Melanie: Welcome to the podcast series from the specialists at Penn medicine. I'm Melanie Cole. And today, we're discussing the waiting game, referral to lung transplantation too little too late, and how late referrals can impact outcomes.

Joining me is Dr. Joshua Diamond. He's an Associate Medical Director in the Penn Lung Transplant Program and an Assistant Professor of Medicine at Penn Medicine. Dr. Diamond, it's a pleasure to have you join us today. Let's start with a little disease-specific lung transplant considerations for key diagnoses, give us some of those and why lung transplant would even be considered.

Dr. Joshua Diamond: There are several specific indications for lung transplantation. In the United States and now worldwide. The number one indication is interstitial lung disease, pulmonary fibrosis, followed closely by COPD, emphysema. The recommendation for a referral for patients with interstitial lung disease really varies dependent on the type of lung disease that the patient has. The more likely the patient has a UIP or IPF diagnosis, the early their referral should be. The ultimate goal is getting patients in for initial meeting with a lung transplant team as early as possible during their course so that we can get to know the patient, learn what's going on, identify potential barriers to transplantation.

For emphysema, on the other hand, transplantation is more of a quality of life improving procedure and not necessarily a length of life improving procedure. Therefore, the timing of referral is really dependent on a combination of both the severity of their disease and their quality of life. Patients with cystic fibrosis, which is the third most common indication for transplant, are really dependent on the severity of their exacerbations, the frequency of need for IV antibiotics and other lung-specific complications, hemoptysis, pulmonary hypertension.

Patients with pulmonary hypertension as their primary indication, which would be the fourth most common indication, should really be referred when they have progressive disease requiring multiple different medications for control and start to have more signs of RV dysfunction and RV failure.

Melanie: Well, thank you for that. So how does early referral for consideration impact survival? And what would you like to tell other providers about the importance of objectively assessing clinical decline?

Dr Joshua Diamond: I think it's an important factor of getting patients in early. What we've noticed over the last five years or so is that patients are getting referred for transplant consideration later and later in their course, because there are more and more options for treatment of many advanced lung diseases.

The downside to this is that patients end up arriving in our offices, meeting us so late in their disease course that the amount of time that we have available to go through the evaluation phase, provide them education, provide their families education about what's involved in the transplant process isn't enough time. We've had patients who've gotten listed and then have had rapid decline after listing such that we've not had enough days, weeks, or months to be able to actually get them transplanted.

So the goal of early referral is to maximize the likelihood that a patient will end up being a candidate, be well-educated in what's required to make a good candidate, both for them and their families, and then provide sufficient time for a suitable match to be identified such that they can be transplanted successfully.

Our goal is to transplant patients when they're within a window in which they're still healthy enough to get the maximum benefit from transplantation, because there is an entity of being too sick for transplant, although that has really shifted further and further away as our ability to maintain and transplant sick patients has improved.

Melanie: So I'd like you to speak about patient selection, Dr. Diamond. Is this based on specific protocol driven multidisciplinary assessment? What does the transplant evaluation process look like at Penn Medicine?

Dr Joshua Diamond: The process kind of depends on how sick the patient is at the time that we meet them first. We have three different pathways that patients can go through. If patients are on the healthier side, oftentimes they'll come meet one of our pulmonologists for initial assessment. It's typically an hour-long visit. We'll review their history, review their records and provide them significant education about the transplant process, and then make a decision about whether the patient is appropriate to move forward with evaluation or whether more monitoring or evaluation is required.

If patients are a bit sicker, but still as an outpatient, oftentimes, we will have a concurrent first visit along with our evaluation. And our evaluation is four days of outpatient testing and it's extremely extensive. We do multiple referrals to our consultants They include a nurse, respiratory therapist, physical therapist, speech pathologist, social worker, cardiac surgeon, financial person. I'm sure I'm leaving out somebody else. There's about nine different people that they meet with. They also meet with our research team. And then we get CT scans, blood tests, ultrasounds, heart testing, vascular testing, and it's organized over a four-day period. About a week later, we meet as a large multidisciplinary team, discuss the entire case and then come up with a plan going forwards as to what is needed.

Now, if patients are even sicker and are already inpatients or require inpatient care, we actually will transfer patients to the hospital and do that evaluation entirely as an inpatient. And we've done the evaluations on people who are ambulatory all the way through full mechanical ventilation, ECMO support, regardless of how sick they are. Those patients typically have a very short window of potential transplantation and so we try to get that evaluation done as quickly as possible. But the input for the decision-making regarding listing is made by all of the people who are involved in that evaluation process.

Melanie: For other providers, Dr. Diamond, what are the absolute contraindications to lung transplant?

Dr Joshua Diamond: This has really changed over the last 10 to 15 years. And the number of absolute contraindications is kind of a moving target. What we've tried to get our referring physicians to do is to send us a message, give us a phone call so that we can discuss patients because oftentimes things start out as absolute contraindications can be intervened upon or fixed.

For example, one of the strict criteria that we use is BMI. And we require our patients to have a BMI of less than 35. But we have had patients who have been referred with significantly higher BMI's and we've provided them education or nutritional support and how to appropriately lose weight, such that they become appropriate candidates.

Other things to consider are things like profound frailty. And so we have a large program at Penn

engaged in trying to mitigate frailty in the pre-transplant phase of care. There are other types of infections that are specifically considered likely to be absolute contraindications. Things like Mycobacterium abscessus active infection and Burkholderia cepacia infection in patients with cystic fibrosis.

But in general, our goal as a team is to try to maximize the likelihood that somebody will be able to become a candidate. And oftentimes, we're able to intervene upon, fix or mitigate things that had historically been considered absolute contraindications.

Melanie: So interesting. Thank you for that answer. Can you highlight for us any progress on the wait-list management of disease, possibly reducing those waiting times? What can the patient expect once they've been placed on the transplant list? And tell us about this experience, how the waiting time is calculated? What are you doing now?

Dr Joshua Diamond: Wait time varies from person to person and it's common for patients to ask, "How long do you think I'm going to wait for transplantation?" But there are several factors that go into how long somebody's going to wait. The first is how sick the patient is. In essence, the scoring system that's used for a lung allocation is the lung allocation score. The LAS tries to estimate the likelihood of survival with and without a transplant and it tries to maximize the difference. In that case, the sicker you are, the higher the score is going to be.

And so for patients who are significantly sick, we have them come in for frequent reassessments because the numbers that are utilized to calculate that score can change from a moment to moment basis. They can have progressively worsening lung function. They can have increasing oxygen requirements. And so the expectation for wait time is directly tied to the severity of illness.

At the same time, there are other factors that come into play. The lungs need to fit in the thoracic cavity. So taller people need bigger lungs, shorter people need smaller lungs. Other factors that go into the decision are the amount of time, blood type as well as other factors related to immune compatibility, specifically related to human leukocyte antigen or HLA compatibility. And this is related to whether somebody has had a prior pregnancy, prior blood transfusion, autoimmune disease, or prior organ transplantation. And all of those factors come into play when trying to estimate how long somebody's going to wait.

I typically quote people that the average survival is about three months. But at the level of the individual, that average might not be applicable. We've had patients who have been listed and transplanted within days, and we have patients who have unfortunately had to wait one to two years in order to get transplanted.

Melanie: So that leads well into the next question. As we're getting ready to wrap up, Dr. Diamond, tell us about the future of lung transplantation. What are some of the constraints to meeting the annual demand for lung transplantation and some of the issues and challenges that you see?

Dr Joshua Diamond: So one of the issues is that there are more people who need lungs and other solid organs than all organs available. And so one of the goals is trying to maximize the donor pool. So here at Penn, recently, we completed a study evaluating the safety and utility of utilizing donors who have hepatitis C viral infection and demonstrated that we can safely treat hepatitis C after organ transplantation. Accepting organs from donors who have hepatitis C can significantly increase the donor pool.

There are other factors that we're interested in trying to improve organ function. Things like predictive algorithms for how a lung is going to function after transplantation. Better understanding of the impact of the different donor risk factors, things like donor smoking, donor drug use, donor age, and how they play into outcomes after lung transplantation.

There's a lot of efforts on our research side of trying to both maximize the utility of donors and then maximize the likelihood that a recipient is going to survive. We have a very large research enterprise focused on the peri-transplant period of care and how to maximize the likelihood that somebody is going to get the full benefit from organ transplantation.

Melanie: Dr. Diamond, as we wrap up, kind of summarize the recommendations for timing of referral, the benefits of earlier referral and if there's an issue, if a provider refers a patient too early,

Dr Joshua Diamond: I think the ultimate goal of most transplant programs and ours in particular is to have patients refer to us earlier. We are happy to follow along with the primary pulmonologist in the community and help to gauge the proper time for actual formal evaluation and potential listing. But the sooner we get to know the patient, the more comfortable the patient will feel with us as their potential providers and the more comfortable we will feel with being able to move forward with the transplant process.

There's really no downside to early referral because of the fact that you get open access to the program and all of the resources that are available to the patient at the level of social work and nutrition and other potential consultations. We help to guide the timing of when testing should be happening such that we can minimize the likelihood that patients are going to need to have repetitive in-person or invasive testing.

We, as a team, are really open to having discussions with community and referring physicians about patients at the individual level. We're happy to have phone calls. Our expanded use of Zoom and other remote technology has really enabled us to be more open and available to have those types of discussions.

We would prefer too early or early rather than too late from a referral perspective, because we've had patients who have unfortunately not been able to benefit from transplant because of referral too late.

Melanie: Thank you so much, Dr. Diamond, for joining us today.

To refer your patient to Dr. Diamond at Penn Medicine, 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. For updates on the latest medical advancements and breakthroughs, please follow us on your social channels. I'm Melanie Cole.