in there in a group of 40 something, who were all deemed as low risk. So when people drop dead of a heart attack in their 50s, and they're slim, and fit, like some of our guys with huge scores are slim and fit, and then people say, "Oh, you know, it's kind of like a bolt from the blue," or, "You know what, it's funny, he didn't smoke, he was slim." But, there's a trend as well, that when you measure the blood glucose after a meal, our guys with the big problem, it's jumping up really high.

Aseem 10:06 That was really good point. I think that highlights the weight and activity, so being so called normal, some weight and being active, should not give people the

illusion of protection. Having said that, I think there needs to be a more specific research about whether these are a separate group. So our athletes with high calcium scores, you know, are they at the same risk as somebody who's a non athlete with a similar calcium score and other risk factors? And my guess is they're probably not at the same risk. But certainly there is more risk in being completely zero, you want your calcium score to be zero, you don't want anything in your coronary arteries. So I think there's probably a more of a nuance there, but certainly it goes against what most people probably believe. They think that if you're a footballer and you're middle aged, and you're slim, and you're active, that the chances of heart attacks is extremely smaller, there's almost no chance of having coronary disease. And I think the data that's there suggests that isn't the case either, that you do get a significant portion of athletes who have significant calcium scores.

Ivor 11:07 Yeah, and events. And actually, I do have one paper on that very topic. And while it is true that the athletes are a little better off in general and they seem to calcify in a more towards density and less volume, as you mentioned earlier, they have a little bit more safety. But when you look at the actual heart attack rates between low and high scoring athletes and the high activity group, they're not that much different than other people. So a high score still means an enormous relative risk. So yeah, our guys who got the highest scores, and in the movie, we're going to go back and rescan them, and it's going to be really interesting data coming out of that. But one of the guys we rescanned, he said he's lost several friends from the sporting community, dead in their 40s and 50s.

Aseem 11:52 So the question then as I suppose, it's important to work out what may have caused it in these people, and then what to do about it. It could be stress, in certain people the stress of exercise, you know? Exercise does cause stress on the body. There are lots of amazing effects on the body, but it could be that it causes a certain stress or the certain amount of exercise and certain and susceptible individuals could cause them to have coronary disease. So that's one mechanism.

12:14 It could be something that, you know, a phrase that I used in an editorial which became very well known, which I wrote with Tim Noakes and Stephanie is that, it could be because of the diet, you can't outrun a bad diet. And certainly, one of the studies that we cited was looking at the availability of sugar and its correlation with the prevalence of Type 2 diabetes. Independent of weight and activity showed a very increased

prevalence of Type 2 diabetes in certain groups in populations, suggesting the high sugar diet, despite even if you're active or slim, is likely to increase the risk of Type 2.

12:50 So I think that it's important if we understand those concepts, and the science is there, then that may explain why some of these people are developing coronary disease despite being active and slim. It could well be that they had a high sugar, high carbohydrate diet. I don't know. It could be something else.

Ivor 13:08 Yeah. Exactly as you say, with more use of calcification, not only will the most important thing happened that a recent paper showed that off the foreseeable heart attacks using the risk algorithm and/or the calcium scan, a third of the heart attacks that happened were only predicted by the calcium scan. So if you've got millions of heart attacks out there and tragedies, a third of those could only be seen by calcium scan. And these are middle risk people. So it's huge. But you're right, with more use of the scan, we get to tease out as well and more around causes. And our guys, definitely, there's a trend towards very high blood glucose after a meal even though their fasting is good, their A1c is good, their metrics look fine, their ratios look okay.

Aseem 13:52 How interesting.

Ivor 13:53 Yeah. So I think that metabolizing lots of sugar and carb intensive...

Aseem 13:58 I think what would be useful if you've got that sample of patients is to see if there's any correlation with liver fat. I know you're going to be speaking to Robert Lustig soon. And these people that have a so called carbohydrate intolerance from their glucose monitoring. So if you're able to get MRIs or DEXA scans look at the visceral fat, it may well be that they are TOFI. They are thin on the outside and fat on the inside. These are slim athletes, but actually, they have excess liver fat.

14:25 I would be particularly interested because that would also make sense. What wouldn't make sense and would need further explanation is somebody that has normal metabolic markers, doesn't have any visceral fat, yet their coronary arteries are full of calcium. Now, that would not make sense to me.

Ivor 14:44 Yeah. It could be I guess, there could be an intermediate state where there's not a huge amount of liver fat, but the dysfunction has established. But we don't really have extensive analysis of these people. But I think if we could start looking at doing trials of this type, we will basically…

Aseem 15:02 But even as an observation Ivor, I think if you could, if you've got a handful, just in those people, it used to be very useful to scan them with an MRI and actually see (you know, it's non invasive, it's safe) have they got any liver fat, especially if they've got you know, exaggerated glucose responses to high glycemic index foods.

Ivor 15:19 True. And the only challenge is the same that we are now post filming. So some of these guys that we've rescanned, they've been doing the right thing for six months.

Aseem 15:28 Ahh, that's fine.

Ivor 15:29 So we may have looked. And originally we just did kind of blood tests. There were some limitations. But interestingly, their liver markers which I went through, were not notable in any way. Interesting enough. Yeah, next time maybe. Great stuff.

Aseem 15:44 Yeah. Fantastic!

Ivor 15:45 Are you looking into some kind of trial, I think you mentioned?

Aseem 15:48 Yeah. I've designed a trial, randomized controlled trial that we want to make sure is, for sure has to have no commercial influence, no one's going to profit result from the results other than the public. But really designed it. I've designed a randomized control trial to actually look at true coronary disease reversal - is this as possible and can lifestyle interventions specifically reduce heart outcomes as in reduce heart attacks, strokes and death. And I think we've got the science to test that. We have observational data. There has been some other studies done showing this is coronary regression or reversal of coronary diseases is certainly plausible. But it hasn't been tested in a rigorous randomized controlled trial. And that's what I've designed. So that's my next bit of work.

Ivor 16:33 Excellent. Well, that is truly a first. Yeah, there are associational studies, I think William "Wheat Belly" Davis

just looked at his patients, and on his treatment regime, which would be quite similar I think to what you're probably thinking about, they had regression and stabilization relative to the population, but it's not controlled, it's not randomized.

Aseem 16:54 Exactly! But the observation itself is still fascinating. It's not something that's well known or discussed in cardiology circles at all. It's all based upon medical therapy and reducing event rates. But coronary regression is something that I, in my whole career, you know, and I've rarely seen, I mean, it's not something that you know, routinely necessarily come across. I've probably managed well over 10,000, maybe 20,000 patients in my career. So, you know, it's… yeah, it's fascinating, it's worth investigating.

Ivor 17:27 It's the holy grail I think it sounds like.

Aseem 17:29 In my genuine view is I think that it is plausible, and there is almost certainly I think that it can be done. But we just need to work out what exactly, you know, to prove that what interventions can do it.

Ivor 17:41 Absolutely. And you know, just a reminder to the audience, I'm hoping the anti are holding a hostage to fortune here, the Hines [Inaudible 00:17:48] next door study and many other studies have clearly declared that calcification is inevitable progress of and can be mathematically modeled for any score or age you are, they've automatically modeled it will go up X percent per year. It's usually 20. That is, on the record the medical world. So if you show, stopping or regression…

Aseem 18:10 It's a paradigm stuff isn't it? And Ivor, it's based upon also the editorial that you remember I wrote in 2017 with Pascal Meier and Rita Redbook? [Inaudible 00:18:18] about, you know, coronary artery disease is a chronic inflammatory condition linked to insulin resistance. So really the scientific basis behind it, you know, and that can be managed by lifestyle interventions, that is the next stage, which is the RCT. [Inaudible 00:18:31] But you know, it's interesting, you say it would be a paradigm shift, but you know, we say the same thing about Type 2 diabetes. Type two diabetes is a chronic irreversible condition that will gradually get worse over time. We know that's not true anymore. So let's look at heart disease reversal next.

Ivor 18:45 It's a perfect analogy. Absolutely. So, game changing stuff, which is always great to be involved in. So thanks a lot, Aseem.

Aseem 18:53 Thanks. Always good to see you.