ANSWERS ABOUT LUNG TRANSPLANTATION FOR PULMONARY HYPERTENSION

Part One: Overview

From the development of epoprostenol in the early 1980s to the discovery of oral and inhaled therapies over the next decades, expansion of medical treatment of pulmonary arterial hypertension (PAH) has improved survival and quality of life over the past 30 years. While research into new medical treatments is ongoing, to date there is no cure.

The first heart-lung transplant was performed at Stanford in 1981 for a patient with primary pulmonary hypertension, and over the next decade, single and double lung transplantation evolved. As surgical techniques and postoperative management have improved, the number of lung transplants has risen every year, reaching more than 3,000 lung transplants in 2009. With improvements in surgical treatments and pre- and post-operative management, lung transplant continues to be a viable treatment for qualified candidates whose disease is progressing despite maximal medical therapy.

When considering lung transplantation, you may ask yourself one or all of the following questions. Part one in this series focuses on general questions about the transplant process.

What types of patients receive lung transplantation for PH?

Lung transplantation is a surgical treatment for patients with PAH due to a variety of causes. Patients with idiopathic pulmonary arterial hypertension (IPAH) account for approximately 5 percent of all double lung transplants; however lung transplant is commonly performed for patients with PAH associated with chronic obstructive pulmonary disease (COPD), idiopathic pulmonary fibrosis (IPF), connective tissue diseases and other lung diseases.

Although we have made considerable progress in the medical management of PAH, not all patients respond equally well to medications. Therefore, lung transplantation is considered in patients who do not respond to medical therapy. Close and frequent follow up after starting PH medications is essential, in case patients worsen and require additional medical therapies or listing for transplant.

What determines if a patient receives a single, double lung, or heart-lung transplant?

By and large, the procedure of choice for patients with PAH is double lung transplant. Although transplantation for PAH began with heart-lung transplant, we have found that in most cases PAH can be effectively treated through double lung transplantation alone. With the immediate changes in pulmonary artery pressures after surgery, the right ventricle is quite remarkable in its ability to heal in the months after transplant. It is important to note that there are cases in which heart-lung transplantation may be required, such as in patients who have poor heart function or irreparable structural problems that they have had since birth.

What are special concerns regarding patients with PAH considering transplantation?

In patients who are progressing with PAH, lung transplantation can provide a promise for a chance at a better quality of life. It is important to emphasize that transplantation requires a lot of maintenance and that in essence, when undergoing transplant, a recipient trades their current medical disease for another medical condition that has a better prognosis. In all recipients post lung transplantation, overall survival at one year and five years are 79 percent and 55 percent, respectively. However, supporting a patient with PAH through transplantation is a complicated procedure, reflected in the 76 percent three-month survival in IPAH patients. When patients with IPAH survive through the first year, their overall long-term survival is significantly higher (median survival 9.5 years) compared to patients with other diagnoses (median survival 6.8 years and 6.9 years in patients with COPD and IPF, respectively). Given the technical challenges early after transplantation for IPAH, it is recommended to be cared for at a center with experience in the PAH patient population.

While pulmonary hypertension medications are no longer needed, the transplant patient must take a combination of medications to help their body accept the lungs, as well as prevent infections. Careful medical follow up at the transplant center is also essential to success, as transplant recipients are at risk for complications, such as rejection, infection, side-effects from medications. Quality of life can be tremendously improved when things go well, but given the regimen that goes into maintaining a lung transplant, as well as complications that may occur, life frequently is

not entirely “normal.” This is discussed further in part two of this series.

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Part Two: What to Expect Before and After Transplant

Part two in our series examines questions about the transplant evaluation, the process of being listed for transplant and what to expect after a transplant.

What is involved in transplant evaluation?

After a patient decides to undergo transplant evaluation, the patient’s physician contacts a transplant center to arrange the outpatient evaluation week. This involves several days of outpatient testing and visits with various doctors and consultants. While some testing is performed by the patient’s primary care physician (routine cancer screening and vaccinations, for example), other testing may be done during the transplant week (lab testing, radiologic studies, catheterizations and other cardiac testing). After this is complete, the center’s committee reviews the data and makes a recommendation on whether or not the patient is a candidate. If the patient is not yet sick enough for transplant, the committee may decide that they could be a candidate in the future but would not list the patient at this time. Instead, the center will follow them closely every three to six months and list when their condition worsens.

The decision of when to list a patient for transplant is complicated, and we often refer to the “transplant window.” Listing too soon may potentially shorten a patient’s life due to the risk of lung transplant itself. Waiting too long may mean a patient’s heart may not recover fully with double lung transplant alone, and they may require heart-lung transplant or even be unable to be transplanted. Therefore, routine follow-up at the transplant center, even prior to listing, is essential to determining when a patient is within the window for listing.

What is involved in listing for transplantation?

When patients meet criteria for transplant, the decision is made by the transplant team and patient to list the patient for transplant. Data from their evaluation week (e.g., age, diagnosis, functional status, oxygen requirement, pulmonary function testing, right heart catheterization data, carbon dioxide levels, six-minute walk distance, serum creatinine) are used to register them with the United Network for Organ Sharing (UNOS). This generates a lung allocation score (LAS), which is a number from 0 to 100 that determines where a patient is ranked on the list with respect to others. A sicker patient will have higher LAS, and thus have a higher priority in obtaining lungs when they become available.

It is known that the formula for calculating the LAS, which is used in all diagnoses (COPD, IPF, IPAH, etc.) places IPAH patients at a disadvantage. To address this, UNOS currently employs an expedited appeals process so that patients who meet certain criteria will be moved to the ninetieth percentile on the list. To meet these criteria, patients must be deteriorating on optimal medical therapy and have a right atrial pressure greater than 15 mmHg or a cardiac index less than 1.8 L/min/m2. These factors are reflective of the stability of the right ventricle, which is ultimately tied to prognosis in all PAH patients. Due to the potential for these appeals, it is important for patients to follow up routinely pre-transplant.

In addition, recent data from the REVEAL study showed that additional factors, if incorporated into the LAS calculation, would more accurately predict survival and thereby better reflect organ prioritization in patients with IPAH. These additional factors include estimates of right ventricular function, which as stated earlier, are key to

determining survival in IPAH. The LAS in its current construct, more heavily weighs factors reflective of “pure lung dysfunction,” like FEV1 (a measure of airway capacity) since these predict survival better for patients with “lung diseases” like COPD. Although IPAH does occur in the lung and is hence considered a “lung disease,” these parameters are not useful in predicting survival in IPAH. This is why it was imperative to have these new “heart-related” parameters added to the LAS. This is currently under review by UNOS, and a revised formula incorporating these changes is now under consideration.

What is life like after transplant?

Lung transplantation involves a complete lifestyle change, and while patients no longer require PH medications, they now require a new set of medications that allows their body to accept the lungs as well as prevents infections. Careful medical follow-up is crucial to success. Lung transplantation is an active medical condition that involves routine labs, pulmonary function testing, and frequent visits to the transplant center for the rest of a patient’s life. The transplant medications often have side effects, and patients frequently require additional medications to treat new conditions such as high blood pressure, cholesterol or diabetes. Although transplant involves active maintenance by each patient, it offers the possibility of helping patients with severe IPAH live longer and improve their quality of life. When all goes well and with close medical follow up, lung transplantation provides patients the opportunity to physically do activities they have not been able to do in years.

In summary, for many patients with PAH, lung transplantation remains a viable treatment option, and if a patient’s disease is severe or worsening, transplant evaluation should be considered. It is better to be evaluated too soon, when a patient is “too well” so that the center can follow along and transplant can remain an option down the road should the patient’s condition worsen. While lung transplant requires a lot of medications and maintenance, it does provide the chance to improve survival and quality of life.

For more information about transplants, be sure to visit **United Network for Organ Sharing**.

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