SPEAKER: Fabry Disease can manifest at multiple time periods during life, specifically for the cardiovascular system. We've done a fair amount of research on patients across multiple ages with Fabry, and we do know that there are cardiovascular implications even in childhood and adolescence.

Some of those are manifestations of conduction disease, for example, such as sinus bradycardia or bundle branch blocks. But we don't typically see an overt amount of cardiomyopathy, per se. But as you get older, it can manifest at pretty much any time. And we have seen patients older in life, 40s or so, that have had essentially clean or unremarkable cardiovascular exams, and then develop a phenotype.

What I would tell you as someone who's been doing this for a while is that when we say people don't have cardiovascular involvement, I would ask you, what is the tool that you're using to do the screening? Because most practices worldwide would leverage echocardiography as the screening tool for cardiovascular involvement, specifically from a cardiomyopathy perspective.

And I'll tell you that that's really not the most optimal way to look for cardiovascular implications. And so for us, we do things such as cardiac MRI. And MRI gives us an opportunity to look at a multitude of things. One is actually, we can get chamber size accurately. We can get volumetrics. We can get good systolic assessment of the RV and LV.

We can do strain on atrial or ventricular tissue. Obviously, that is important as well. But there are a few other things that we can capture on the MRI that I would suggest really argue strongly that MRI should be the longitudinal test of choice for patients with Fabry. And we'll talk a bit more where echo comes into play. But for most of what we're talking about, MRI will give you most of the information you're going to need.

So a few of the things that we alluded to a little bit earlier in other segments are that there are other pathologies we need to be cognizant of in people that have Fabry. So specifically, they can develop aortic dilatation, so where it can become mildly aneurysmal. And obviously, this is a silent disease.

As you know for anyone who's cared for any thoracic aortic aneurysmal patients, it's a silent disease until it's not, when that dissection occurs. And so that's an important thing for you to know, because you want to watch it. But you also want to potentially treat it medically. We capture that information just on the MRI just because it's there. We don't have to do additional testing for that.

The other thing, though, is that we can look for myocardial characterisation. And for people that have genetically-triggered cardiomyopathies, that's a very important opportunity, because in most diseases, we're going to see changes in the myocardium before we see changes in systolic function.

So meaning we could do an MRI-- and traditionally, we would use gadolinium as a contrast agent, so intravenous, give that, and look for evidence of late gadolinium enhancement. And that gives us an idea of abnormalities in the myocardium, remembering it's a surrogate. But many times, it will be representative of scar or fibrosis. So that's an important thing to know.

And I'm saying that we may see fibrosis on a cardiac MRI well before I see a decline in systolic function, and even before I see a change in ventricular thickness. And if someone asked me, does that patient have a cardiomyopathy? I would say, yes. As such, that would potentially lead to them receiving enzyme replacement therapy.