

Autoimmune disorders: An emerging risk factor for CV disease

DR. SHARON MULVAGH: Greetings. I'm **Dr Sharon Mulvagh**, professor of medicine and director of Mayo Clinic Women's Heart Clinic. During today's Mayo Clinic Talks we'll be discussing autoimmune disorders, an emerging risk for cardiovascular disease.

I am joined by my colleague, **Dr Rekha Mankad**, instructor in medicine, who works with us in the Women's Heart Clinic and has a special focused interest in autoimmune disorders and the risk for cardiovascular disease.

Rekha, it's really interesting that this recognition of the fact that autoimmune disorders, particularly rheumatoid arthritis, lupus, and psoriasis, the first two of which occur far more commonly in women, now are known to be risk factors for cardiovascular disease. How did this evolve? And tell us [what led us to recognize this fact] over just the last couple of years.

DR. REKHA MANKAD: Yes, it is interesting, Sharon. This risk factor has actually been identified long before, if you look at the literature. Reviewing the rheumatologic literature, the rheumatologists have seen that patients with rheumatoid arthritis and lupus are having a higher rate of cardiovascular morbidity and mortality, and this dates back for several decades.

I think that the cardiologists' recognition has been more recent, probably because of the higher focus that we have about the inflammatory mechanism of atherosclerotic disease. So I think starting in the '90s to early 2000s, as we started talking about inflammation being the big risk for atherosclerotic disease, we went backward a little bit and looked at that rheumatologic disease entities, the inflammatory rheumatologic diseases, and seeing that there was this link. And I think that's how we came about now to talk about this as a risk factor.

So I would actually say it's not an emerging risk factor. It's been one that's been recognized, but we cardiologists, I think, are just now getting on the bandwagon.

DR. SHARON MULVAGH: Interesting. The issue really becomes what we do with these patients. How do we look at the traditional risk factors for cardiovascular disease in the context of the additional risk of having a diffuse autoimmune disorder?

DR. REKHA MANKAD: That's a great question, and I think that there's still some controversy, and we're just collecting a lot of data about this. And again, both lupus and rheumatoid arthritis, which are the ones we are going to concentrate on, are relatively uncommon entities. So we don't have a lot of patients with these diseases to have a lot of cohort studies. Rheumatoid arthritis has a bit more epidemiologic studies than lupus, but we're really getting this from that analysis.

So what we see first is, again, cardiovascular mortality is higher in both of these groups and seems to happen at a much earlier age. That's particularly true in the lupus patient.

But if you start talking about why these patients are having this disease, first you look at the traditional risk factors, and they do have the standard traditional risk factors such as hypertension, dyslipidemia, smoking history, and insulin resistance, as [in] the general population, but it may be that those particular entities have different influences in the rheumatologic patient because of the concomitant inflammation that's going on.

What we have seen in the literature is that if you control for those traditional risk factors, these patients continue to have higher rates of cardiovascular mortality and morbidity, so that there's something beyond the traditional risk factors, and those traditional risk factors may impart different roles and different sort of weights in this patient population.

DR. SHARON MULVAGH: How is it that the medications that the patients are on with autoimmune disorders play a role or perhaps the intensity of their disease process at the time, are those that are in more active flare more likely to present with acute coronary symptoms? Has there been any association like that? What about the mechanisms of the treatments that are provided for the folks with autoimmune disorders?

DR. REKHA MANKAD: When we talk about the disease activity with these disorders—and again, the two are different and have different ages of presentations and different flares, but for the most part we'll group them together as inflammatory autoimmune disorders. When you talk about the inflammation, what we see is those with higher disease activity, higher incidence of inflammation, so higher [sedimentation] sed rates, CRP, seem to have higher cardiovascular events, not necessarily during the flare itself, but just if you look at

their sed rates that over the period of time before the event, they seem to be running higher. So again, inflammation seems to be the major underlying mechanism or one of the major underlying mechanisms.

So what we've seen in rheumatoid arthritis is that the longer you have the disease, the higher likelihood you would have a cardiovascular event, so disease duration, being older at the time and, again, this disease activity score. So the more that the disease is destructive or inflammatory seems to play a role for both of these entities.

So what does that mean as far as the treatments? Well, as you know, we use nonsteroidal anti-inflammatory drugs in these patients as well as steroids, at least during flares, and both of those may not be the most beneficial from a cardiovascular standpoint. Nonsteroidal anti-inflammatory drugs have been associated with higher rates of cardiovascular morbidity.

So how do you use those? But like I said, inflammation's playing a role, so you want to control the inflammation. Right now the way those drugs need to be used is to control flares and use the lowest dose to control symptoms. But that the biggest component is to control the disease itself and the inflammation of the disease long term, and that's where these disease-modulating antirheumatic drugs play a big role, **methotrexate** being one of them. And what we've seen is patients on those drugs actually have a lower rate of cardiovascular events.

And so the goal is to try to treat the disease early and maybe at milder stages to control that inflammation. There's the TNF, anti-TNF factors as well, and those are used sort of later in the course of some of these diseases, but again, it seems that using those agents to control the underlying inflammation of these diseases may be beneficial in relationship to the cardiovascular events.

DR. SHARON MULVAGH: Is there anything that you do in this disease population—you know that the patient is coming with this risk factor, this novel type of risk factor. Is there anything that we should be doing to address our patients beyond our usual screening assessments for cardiovascular disease, you know, checking the lipid profile and the blood sugar? What about early atherosclerosis detection?

DR. REKHA MANKAD: This is a great topic, but it's something that's still a little unclear and unknown. I think, again, the first thing is to understand that this risk exists. We can go backward and say this is

how we came about with women and heart disease and recognizing that women were having high rates of heart disease. Same thing about these rheumatologic conditions. First, we need to understand that it is a risk factor, and in some of the literature it's been equated to diabetes as a risk equivalent.

We need to first understand that these patients are at risk, and we need to look at their traditional risk factors because what the literature would tell us is that their traditional risk factors may not be adequately being recognized or treated. Their hypertension may not be adequately controlled. Their lipids may not be adequately controlled. Talk about lifestyle modifications, weight loss, exercise, all need to play a role. So I think that's the first thing is to make sure you know that this person's at risk and look at their traditional risk factors.

Now beyond that, looking at early atherosclerosis, I think this is a great topic because this may be where we need to go, where we start screening these people earlier for subclinical disease. And literature has shown us that these patients have higher rates of carotid atherosclerosis, nonobstructive. They also have higher calcium scores on CT scans for [coronary calcium] studies. So we know that they have more subclinical atherosclerosis, so perhaps by identifying that early we then have an additional factor to look at their risk profile and then can go after their traditional risk factors more aggressively and also talk with our rheumatology colleagues about how best to modulate their disease as well.

DR. SHARON MULVAGH: Diseases underlying, exactly. Now, are there official guidelines for the management of patients, recognizing now that this is a newer risk factor for cardiovascular disease, particularly the recent **American Heart Association** Guidelines for Prevention of Cardiovascular Disease in Women by **Dr Lori Mosca** and coeditors? What's the statement there, and what's the approach, and what do we do here at Mayo? Maybe we could elaborate.

DR. REKHA MANKAD: Sure. The most recent guideline update added autoimmune disease to the at-risk population. So automatically, if you have one of these inflammatory rheumatologic conditions (lupus, RA), it puts you at risk through your lifespan of having a cardiovascular event. It's in the at-risk category. It is not equal yet to diabetes, although, again, the literature would say that they may be equivalent.

The Europeans use rheumatologic conditions and inflammatory conditions in their risk assessment, and they actually have a factor

that they use for rheumatoid arthritis to show that those patients are at more risk, and they just put a random number sort of score if you have RA and if you've had it for a longer duration and certain antibodies, etc. We don't do that here.

So the first thing, again, is we need to collect more data. So we need to look at these patients, probably, you know, look at them across different institutions, collect all this data to see how best to treat these patients and what we should do.

So what do we do here? I think the first thing—and this is how I got interested—was that the rheumatologists were sending these patients for risk assessment, and that's how I realized, wow, these patients are at this really high risk.

DR. SHARON MULVAGH: And a lot of them are women so you were seeing them in the Women's Heart Clinic.

DR. REKHA MANKAD: And they're young. So that's the other key and the lupus young women—

DR. SHARON MULVAGH: Yeah, and lifetime risk increased.

DR. REKHA MANKAD: Increases, because the rheumatologists have gotten so good at controlling their disease, clearly we're talking about many, many years of living with this disease. And so we really have to look at lifetime risk.

So what we are doing—and we are just getting into the stages of this and hopefully having a clinic within our Women's Heart Clinic to deal with these patients—is to, again, address their traditional risk factors first, sort of be the center player to look at traditional risk factors and then decide about early atherosclerosis screening, decide about assessment for endothelial dysfunction, carotid atherosclerosis, etc, and then follow these patients long term to see if what we're doing is changing outcomes.

DR. SHARON MULVAGH: Are there any centers in the world that have experience with this as well?

DR. REKHA MANKAD: There is a center in Norway, a colleague of ours that we met through **Dr Sherine Gabriel** from rheumatology, actually has a clinic in Norway where she follows these patients and she sees all the autoimmune patients who have potential for cardiovascular risk

and, again, mostly rheumatoid arthritis and lupus but the other conditions as well which are a little bit rarer.

So she does track their lipids, looks at their risk profiles. She is also assessing carotid atherosclerosis and even doing echocardiograms to look for diastolic dysfunction and heart failure.

DR. SHARON MULVAGH: Well, Rekha, I really appreciate you enlightening us in this; really it is an emerging awareness of this risk, this added risk of autoimmune disorders with their chronic inflammation in lifetime risk for development of cardiovascular disease.

I would like to mention to our listeners too that indeed because we do feel that this is such an important topic, we will at the upcoming American Heart Association sessions this November have a satellite session entitled "Cardio Rheumatology Mechanisms and Management," and it will be on the Saturday of the meetings, and we would certainly invite you all to come. There's a lot of very exciting and interesting information that will be presented there as well.

So thanks again, Rekha, for these very important insights, and thank you to our listeners for tuning to Mayo Clinic Talks.

DR. REKHA MANKAD: Thank you.