RA Risk Radar: Heart Disease, Infection, and Malignancy

Podcast Transcript

Dr. Jeffery Curtis: Welcome to RheumNow. This podcast is sponsored by AbbVie US Medical Affairs. I'm Dr. Jeffrey Curtis and I'm a professor of medicine, epidemiology and computer science at the University of Alabama at Birmingham. Today I'm joined by Dr. Jon Giles. Jon, could you introduce yourself?

Dr. Jon Giles: Hi, I'm Jon Giles. I'm an associate professor of medicine and the director of the Inflammatory Arthritis Center here at Cedars-Sinai Medical Center in Los Angeles, California.

Dr. Curtis: Thanks, Jon. Today we're going to talk about comorbidities that can occur as a consequence of uncontrolled, or under-controlled, inflammation in rheumatoid arthritis, or RA.

As rheumatologists, it's quite natural for us to be focused on the hallmarks of the rheumatic disease that we're treating, as well as the medication-related side effects that we have to think through. However, we also need to be thinking about patients risks for comorbidities, as well as multimorbidity.

Multimorbidity is a newer term that can be thought about as all of the other medical conditions that may be impacting a patient's care. It's a little bit of a paradigm shift for rheumatologists that typically focus on one disease, in this case, RA. And yet that's probably not how patients think about their own health. For them, rheumatoid arthritis may simply be one of several important and chronic health conditions that they need to think about, and I think this will have important impact as we think through how we consider tradeoffs and risks of controlling inflammation, some of the side effects of under-controlled inflammation, and some of the medicines that we might use to get the disease under control.

Quite recently, I think as a field, we've had a lot of discussion around cardiovascular risk, as well as other risks for serious infections and malignancy. So, the topic for today is to discuss how we can mitigate comorbidities and reduce the overall risk from multimorbidity, and continue to address the top priorities that patients have to control their RA.

So, with that as context, Dr. Giles, why is it important for us as rheumatologists to be thinking about comorbidity risk in RA?

Dr. Giles: Well, I think we often think about RA as being just a disease of the joints, but in reality it's a disease of the entire body. And there are a lot of high impact comorbidities that make a big difference for our patients in terms of their quality of life. It could even reduce their lifespan in certain circumstances. And the top ones here are cardiovascular disease of all types. We're thinking about atherosclerotic cardiovascular disease, cerebrovascular disease, and even heart failure. We know our patients get serious infections more frequently, and pretty much across the board, their risk for most malignancies, with maybe the exception of colon cancer is higher. And two of the highest risk malignancies are actually lymphoma and also lung cancer.

These of course, are some of the biggest contributors to mortality. They're the highest risks of death in the general population. And that's even higher in our RA patients.

ABBV-US-01757-MC Approval date: September 2024 v1.0

Dr. Curtis: That's a great point. And I think that as we focus a lot, as specialists, on the risks of medications used to treat the disease, often what goes unrecognized is all of those other considerations that you just spoke about.

I'm reflecting on an RA patient of mine as an example. And she has some of these same issues that surfaced in the course of treatment discussions but where some of the topics that you brought out really were under-recognized and I think were helpful to think about with her.

She's 59 and she has had, frankly, longstanding under-controlled rheumatoid arthritis, and has been in, frankly, moderate disease activity even despite a couple therapies in the past. She's now on her second TNF inhibitor. And she's had RA for 25 years. She's a half pack a day smoker, and we've had a tough time getting her off prednisone.

Due to uncontrolled inflammation, as well as some of these other risk factors, I've discussed with her, her increased risk for cardiovascular disease, as well as some of the risks for infections and malignancies. But due to her concern for potential side effects of changing her RA medications, she actually hasn't been willing to change from her TNF inhibitor to a different mechanism of action.

So, with that as an example, I'm curious, Jon, how you approach a patient like this, where you're having these kinds of discussions: there's the things she's worried about, and then there's the things that you and I might be worried about. How do you resolve what might be a mismatch?

Dr. Giles: I think first is educating the patient about the increased risk and describing that there's a background amount of risk they have from their traditional risk factors that are often amplified because of features of their RA, whether it be other comorbidities or whether it be the inflammation of their disease.

And I think we take it for granted that patients understand that inflammation itself is a risk factor for these things, but they often don't. And I think we have enough data, at least for cardiovascular disease, to suggest that by decreasing inflammation in our patients, systemic inflammation and articular inflammation, that we can actually reduce these risks over time.

So, first is education for our patients. And the second is quantifying their risk. So, for cardiovascular disease we have a number of risk calculators that we can use in the general population. For the US population it is called the PREVENT score. That uses a number of traditional risk factors, like their age, like blood pressure, etc. that can be put into a calculator that's readily available on the internet and give an idea about what the person's risk of having a major cardiovascular event in the next ten years is. And we can share that information with them regularly and let them know about their risk.

In addition, we know that the risk is probably higher than what those scores give us. And the nice thing about that score is it's actionable based on what the score is, in particular, adding things like statins to a person's treatment regimen.

For infections there are also some risk calculators, mainly related to age and frailty type features but also related to disease activity. These aren't quite as actionable because they give us an idea the patient is at higher risk, but there's really not much else we can do in that circumstance except for maybe reducing prednisone.

For malignancy there are also a number of underutilized screening tools. One is doing yearly low-dose CT scanning of the chest for lung cancer screening in smokers. We know our patients have smoking as commonly as a risk factor and that we are underutilizing lung cancer screening in our patients because we know their lung cancer risk is higher, especially if they have comorbidities like for interstitial lung disease.

So, I think we're underutilizing the tools that are already recommended for the background population. If we talk to our patients and emphasize that their risk is even higher than the background population, I think they can understand that these risks are higher and engage with those types of screenings and studies.

Dr. Curtis: I agree, although I, I confess that sometimes entering data into any of those calculators may impact a clinician's busy workflow. So, how important is it, do you think, to use any of those risk calculators to quantify risk versus to talk about it in general terms? And then maybe you could also speak to how you think of those calculators' output as a starting point, and then modify somebody's level of disease control from their RA as one of the modifying factors.

Dr Giles: Yeah, I think that's a good point. I mean, they do take a little time, but they don't have to be done every single time you see a patient. There are ways to automate your practice so that maybe you're not doing it. Maybe the nurse is doing the calculator and giving you the numbers, or maybe the patient can even do the calculator themselves and give you the numbers.

In terms of mitigating risk, I think the other aspect that we can bring, which is the example of your patient, is if the patient is reluctant to change their therapy because their content with their level of disease activity, but we know that it's higher than it should be, we can always bring that up into the equation of you have these other risk factors. Maybe we already know that they have atherosclerotic cardiovascular disease. And we can use that and say that not only will a change in your medications likely make your joints feel better, but it may have a role in controlling these other things. And having a heart attack is maybe a little scarier than, you know, having a few swollen joints in the fingers.

And we do know that, we have some good, evidence that this is the case, that we can actually intervene on these by reducing inflammation. There's circumstantial evidence that shows that cardiovascular disease outcomes have improved over time, and that they're tied to disease activity. We know that when people have flares, they have more cardiovascular events. So, this really intimate relationship with disease activity really seems to have a good evidence base behind it.

Dr. Curtis: Yeah, I agree with you. And I also use some of the output from those calculators to also make the point of the modifiable risk factors that really are under our or perhaps patient's control. You know, you don't want to take a statin and you don't want to stop smoking, and you're unwilling to let me try to decrease you from ten milligrams a day of prednisone – those are things that to some extent we could perhaps work on or work through. And while people may focus on medication-related side effects, I think some of those other risk factors or lifestyle factors, side effects, go unrecognized.

And so I use some of those risk calculators' findings and the quantitative aspects of them to point out, you know, here's the incremental risk, at least for groups of patients, related to some of these things that we could talk about you giving up or trying to quit, if this were smoking. So, I find that very helpful.

I talk about cardiovascular risk as one of the risks associated with poorly controlled RA. And sometimes poorly controlled RA doesn't seem to have risks explicitly like maybe a treatment or a surgery has risks, and yet it very much does. And I want to put that on the table and say, look, let's think through - for you - the risks and benefits of treating this in a certain way, or not treating this and just letting RA, you know, roam unchecked. And I think that's helpful when you can put that silent or sometimes hidden set of risks of under-treating RA on the table as something that patients need to grapple with.

Dr. Giles: I agree with you 100%.

Dr. Curtis: You touched on inflammation in its contribution and interplay with disease activity. You were part of a very important study, the TARGET trial, that I wondered if you can help us glean some of the most important insights from that study and how we can think about that interplay between inflammation and RA disease activity and some of the side effects on the non-joint organ systems that were uncovered as part of that.

Dr. Giles: Well, we were interested in finding out if our medications could reduce inflammation in the blood vessels. So inflammation in your arteries, like your coronary artery, your aorta, your carotid arteries, those are associated with atherosclerotic plaque formation and also with the plaque rupture, which is the cause of myocardial infarction. So we were interested to test whether the inflammation in the blood vessels got better with our treatments.

There were two treatments, a TNF inhibitor arm and a triple therapy arm. And what we found was interesting. Both arms reduce the inflammation in their blood vessels equally. And it was not necessarily tied in with their traditional inflammation parameters. So they both got better. It wasn't intimately tied to inflammation, but we're trying to understand if there are some other more specific inflammation pathways that are related. But it backs up the idea that reducing disease activity through therapy in our patients can be associated with a reduction in cardiovascular risk.

Dr. Curtis: Yeah. I think that's so important. And I've experienced in my own discussions with patients, many of them are very surprised when they come to me talking about rheumatoid arthritis, that when I bring up cardiovascular disease, I sometimes get a blank look, like, "What are you talking about?" and like, "I never even thought about that." Or, you know, for projects that we've done to help mitigate cardiovascular risk, where many RA patients are very surprised, "why did my rheumatologist never tell me about that?"

But again, as part of the benefits of getting RA under good control, I put this in the so-called good side effects column, that if RA is under good control, not only are you going to feel better, your joints are going to be less subject or at risk for damage, but your heart and your lungs may thank you as well.

Dr. Giles: And especially, you know, we don't have all the data to back it up, but if we can also tell them that your risk for getting cancer would be less too, I think many patients would be very responsive to that. Everybody's afraid of cancer. And we don't necessarily have that data about treatments and cancer risk right now, but there's circumstantial data to suggest that there is a link.

Dr. Curtis: I absolutely agree, and I think some of the more recent, EULAR guidelines provide some guidance backed by a substantial literature base, now, for people who have had a history of cancer that's well treated, that may be able to be effectively treated with biologics, where it really doesn't look like there is any or much incremental risk, will probably be quite reassuring that some of our most potent therapies are on the table and now have some evidence to reassure both clinicians and patients that keeping RA under good control, even for somebody who's high risk or with a history of cancer, is an option with more evidence than ever before.

So, let's switch gears a little bit and let's talk about serious infections. And perhaps like cardiovascular disease, there definitely are things that we can be doing to help mitigate and attenuate risk for serious infections.

The fairly recent American College of Rheumatology guidelines for vaccination that Anne Bass was the first author, I think was very helpful, not just in RA but across a number of rheumatic diseases. Of course, there's updated guidance about flu vaccination, the vaccination against shingles, pneumococcal and updated COVID vaccination.

I think it's quite recognized now that older patients and those taking certain immunosuppressive medications are supposed to get all the recommended vaccines that probably many of us are quite aware of. That said, particularly for COVID, there's a gigantic amount of vaccine hesitancy. And I wondered if you could share some of your insights about how you've approached the huge amount of vaccine fatigue that seems to be pervasive, that affects not only COVID vaccination, but at least in my practice, probably all of the others, as a spillover effect.

Dr. Giles: Well, I think patients need to understand the medications that we use to treat their inflammatory disease also have a role in reducing the efficacy of vaccines and also potentially on how well the vaccines can start working.

Patients may not understand that. In addition, we need them to know that they are at risk for serious infections, that anything we can do to reduce that is important. So, I start out with education, as always, and then, again, sometimes these are things that slip through the cracks in your practice because you're busy working through other things. So I think practice optimization. Maybe it's not you, but again, maybe it's the nurse or someone else in the practice who can check off whether vaccines are due as part of the routine aspects of taking care of those patients.

Dr. Curtis: Yeah, I think that's a great point. And honestly, although people may work in different practice settings, perhaps, like you, my experience is the same. If you want something done well and systematically, probably giving it to your office staff is a great way to go because then you can implement it as a standard rule or practice. You know, in my practice, having the staff ask, "have you ever gotten a pneumonia shot? Have you gotten this year's flu shot? Have you gotten a COVID vaccine?" Just some simple screening questions, so you at least know what you're headed into as you start a discussion with the patient. But having them collect that data in a systematic fashion to maximize quality of care so that people aren't slipping through the cracks, I agree with you, can be a really important part of making sure that the right things are done, or at least offered to patients.

So, when thinking about any closing thoughts, maybe you could speak to how you have found it effective to work with other specialists or primary care doctors to co-manage care, because not everything we might do in this space, particularly in the cardiovascular risk space, is necessarily going to be eagerly done by rheumatologists. So, how can we best partner for care co-management with other providers?

Dr. Giles: I think multidisciplinary conferences, at least in the academic setting, are important. And working with our cardiology colleagues, many of them don't recognize that there's a higher risk in our patients. So, if we just tell our patients, "go to the cardiologist," they may not treat them as having higher risk.

So, I think, educating each other about these things, keeping up with what we all do together in terms of new risk calculations, and new therapies, and being willing to be the initiator of some of these conversations as well. I think we have busy practices, but we need to own comorbidity screening and management as part of what we do. Just like we get bone density scans on patients and send them to the eye doctor for hydroxychloroquine retinal toxicity management. That's something that we should be doing as well.

Dr. Curtis: Yeah. I think you brought up some excellent points. Even if you're not the one who is ordering the cholesterol test, or even if you're not the one who is managing it or prescribing the therapy, making sure it gets done, like in your ocular toxicity example, where you're not doing that evaluation or you're sending them to

ophthalmology, but you're still the responsible party as the conductor of the orchestra, amongst that multidisciplinary team. I think that is very much a role for most rheumatologists in clinical practice.

Well, this is all we've had time for. It's been a great discussion. Thank you so much, Dr. Giles, for participating.

Listeners, if you'd like to learn more about comorbidity risk in patients with RA, please take some time to visit the RA Risk Radar therapeutic update on the RheumNow page to see some of the data supporting the topics that we've discussed. Thank you so much for listening.