**Transcript Details**
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Investigating the Link Between Heart Disease Risk Factors & Psoriasis

Dr. Greenberg:
Welcome to *DermConsult* on ReachMD. I'm Dr. Michael Greenberg, and joining me today to discuss heart risk factors in psoriasis patients is Dr. Nehal Mehta, Head of the U.S. National Heart, Lung, and Blood Institute Lab of Inflammation and Cardiometabolic Diseases.

Before we dive into your study, Dr. Mehta, can you tell us what was previously known about the link between psoriasis and the risk of heart disease?

Dr. Mehta:
So, it's long been known that inflammation is a driver of early atherosclerosis, and atherosclerosis itself is one of the leading causes of heart attack and stroke. And if inflammation has been driving atherosclerosis, then one might add that if psoriasis is an inflammatory skin disease that it itself may have some previous position to atherosclerosis and cardiovascular events. So, before our study for about 15 years now, there's been an accumulation of literature showing that psoriasis itself is a systemic inflammatory disease, that it does extend beyond the skin, and that it affects multiple organ systems in the body, and it does so at different points of life.

So, in 2006, the first study came out that when one had severe psoriasis compared to no psoriasis, you had approximately a two-fold risk of having your first heart attack. And what was striking was that in 40 to 50-year-old individuals, there was an age-interaction whereas somebody who was younger compared to an older person with psoriasis, they would actually have a two-fold increase of having that first heart attack in their forties.

So, then the next series of studies that showed that psoriasis affected vascular disease came by way of looking at imaging using vascular techniques, PET CT and coronary CTA, and up until the mid-2010 to -20 decade, it was known that the events were predisposed in psoriasis but there wasn't a reason why. So, the other lines of evidence before the study was done had been that psoriasis affects lipid function, so you have lipid handling disturbance. It affects your ability to handle sugars, you have insulin resistance. There's a signal for obesity, meaning that people with psoriasis tend to be obese.

So we can say that before this study, in addition to having increased cardiovascular events, as well increased traditional risk factors for cardiovascular disease, coronary CT angiography also showed that patients with psoriasis had a higher risk of sub-clinical, meaning they had no symptoms, sub-clinical heart disease, and that was found on coronary CT angiography in the form of what we call early non-calcified plaque. So leading up to this study, psoriasis almost acted like a risk factor for heart disease.

Dr. Greenberg:
And so with that being said, how did your study aim to fill in some of our knowledge gaps? How was it designed?

Dr. Mehta:
So the question that our study was asking was built on three pieces of evidence. Number one, psoriasis patients tend to be obese. And this obesity is associated with pre-diabetes, or something called the metabolic syndrome. So we asked whether knowing that if there was obesity in psoriasis and an increase in metabolic syndrome, and we knew that there was an increase in sub-clinical atherosclerosis by CCTA, the kind of plaque that causes heart attack, what if we started identifying patients with psoriasis as having the metabolic syndrome in order to make patients understand that they are at higher risk for developing this higher risk plaque, this non-calcified plaque.

So what our study did was it followed 300 individuals for a total of a year and asked, 'If you had psoriasis and you had metabolic

syndrome, was that differentially associated with your risk of having this sub-clinical atherosclerosis on CT angiography?'. And what the study was really trying to do was make people aware that when you're obese and you have psoriasis, there's a very high chance that you have the metabolic syndrome, and we'll talk about what that is. And when you have the metabolic syndrome, you have this higher risk for having future risk of heart disease.

So what we did was we asked, if you classified people as having the following five abnormalities. And one of them was being obese, so that's one of the things, your body mass index is above 35, or 30 if you're looking at it for just general obesity. Do you have high blood pressure? Do you have high triglycerides? Do you have a high sugar? And the combination of three of those five diagnoses metabolic syndrome. And what our study was trying to do was say, 'When you're obese, and if you have other risk factors for heart disease, such as high blood pressure or dysglycemia or pre-diabetes, or high triglycerides, your body is probably in an insulin-resistant state and that may be a marker for future risk of heart disease.'

Dr. Greenberg:
So Dr. Mehta, can you tell us why you chose this point in time to do this study?

Dr. Mehta:
Yeah. So there's accumulating literature that visceral adipose tissue, which is the type of tissue that's around the middle of the body, was up-regulated in inflammation. So, inflammation in the last five years has received a lot of attention in cardiovascular disease because the CANTOS study showed that treatment of people with post-myocardial infarction within that first window with an anti-IL1 beta therapy, a biologic therapy, reduced the second heart attack risk. Furthermore, we were sitting on the heels of COLCOT which showed that with treatment of colchicine at low doses post having a myocardial infarction one can lower the re-event rate. So, the inflammation access had been right at the intersection here. But then we had also seen that inflammation also drives this visceral adipose tissue. So this study was positioned in an inflammatory population who's predisposed to visceral adipose tissue, as well as obesity to ask whether the simple identification using clinical definitions of the metabolic syndrome would impact risk of heart disease.

Dr. Greenberg:
And what were your findings, Dr. Mehta? Were you surprised by them?

Dr. Mehta:
The findings of our study were three-fold. The first one. Patients who had psoriasis with the metabolic syndrome had worse lipid function, had more systemic inflammation, and had more visceral adiposity, which is a type of fat tissue that is higher risk for having future diabetes and heart disease risk.

The second finding was that in patients who had the metabolic syndrome, they had more evidence of sub-clinical atherosclerosis, meaning they never had symptoms, but they had presence of non-calcified plaque in their coronary arteries.

And the third thing that the paper showed is that when you look at  controlling for all the other risk factors for heart disease including the metabolic syndrome features, themselves, blood pressure and obesity remained independently associated with non-calcified burden. Which means that even if you look at all the other factors as equal, being obese and having high blood pressure were the single most important risks for driving that non-calcified plaque. And so the take-home was that A) look for metabolic syndrome in the patients, and B) if you do find it, really focus on getting the weight down and getting the blood pressure under control in order to mitigate risk of future heart disease.

Dr. Greenberg:
So, Dr. Mehta, now that we know the results of your study, let's take a look at their implications. What might your study mean for our patients?

Dr. Mehta:
The major implication of this study is to look for cardio-metabolic features in our patients with psoriasis. And what are those cardio-metabolic disease features? Look for obesity. I should not be the first person telling patients that they are obese. Body mass index is a height divided by a weight with an index factor. Secondly, there should be general education for our patients of their cardiovascular risk in psoriasis that they may be walking around with "just a skin disease" but in reality, it's not just a skin disease; it actually has implications on cholesterol, on sugar, on blood pressure, on weight. And these are the most important cardiovascular risk factors anyway.

I think what this study sheds light on most is the fact that something could be right in front of you, ready to give you a clinical answer and you don't look for it. So this requires a little bit of work on the healthcare provider's part. It requires getting the three B's, I've always said that the meta 3 B's are get a body mass index, get a blood pressure, and check the blood for cholesterol and glucose. And if people get

those three B's done in psoriasis and in general, you could calculate your metabolic syndrome presence or absence. So, something sitting right in front of you ready to calculate, I think we've given this the justification it needs that you should be identifying this in your patients with psoriasis.

Dr. Greenberg:
So as clinically practicing dermatologists, what's our role in all this? Can we really help prevent heart disease in patients with psoriasis?

Dr. Mehta:
I am really glad that you asked that question. I think that it is not the role of the dermatologists, per se, it's the role of any healthcare provider for that patient to remind that patient, whoever they feel most comfortable getting those 3 B's done with, they need to have them.

I do believe that the role of the doctor in dermatology is to keep the cutaneous disease at bay. The role of a rheumatologist is to make sure that we stave off or treat any psoriatic arthritis, one in three patients will get psoriatic arthritis. And I think that the role of any general medical provider should be in general preventive medicine. And that is including identifying obesity, identifying cardiovascular risk factors, and this doesn't start too early. Some of our studies from my lab have shown that these psoriatic patients who have diseases in their early ages, in their 10 to 13 years of age, they are developing insulin resistance and cholesterol dysfunction in their teens, so this makes sense why in their forties they're having heart attacks and strokes.

And then why I was glad you asked that question is that actually the next wave of studies coming out of our group, in conjunction with some collaborators at University of Pennsylvania, we've designed the prevention of cardiovascular disease in psoriasis and psoriatic arthritis study where we're understanding the factors needed to overcome getting statin prescription or prescription of HMG-CoA reductase into the hands of derms and rheums. Because here what you're saying is, 'Well whose job is this to look at this risk factor profiling?' I don't think we really do a good job, in general educating about the risk and then doing something about it.

So our study is going to ask, 'Well, what are the barriers, why aren't people asking and educating?', so we're done with phase 1 of the study. And then phase 2 is going to be rolling out getting the prescription of lipid-lowering therapy into the hands of the people who see these patients.

Dr. Greenberg:
Dr. Mehta, what's next for you and your team? Do you plan on expanding this knowledge base?

Dr. Mehta:
The most important thing for what's next is moving the dial forward. So, in 2009, we coined the term, 'more than skin deep,' that one, one psoriatic plaque was really more than skin deep, it was going to the brain and being associated with things like anxiety and depression. It was impacting liver disease, it was impacting the joints. It was impacting the vascular system. And then years later, we said that we now know it's more than skin deep, and we coined the term 'even one plaque is too much.' So even having gone plaque on the body gave you this low-grade inflammation and even having palm or elbows and knees psoriasis was associated with earlier non-calcified plaque in our cohort.

And so then in 2018, we saw the guidelines recognize that psoriasis is actually a risk factor and for initiation of early statin therapy. And that was very good because for the field that showed that we now have moved the dial forward. So, what's next for this field? Is really my next term is, 'let's move the dial.' And in order to move the dial, we've planned the CP3 study, which is getting statin prescription into the hands of derms and rheums. And we've also planned another set of trials to test whether aggressive control of skin disease, as well as treatment of cardiovascular risk factors will in fact impact the progression or regression or stabilization of these non-calcified plaques.

We're very pleased that our work has reached so many different agencies, bodies of guideline producers, as well as has now started hitting more of the lay press in the sense that psoriasis has demonstrated that untreated inflammation is not good for the body. So what's next for the program is continue to move the dial forward. And to continue to educate about the general well-being that's needed to approach this inflammation and to combat it.

Dr. Greenberg:
Well that's a great way to end our discussion. I want to thank Dr. Nehal Mehta for being on the program today.

For ReachMD, I'm Dr. Michael Greenberg. To access this episode and others from this series, visit ReachMD.com/DermConsult, where you can Be Part of the Knowledge. Thank you for listening.