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ReachMD
www.reachmd.com
info@reachmd.com
(866) 423-7849

The Role of Imaging in Determining Treatment Escalation in Spondyloarthritis

Announcer:

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Here's your host, Dr Ethan Craig.

Dr Craig:

So, I've worried with some of these episode introductions that I may be starting to get repetitive. Some themes just keep arising, and today's episode covers one of those: That disease activity in spondyloarthritis, or SpA for short, can be pretty challenging to assess. From the involvement of joints that simply cannot be assessed clinically to the role of enthesitis, which may be difficult to disentangle from pain sensitization and mechanical diseases, and the difficulty of gauging improvement in a patient with only a few joints involved, clinical disease activity assessment can be very difficult in SpA. Making matters worse is the relative absence of biomarkers beyond the trusty CRP. So there's a great interest in improving our ability to monitor disease activity, especially surrounding decisions to escalate therapy. In today's podcast, we'll discuss the role of imaging and treatment escalation in SpA.

This is ReachMD, and I'm Dr Ethan Craig. And there's no one I'd rather have join me to discuss this topic than our guest, Dr Catherine Bakewell. Dr Bakewell is a rheumatologist at Intermountain Healthcare in Salt Lake City, Utah, and she's an active member of multiple spondyloarthritis research groups, including SPARTAN and GRAPPA, and continues to actively mentor and teach rheumatology ultrasound trainees through various CME efforts, as well as the Ultrasound School for North American Rheumatologists, or USSONAR program. Dr Bakewell, thanks for being here with us today.

Dr Bakewell:

Thank you for having me.

Dr Craig:

So, I'd like to start off with talking about peripheral SpA, going through the monitoring of its varied manifestations, and then maybe we'll move on to axial SpA. So let's start with arthritis.

Certainly, we've all run across the patient on treatment for SpA who has, say, new pain in a hip or a shoulder that's challenging to examine, or maybe has some new hand pain without apparent synovitis on exam. So, taking these examples, do you see a role of ultrasound or MRI to determine if there's a need for treatment escalation? I guess put simply, do we have anything for SpA that's akin to the ARCTIC trial, Aiming for Remission in rheumatoid arthritis: A randomised trial examining the benefit of ultrasound in a Clinical Tight Control regimen trial in rheumatoid arthritis?

Dr Bakewell:

So to date, we don't have any specific spondyloarthritis trial at the scale of ARCTIC for rheumatoid arthritis. But I can tell you that when we do those trials, I hope we will structure them differently, since the final take-home from ARCTIC was that there was not really room

for ultrasound on the treat-to-target paradigm for rheumatoid arthritis. But again, some may disagree, and I think it is helpful to highlight the actual phrasing of the conclusion on the ARCTIC trial was that the systematic use of ultrasound in the follow-up of patients with early rheumatoid arthritis was not justified based upon their results. And this has to do, in the opinion of some, with the way that ultrasound was applied to every patient at every visit in the ultrasound tight control arm, as opposed to how we apply this modality in clinical practice, which is more the patient that you are highlighting above, which is to say the patient with either new onset or cryptic shoulder or hip pain. These are difficult-to-examine areas. Or the patient with hand pain with not much on exam. It's these areas of either difficult examinations, or equivocal or clinically discordant examination and patient report of their experience or discomfort that the ultrasound is critically helpful. And so, my hope is that when we go about a systematic approach or review of the use of musculoskeletal ultrasound and a treat-to-target paradigm for the spondyloarthropathies that we really reserve it for where a clinical question exists, as opposed to every patient, every visit, in a highly protocolized way.

Dr Craig:

So then, if we move on to enthesitis, the picture is kind of similar. We often have patients with new areas of pain, where we may be asking whether this is enthesitis, myofascial tender point, or a mechanical injury. And it does seem that ultrasound is helpful in sorting that out. But is there a role to play in monitoring of enthesitis over time with ultrasound or MRI?

Dr Bakewell:

Yes. So, in my opinion, there's absolutely a role, in particular for ultrasound and monitoring enthesitis. It is real time, it's bedside, it's highly accessible to the patient and the clinician, and we do have some proof-of-concept studies that demonstrate that entheseal Doppler signal improves with biologic therapies such as TNF factor inhibitors or interleukin-17 inhibitors. But enthesitis is somewhat more difficult to evaluate ultrasonographically for a number of different reasons. It is subject, at least the power Doppler aspect of it, to some of those same qualifiers or caveats that synovitis is, which is to say, it's sensitive to the time of day and room temperature. But enthesitis, in particular, is sensitive to patient position. And there may be discordance in the patient position that we recommend for a synovitis exam and contradistinction to an enthesitis exam.

So for example, at the level of the knee, we will teach our young ultrasonographers to examine the patients with the knee in 30 degrees of flexion, so with a pillow tucked under the knee or a towel, because that is how you can get the highest synovitis scores. But when you're looking at the enthesis, so quadriceps or patellar tendon, it was actually Marwin Gutierrez first in 2011 that published a paper showing that you get higher power Doppler signals at the enthesis with the patient in a neutral position. So you would remove the towel, remove the pillow, and examine the knee again. So, this is what we have done since 2011, not only in our clinical practice, but also tried to routinely apply this in clinical trials when we're looking at ultrasonographic endpoints.

And specifically, since the question is, can we monitor enthesitis? I do want to highlight one clinical trial that attempted to answer this in a validated, systematic way, which was the ULTIMATE trial. And it was unique because it was the first of its kind in that it was a randomized, double-blind, placebo-controlled trial that examined the effect of an IL-17A inhibitor and it had an ultrasonographic primary endpoint, which was a synovitis score. So, it met its primary endpoint, but it also concomitantly examined enthesitis scoring systems and was able to show a correlation between the SPARCC, or the Spondyloarthritis Research Consortium of Canada clinical enthesitis exam, and 2 different ultrasonographic enthesitis scoring systems, which was one including grayscale and power Doppler, so that would be hypoechogenicity, thickening, and power Doppler signal at the level of the enthesis. That was definition 1. And definition 2, which a minority of patients, only 33%, met this definition, but it was exclusively power Doppler signal. But both of these definitions were able to demonstrate a similar diminution to the clinical index. So, this really was the first step towards the development of an ultrasound enthesitis scoring system for our psoriatic arthritis patients that I hope to see validated across the spondyloarthropathies.

Dr Craig:

Thank you for that. And I have to say that getting to name your trial the ULTIMATE trial is pretty fantastic.

So, this finally leads to axial disease, so let's take a case. So, let's say we have a 25-year-old man. He has a history of morning stiffness in the low back, he's got uveitis and a positive HLA-B27. He had a prior MRI of the SI joint that showed a few erosions and deep bone marrow edema. At the time of the diagnosis, he had normal inflammatory markers, so we can't track those as easily. So, he's been on NSAIDs for over a year and his morning stiffness has improved, but he still has this, like, 15 to 20 minutes of stiffness each morning and some low back pain that's gotten somewhat better, but still persists. So, his ASDAS score is consistent with low disease activity, but he wants to know, you know, what about these erosions we saw before? So, should we be thinking about then monitoring patients with repeat MRI to make sure there are not any changes? And how do you answer patients when they ask you about this?

Dr Bakewell:

That's a great question. And in the absence of his specific question, but just simply from a clinical perspective, if you have a patient who has low disease activity, and they're feeling significantly improved, there's really no need for routine MRI unless there is a clinical question, and I'll give you some examples. If the same patient were to have sudden worsening of back pain or a new location of back pain, this would be a time that it would be appropriate to re-MRI. But not necessarily to give us assurance that yes, in fact, you are in remission, even though by our best disease activity measures you are currently in either remission or low disease activity.

So, similar to what I was saying with ultrasound, we really want to reserve these imaging modalities for where there is a clinical question to be addressed. We don't have a treat-to-target paradigm where we serially perform MRI for patients with axial disease, and there's no guideline for its use for re-evaluation.

We know that there are barriers to routine use, more so for MRI than for musculoskeletal ultrasound, which again, is real-time and bedside and relatively inexpensive. When I order an MRI for my patient, it has to first be approved by insurance, and then scheduled, the patient has to come back, and they may be in a small claustrophobia-inducing tube for up to 45 minutes. And so you don't want to just be saying, 'Oh, every 2 years, we need to, you know, re-MRI your spine.' You want to monitor your patients, if their inflammation goes up, and either morning stiffness, ESR, CRP, or their clinical status changes, then it is absolutely appropriate to re-image.

Dr Craig:

And I think that's a great way to round out our discussion on this topic. I want to thank my guest for helping us think in depth about imaging in SpA, and how we can use it to determine treatment escalation. Dr Bakewell, it was great speaking with you today.

Dr Bakewell:

Thank you very much for having me.

Announcer:

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