The Latest Gout Research at a Glance

Transcript

Suneet Grewal, MD (Guest): There [are] a lot of misconceptions that still exist that are barriers to us providing care and identifying gout in patients.

Ada Kumar, MD (Guest): So, it is really starting to shift the way that we think about gout, not just as a disease of the joints, but really as a systemic, chronic inflammatory disease, which I think is really revolutionary.

Meghna Rao (Host): Welcome back to season 2 of the *Rheumatology Advisor* podcast, Rheum Advisor on Air. I'm Meghna Rao, the senior editor of *Rheumatology Advisor* and the host of this podcast.

In this series, we will be joined by expert clinicians and researchers to discuss emerging and compelling topics in rheumatology. These perspectives may be related to the management of rheumatic disease, guideline updates, patient care, data from conferences and scientific meetings, and much more.

In the next set of episodes, we're talking with some of the presenters of the all-virtual American College of Rheumatology (ACR) Convergence 2021.

So, let's dive in!

Meghna: What were some of the most compelling research in gout presented at ACR Convergence 2021?

To talk more about that, we have with us Dr Suneet Grewal, a rheumatologist at East Bay Rheumatology Medical Group, and Dr Ada Kumar, medical director in medical affairs at Horizon Therapeutics.

Welcome to the both of you, and thank you for joining me today!

Dr Kumar: Thank you for having me.

Dr Grewal: Yes, it is a pleasure to be here.

Meghna: Of course. I guess I am asking everyone this, but how did you like the all-virtual ACR meeting this year? What did you think were some of the most interesting aspects of it?

Dr Kumar: I thought the virtual ACR meeting this year was fantastic. Obviously they did the best that they could considering the circumstances. I do think compared [with] last year, there was quite a bit of improvement. I thought that there was a lot more engagement, a lot more virtual engagement, the chat functions were much more robust. I really enjoyed the session a lot.

Meghna: What about you, Dr Grewal?

Dr Grewal: Yeah, I enjoyed the same. I think the second year in, we are getting better at these virtual platforms, so I really enjoyed the flexibility and felt that I was able to cover more virtual ground than actually being at a live meeting.

Meghna: Yeah, I think I tend to agree. Although it was spread out over more than a week of sessions, [there were] a lot of interesting data from very compelling studies.

Now, we're here specifically to talk about the gout research presented at the conference. Maybe we can start with you, Dr Grewal, would you like to provide an overview of what you thought were promising studies in gout this year? Dr Kumar, of course, feel free to chime in.

Dr Grewal: Yeah, of course. So yes, it was very encouraging to see as in years past that gout did have a strong presence at the meeting. I think there has been a shift, especially since the ACR 2020 guidelines came out in the treatment of gout with this focus on treat-to-target [therapy]. I think some of the publications and posters that really stood out highlighted the long way that we still have to go.

So, there were several posters highlighting some of barriers that we still face in treating patients. One in particular was by Mark Russell et al [about] processed mapping gout hospitalization. This was a poster; although the study took place in the UK, it highlighted the fact that hospitalizations for gout are still on the rise. We know in the US that gout flare hospitalizations have doubled between 1993 and 2011.

An interesting finding from the study was that 59% of the participants admitted to the hospital with preexisting gout, of those, only one-quarter were [receiving] urate-lowering therapy. So, there is still suboptimal treatment for these patients, while hospitalizations are on the rise for these patients.

So, that was 1 poster that stood out. But really, this focus on the need for better education, better treatment.

Dr Kumar: Yeah, I agree with Dr Grewal. I think 1 of the big reasons for this is – there was another really interesting poster about gout stigma. They actually surveyed [more than] 100 practicing rheumatologists to see what do they think about gout and they used rheumatoid arthritis as a comparator. What they found was that rheumatologists perceived that there was a higher level of patient responsibility for patients [affected] with gout compared [with] those with RA.

I think it is that longstanding stigma that surrounds [patients with] gout compared [with those with] other inflammatory arthropathies that may be the result of undertreatment or mismanagement in our patients with gout.

As Dr Grewal said, it is really amazing that even though hospitalizations are on the rise, only about 25% of patients are given any type of urate-lowering therapy in those hospitalized patients. That doesn't even include patients [who] were on treat-to-target therapy, as recommended by the ACR guidelines.

Meghna: That's really interesting. And another thing that I found especially interesting was when you were talking about stigma; I was [closely] watching 2 studies. One was about the

association between diet and genetic predisposition in risk for incidence gout. And then, also, there was this other study about hyperinsulinemic diet, which may increase risk for gout. But these were particularly conducted among women.

I know [in] gout mostly the populations have been male, but I think this was interesting that [it was] studied among women.

Dr Grewal: That absolutely was very interesting. I think in clinical practice, this is a conversation that we have with our patients all the time. This is, kind of, a misunderstanding that gout is predominantly in men, and actually, after menopause, women are at equal risk as men.

So, yes, I agree that there [are] a lot of misconceptions that still exist that are barriers to us providing care and identifying gout in patients.

Dr Kumar: Yeah, and I think it is that core identification and the undertreatment of patients with gout that are leading to these some of these poor outcomes.

There was a really interesting paper on the rate of amputations, particularly lower extremity amputations in patients with gout. [Researchers] found that there was a 33% increase in the risk [for] lower-extremity amputations, particularly below-the-knee amputations, and that was independent of other comorbidities, including diabetes, for example. So, we really are not doing our patients with gout a service.

There was another really interesting retrospective analysis from a [Veterans Affairs] (VA) database looking at [more than] 500,000 patients. When [researchers] looked at those [who received suboptimal treatment], they had a 24% higher risk for all-cause mortality.

So, it really is a lot of these abstracts that were presented at the ACR highlighted a couple of things. Number 1, [t]here is a gout stigma; because of that gout stigma, we are thinking more about lifestyle options as opposed to therapeutic interventions. Therefore, a lot of our patients with gout are undertreated, they are not being treated to a treat-to-target strategy, like the ACR guidelines recommend, and therefore, they are suffering from poor outcomes.

So, I think, it was really a call-to-action amongst our colleagues to say, we need to do a better job in treating our patients with gout.

Meghna: I think that's interesting. Dr Kumar and Dr Grewal, I know that we have been tracking pegloticase in gout even among kidney transplant recipients. So, tell us, were there any interesting studies that came out of ACR this year with respect to that?

Dr Kumar: Yeah, so there were a couple of really interesting abstracts in relation to pegloticase [w]hen we are talking about undermanaging our patients with gout.

Pegloticase, for those who don't know, is an uricase, and so it drives our urate – the serum uric acid levels down to basically zero. But 1 of the biggest barriers to pegloticase is that it is a biologic and so a lot of patients can develop antidrug antibodies to this particular medication, which can then lead to patients no longer responding to the medication.

There were a few really interesting abstracts on this, basically highlighting the use of concomitant immunomodulation with pegloticase [and] showing that patients [who] were

[receiving treatment with] low-dose immunomodulatory agents actually had higher levels of response to pegloticase. In some cases, up to 90% of patients [who were receiving] these immunomodulatory therapies were actually able to complete their pegloticase treatment without becoming what we would consider a "nonresponder" because of the development of antidrug antibodies.

So, I think that is really fantastic. It is becoming almost the standard-of-care now. Dr Grewal, I would love to hear your experiences with it as well. But I think it is almost become standard-of-care with pegloticase to use a concomitant immunomodulatory therapy. And those were some abstracts that were highlighted at the ACR this year as well.

Dr Grewal: Yeah, I completely agree. We are seeing this trend amongst community rheumatologists as well. One of the posters that you referred to by Dr Aaron Broadwell et al pointed out that this is happening in the community rheumatology clinics. You're right, they did find that patients who were [receiving] immunomodulation along with pegloticase. Of their patients, nearly 90% were able to achieve a treatment response.

So, this is a very dramatic improvement beyond what the pivotal trials have originally shown without immunomodulation. So, this is very exciting to see that we are adopting the use of immunomodulation and we are seeing results. We are able to get these patients to the finish line.

Dr Kumar: Yeah, and in the pivotal trials, it was only about 42% of the patients [who] were "complete responders," and now we are up to almost 90%. So, like you said, Dr Grewal, we are almost doubling the number of patients [who] can stay on therapy, which is truly incredible.

Meghna: I think that is incredible. What else did we see that you thought were compelling?

Dr Grewal: Well, I think the body of evidence with gout imaging is also growing, which is very exciting, and specifically referring to the dual-energy [computed tomography] (DECT) scans. And, of course, I would love to hear Dr Kumar weigh in on this, as she is a radiologist.

But that has been really exciting. I talk about this with my patients. I show them pictures of DECT scans and for those who are involved with clinical trials with pegloticase, we are able to utilize the DECT scans. But those are really showing us the unappreciated burden of gout that really does exist in these patients. So, that has been really exciting as well to see more and more publications come out looking at the true burden of gout through DECT scans.

Dr Kumar: Yeah, I agree. What is really exciting is that with the D E C T scanners or the DECT scanners, not only are we seeing a larger overall urate burden in the extremities, but now we are starting to see urate deposition occurring outside of the extremities.

There was an entire plenary session about imaging and gout, really focusing on the joints using ultrasound and dual-energy CT, and there was an abstract correlating ultrasound and dual-energy CT in the joints, showing that they can both really be great ways to image patients with gout.

But then, there was a really wonderful oral presentation out of [New York University] (NYU) where they used this technology, the DECT technology, to look for spinal urate

deposition. That is a really a new kind of field in gout is this thought of or this evidence of urate depositing now within the spine of patients with gout.

[Researchers] used the DECT imaging to look at the lumbosacral spine, and what they found was that patients with gout had a significantly higher rate of urate deposition within their lumbar spine compared with nongout control [participants], and then it correlated actually with back pain scores – Aberdeen back pain scores – which was very, very interesting.

In addition, that study found that patients with gout had higher inflammatory biomarkers. So, the [erythrocyte sedimentation rate] (ESR) levels were significantly elevated in [patients with] gout compared [with] nongout control [participants]. This was being studied during that intercritical period, so during that period where we think patients with gout are clinically quiescent.

But we now know through a lot of work that systemic inflammation or chronic systemic inflammation is actually very detrimental, particularly when we think about cardiovascular outcomes. So, that was a really interesting study.

Then there was another study showing urate deposition within the vasculature in patients with gout. It was a podcast or a vodcast highlighting some of the studies that have shown urate deposition within, for example, the coronary arteries, in patients with gout; at almost an 85% prevalence of patients with gout having a urate deposition within their arteries through this dual-energy CT technology.

So, it is really starting to shift the way that we think about gout, not just as a disease of the joints, but really as a systemic, chronic inflammatory disease, which I think is really revolutionary and is going to change the way we think and treat [patients with] gout.

Meghna: Excellent. I think those were some wonderful insights from you, Dr Grewal and Dr Kumar, thank you again for that.

Dr Kumar: I just think we are in a really exciting time right now in gout. Our mindset is starting to shift in thinking of it as just not only as a joint disease, but really think about the overall urate burden in our patients with gout, the systemic impacts of gout, and then, how are we going to optimize the way that we are treating patients with gout? And really, emphasizing those ACR guidelines, the treat-to-target guidelines of trying to drive the [serum uric acid] (SUA) levels to less than 6 in order to really improve outcomes in our patients with gout.

I think we are at a really exciting time, and so, I think it was a fabulous ACR. What do you think Dr Grewal?

Dr Grewal: Yeah, I completely agree. I think this shift in our thinking and how we approach gout is wonderful; it's long overdue. I think these studies that were done and the posters that were presented are just reminding us that we really do need to chip away at these negative stereotypes, take a fresh approach, [and] adopt these treat-to-target guidelines. We have great urate-lowering therapies in our hands, available to us, as well as pegloticase

[and] the biologics. So, we really are on the right path to treating [patients with] gout in a much more efficient and effective way.

Meghna: Absolutely. I completely agree with the both of you. I have [also] been seeing a lot more of gout research on our site and a lot of interesting papers come out as well, even after the conference.

I thank you again for joining us on this episode, Dr Grewal and Dr Kumar. Thank you.

Dr Kumar: Thank you so much.

Dr Grewal: Thank you, this was great.

Meghna: Please stay tuned for more episodes in this series. For more information on *Rheumatology Advisor* and this podcast, you can reach out to us at editor@rheumatologyadvisor.com.

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