Melanie Cole (Host): Welcome to the podcast series from the specialists at Penn Medicine. I'm Melanie Cole and today we're examining lung transplantation for connective tissue disorders, the new International Consensus Statements for optimal patient outcomes. Joining me is Dr. Maria Crespo. She's the Medical Director of the Penn Lung Transplant Program.

Dr. Crespo, it's a pleasure to have you join us today. Can you tell us about the new guidelines for lung transplantation in patients with connective tissue disease from the International Society for Heart and Lung Transplantation and how have they evolved from the existing literature?

Maria Crespo, MD (Guest): Yes,-previously the International Society for Heart and Lung Transplantation Consensus Guidelines for the selection of lung transplant candidates suggested that patients with connective tissue disease, can be acceptable candidates if they didn't have severe esophageal disease. That means gastroesophageal reflux disease as well as esophageal dysmotility. However, there are numerous publications from the US and Europe, particularly on scleroderma which is a type of connective tissue disease -showing comparable lung transplant outcomes with other patients with lung fibrosis, without underlying connective tissue disease who *have* severe esophageal disorders. However, there's substantial variability between lung transplant centers on the transplant evaluation, selection and post-transplant care of these patients.

This motivated the need to create a new ISHLT Consensus Guidelines specific for patients with connective tissue disease, due to their underlying complexity. This consensual workforce included a multidisciplinary international expertise in lung transplant and connective tissue disease which included pulmonologists, surgeons, cardiologists, transplant pharmacists, nutritionists, nurses, anesthesia, critical care, and rheumatologists.

And the aim of the consensus was to standardize the evaluations, the selection, including absolute contraindications to transplant, and the post-transplant care.

Host: It's very interesting topic we're discussing. And we're going to expand a little bit later on that multidisciplinary subspecialty team you were talking about but how will these guidelines impact patient selection for lung transplantation? Why is this so important Dr. Crespo, as we look at the principles for the allocation of donor lungs?

Dr. Crespo: Well, it will guide the lung transplant communities during the evaluation, making sure that the appropriate testing and consultations are done

at making the best decision at the selection of candidates to list. Also, this consensus will improve consistency between centers in regards to these patient selection, surgical, and multidisciplinary post-transplant management.

I mean, one of the things is that because of the shortage, like you mentioned of donors, we want to make sure that the selection of these patients are actually the correct ones. Because that also will impact having a good lung transplant outcome, too.

Host: So, now I'd like you to expand for us on that role. You mentioned a bunch of different team members. Tell us about that as pre and post management of this population's extra pulmonary issues and why this is so important for these patients.

Dr. Crespo: For patients with connective tissue disease, an autoimmune disorder, they have multi-organ involvement. So, it's not just the lung or their heart that this involves, they have also skin involvement. The kidney can be involved, for example, rheumatoid arthritis, they can have joint involvement. That's the reason why, contrary to other patients without connective tissue disease that undergo lung transplant evaluation, due to these extra pulmonary conditions, these patients actually require a multidisciplinary team in their evaluation.

And here at Penn, our patients with connective tissue disease, they are being evaluated by the team of rheumatologists, as well gastroenterologists. Why is that? Because it's very important that these extra pulmonary manifestations are stable and won't be of concern for the post-transplant care.

For example, extra pulmonary manifestations like severe arthritis. Patients that have rheumatoid arthritis and they have very bad joint pains, that can be of concern. And we want to make sure that these patients, they go for a lung transplant once the pain is well controlled on medications, because that can jeopardize or compromise the potential rehab after transplant. Also, the gastroenterologists play an important role in these patients. They need to have a very thorough gastrointestinal evaluation to make sure that they don't have severe esophageal disease and also to assess the risk post-transplant of potential aspiration due to severe gatroesophageal reflux disease or due to esophageal dysmotility, which can put the patient at risk for lung rejection. And this multi-disciplinary subspeciality team that we have at Penn, that actually is part of the longitudinal care pre and post-transplant in these patients, which is fundamental.

Host: Now earlier you mentioned, Dr. Crespo, scleroderma. So, can you tell us the recommendations for timing of referral for lung transplantation in patients with scleroderma and does the presence of this and other connective tissue disorders affect short and long term outcomes for lung transplantation?

Dr. Crespo: So first I'm going to just answer your question about the lung transplant outcomes in patients with scleroderma or other connective tissue disease. There's plenty of publications from US, as well as, Europe showing the short and long-term outcomes in patients with scleroderma are comparable with patients who have other interstitial lung disease, not related to connective tissue disease and that the quality of life is actually very good. The key is to make sure that the patients are selected appropriately.

In terms of, when is the time actually for patients to be evaluated, early evaluation is essential. Those patients with connective tissue disease who have advanced lung disease, whose clinical status has progressively declined despite maximal medical therapy, or if patients have secondary pulmonary hypertension which is getting worse despite maximal therapy, they need to be seen early at the lung transplant center. That is just related with the underlying medical complexity in this particular patient population. And also, to determine the potential risk and benefits of lung transplant.

Host: Well, thank you then, Doctor are the lung transplantation risk factors for mortality different in a patient with scleroderma?

Dr. Crespo: Yes, it is actually by the, issues that I mentioned before. The patients, particularly with scleroderma, they often have severe underlying esophageal dysmotility and gastroesophageal reflux which has been associated to an increased risk for chronic rejection and obviously putting these patients at a higher risk for early mortality.

Another of the concerns is that patients with a connective tissue disease often have severe pulmonary hypertension and they are considered actually to be a very high surgical risk.

Host: So then is that why there's controversy regarding the use of lung transplant in patients like this?

Dr. Crespo: Yes patients with connective tissue disease, but particularly scleroderma, they continue to be considered suboptimal candidates for lung transplant at some centers and they're not willing to accept these patients.

So, who are the centers, who are willing to consider these patients? Willingness to accept any risk may vary between centers. And sometimes it depends on the center’s expertise. There are centers that have very small lung volume that don't have the expertise from the multidisciplinary team of anesthesiologists to take care of these patients in the operating room; to critical care specialists when the patients come from the operating room to the ICU; and as well as rheumatologists and gastroenterologists and pulmonologists who evaluate those patients before the transplant.

Host: So Doctor, I was reading these new guidelines. What's your role in the new ISHLT guidelines regarding lung transplantation in patients with scleroderma and who are the other major contributors? Speak about this collaboration for us.

Dr. Crespo: I was the main leader in this important consensus statement, which has three parts, divided into three papers. The first part, involved the epidemiology, the assessment of the extra pulmonary conditions, candidate evaluation, and selection criteria. The second part was focused on the cardiac manifestations, the surgical perioperative, operative and postoperative challenges and management. And the last paper was in pharmacology, medical and surgical management of post-transplant extra pulmonary conditions. So, I'm very fortunate to have worked with great international lung transplant colleagues and I'm particularly honored for this consensus to have had a significant Penn representation from our multidisciplinary expertise team of transplant pulmonologists, nurses, surgeons, cardiologists, rheumatologists, nutritionists, anesthesia, critical care and pharmacists. This consensus will help the lung transplant communities during the evaluation, selection and management of patients with underlying connective tissue disease.

Host: Thank you so much, Dr. Crespo for joining us today. What a great topic.

To refer your patient to Dr. Crespo at the Penn Lung Transplant Program, please visit our website at pennmedicine.org/refer. Or you can call 877-937-PENN. That concludes this episode from the specialists at Penn Medicine.

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