The Breath-Taking Lungs and Scleroderma

Transcript

Toby Maher, MD (Guest): I think, there is great importance in having a pulmonologist who understands [interstitial lung disease] (ILD) involved in the care of these patients.

Meghna Rao (Host): Welcome to Rheum Advisor on Air, the official podcast of *Rheumatology Advisor*, one of Haymarket Media's leading publications that focuses on the latest news and research in rheumatology to inform clinical practices. I'm your host Meghna Rao, the editor of *Rheumatology Advisor*.

In this series of episodes we're talking all about the exciting research and compelling data presented at the [European Alliance of Associations for Rheumatology] (EULAR) 2021 Virtual Congress.

So let's dive in!

Meghna: Research has revealed that more than 80% of patients with systemic sclerosis (SSc) have pulmonary involvement, with interstitial lung disease or ILD and pulmonary arterial hypertension [(PAH)] being the most common of these lung manifestations. In fact, both these conditions have been identified as the leading causes of systemic sclerosis-related mortality.

In this episode of the EULAR 2021 series, we're speaking with Dr Toby Maher, professor of clinical medicine at Keck Medical School of [University of Southern California] (USC), the British Lung Foundation chair and respiratory research, and a clinician scientist at the National Institute for Health Research UK. Dr Maher is also a professor of interstitial lung disease and the head of the Fibrosis Research Group at the National Health and Lung Institute at Imperial College, London.

I hope I did your introduction justice, Dr Maher, and welcome to the *Rheumatology Advisor* podcast.

Dr Maher: Thank you very much. Yeah, it sounds like far too many titles, doesn't it?

Meghna: You know, ILD, one of the most common lung manifestations of systemic sclerosis – research has shown that there is significant variability in screening patients for ILD.

Dr Maher, first, why do you think this may be, and second, along the same lines, can you maybe provide some insight into why ILD is potentially being underdiagnosed among patients with systemic sclerosis, despite its significant prevalence? [Are] the sensitivity of the screening methods, such as

imaging and pulmonary function tests, insufficient, or is it because ILD may mimic some other conditions, and/or are there other reasons that you can tell us about?

Dr Maher: So, I think there are a handful of reasons why historically it's been underidentified. Until we have the recent approvals of nintedanib and tocilizumab as treatments for systemic sclerosis-associated ILD, we actually have very little that we could do in terms of treating the ILD independent of treating the scleroderma. So, I think that's historically been one of the reasons.

Another reason has been the concern about radiation exposure. Patients with systemic sclerosis are typically [women] in their 30s or 40s, and, of course, there is a concern about extensive radiation exposure in that age group and the risk of it increasing cancer. I think that was much more of a concern 10 or 20 years ago when [computed tomography] (CT) scans were associated with high exposure to radiation.

And then, I think, the major common reason nowadays is that people don't always know what to do with the results of a CT scan, particularly if it shows trivial interstitial lung disease. I think we understand what we should do for patients who present with extensive fibrosis on a CT scan. We understand less well what it means if we find very trivial change in the absence of symptoms.

My own personal feeling would be that it's important to know which patients have [I]LD because when it comes to managing lung problems, it's not only the pharmacotherapy that we think about, it's not just important to get patients on drugs. There are other things that we can do to improve lung health: exercise, vaccinations to avoid infection, [and] avoidance of cigarette smoking, etc.

Meghna: It's interesting that you should say that because some data published earlier this year reported on the unmet needs in the management of patients with SSc-related ILD. Some of the barriers reported were the lack of disease-specific knowledge, gaps in the health care system, and insufficient information and support for patients and caregivers.

Dr Maher: And I think that problem is common across rarer diseases. For a patient with a rare disease, whether it's systemic sclerosis or another rare disease, they confront many challenges.

One is that friends and loved ones will have never heard of the disease, so they won't understand how significant of a condition it is. Their primary care physicians might have learned about these things in medical school, but often they won't have seen a patient with systemic sclerosis in their professional lifetime, and so, that means that patients often have to educate their own primary care physicians each time they present with problems. And even when [patients] go to secondary care, they don't always meet people who

understand the multisystem components of the disease. Often in countries, there are only a small number of dedicated centers for patients with systemic sclerosis, which means patients are often traveling a long distance to get high-quality health care, and I think that adds to the stress of dealing with the condition itself.

Meghna: Just another aspect that could be potentially important to recognize is the lack of clinical guidelines for SSc-ILD, and I wonder if we'll see some changes to that regard soon.

Dr Maher: Yeah, I think as we discussed earlier that the absence of treatments historically has meant that there has been limited rationale for having guidelines, and added to that, there was a relatively limited evidence-base on which to build any guidance.

I think that has changed a lot in the last few years. I think we are understanding SSc-ILD much better. I think there is much wider use of screening CTs. So, we are beginning to get a better understanding of the natural history of ILD and patients with systemic sclerosis. And, of course, we have now seen several trials – both the academically run trials with mycophenolate and cyclophosphamide, but also the industry-sponsored trials – that resulted in drugs being approved.

[T]hings have changed quite dramatically, and, I think, that will lead to evidence-based guidelines. I think that's important for a number of reasons. One is it helps ensure standardization of care, but the other benefit of guidelines is the whole process of developing them often identifies the gaps in our knowledge, and so, it provides a useful framework for future research to make sure that we continue to improve the standard of care we are offering to patients with SSc-ILD.

Meghna: Dr Maher, as a practicing pulmonologist and a specialist in ILD, what would you like your colleagues in rheumatology to know about diagnosing ILD in systemic sclerosis? Can you also speak to the importance of collaboration and communication between the 2 specialties to provide appropriate care?

Dr Maher: Yeah, so I think, as we've touched on in some of the earlier discussion, there is great importance in having a pulmonologist who understands ILD involved in the care of these patients because I think there is much more to the management of interstitial lung disease than just the pharmacotherapy. I think there is a package of care that can be put in place for patients, both to improve their quality of life and to minimize the chances of them suffering complications of their ILD in the future. There are things like pulmonary rehabilitation, so working with respiratory therapists within the pulmonary department to improve patients' exercise capacity. There are things that we can do to treat symptoms like cough and breathlessness. There's also, for more advanced disease, the importance of using oxygen and providing supportive care at end-of-life. And I think, all of those are things

that we do very well within specialist ILD clinics, and [i]t's important for patients with SSc-ILD to have access to that.

I think, historically, rheumatologists who look after SSc are used to collaborating with other disease specialists – we have seen improvements in the care of renal disease in patients with systemic sclerosis; we've seen improvements in the care of the gastrointestinal disease in pulmonary hypertension. And all of that is required collaboration with different disease area experts and, I think, the same is true of ILD. It just means that the expert teams that are involved in the care of patients grows slightly bigger. As you alluded to in your question, it is important that we provide integrated care, that everybody is talking together to ensure that there is joined up thinking when it comes to the treatment of the patient.

So, I think, the rheumatologist's role in all of that is, really sort of, the "captain of the team" to make sure that all the different bits are brought together effectively and that there isn't unnecessary duplication or oversight of certain aspects of an individual's disease.

Meghna: While we have a minute, I also wanted to touch upon the diagnosis and treatment of pulmonary arterial hypertension, one of the other leading causes of death among patients with systemic sclerosis.

Now, since there is no cure for SSc-related pulmonary arterial hypertension and treatment options are limited – although there are positive results from recent trial about rituximab treatment – how can patients' conditions be effectively managed in clinical practice? Again, you know, emphasizing the combined role of the pulmonologist and the rheumatologist?

Dr Maher: Yeah, so, as with the previous answer, it is about collaboration with relevant experts within pulmonology for the management of pulmonary hypertension. We often tend to collaborate with dedicated PAH specialists who, in turn, directly collaborate with cardiology departments. I think it's about making sure that the team of clinicians looking after the patient is the right one, and, I think, ensuring that patients are screened for pulmonary hypertension, both at diagnosis and over time, in the same way [that] I feel they should be screened for their ILD.

[I]t's worth saying that the ILD and PAH tend to occur in separate patients, but in a small number of patients, there is an overlap between the 2 disorders. So, it is something that is constantly important to think of as a potential diagnosis, particularly as we have availability to potentially disease-modifying therapies.

Meghna: To sort of tie everything up here, where do we currently stand in terms of research and therapy with pulmonary involvement in scleroderma? Can you share any data that you've come across with potentially clinically meaningful results, Dr Maher?

Dr Maher: I think the real shift forward in the last 18 months has been the publication of the various trials of novel therapies.

With nintedanib, now, we have evidence that use of an antifibrotic drug slows disease progression, independent to taking an immunosuppressant approach, which is what we have historically used. Then, with the tocilizumab studies, I think there were 2 important things to come out of that. The first was the observation about how rapidly ILD can progress in newly diagnosed patients, particularly those with an extensive inflammatory phenotype. And the second important observation was the therapeutic benefit of early intervention with tocilizumab, even in patients with very trivial or limited interstitial lung disease at the point they entered the study.

So, I think, those 2 things, in particular, are changing our approach to SSc-ILD that are driving a rationale for identifying patients early and for considering early intervention as to prevent significant and irreversible scarring of the lungs in these patients. And hopefully, the knock-on benefit of that will improved quality of life and reduce mortality going forward.

Meghna: Yeah, absolutely. [T]hose are such exciting trials and data that you've shared with us.

Dr Maher, I know we have only begun this conversation about the impact of lung manifestations in patients with systemic sclerosis, but I thank you for taking the time today and speaking with me.

Dr Maher: It's a pleasure; well, thank you for having me on, I think it's an important topic, and, as you say, I am sure there will be plenty more discussions to be had in the future.

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. We, at *Rheumatology Advisor*, look forward to delivering timely, evidence-based news to you. You can also sign up for our free enewsletters on the site.