Lung Transplantation for Pulmonary Arterial Hypertension


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The past decade has witnessed enormous strides in the treatment of pulmonary arterial hypertension (PAH). Currently available pharmacologic agents are capable of inducing sustained clinical improvements and reducing mortality, particularly for idiopathic PAH (IPAH). However, response is variable, and morbidity and mortality remain unacceptably high in this relatively young population.[1,2] Lung transplantation, therefore, remains an important option in the face of progressive disease.

PAH holds a unique place in the history of lung transplantation. The first successful human lung transplantation, in the form of a combined heart-lung procedure, was performed in 1981 by Drs Bruce Reitz and the late Norman Shumway at Stanford University on a 45-year-old woman with IPAH.[3] The patient, Mary Gohlke, wrote a book about her experience titled *I'll Take Tomorrow*. With the advent of isolated lung transplantation in the 1990s, both single and bilateral lung transplants were widely applied to patients with advanced parenchymal lung diseases as well as PAH. As a result, the number of heart-lung transplantations reported to the Registry of the International Society for Heart and Lung Transplantation (ISHLT) [4] has fallen considerably from a peak of 239 in 1989 to 78 in 2004. Nevertheless, this procedure remains relevant for selected patients with PAH.

As of June 2005, more than 21,000 lung transplantations had been recorded worldwide by the ISHLT registry.[4] Whereas the proportion of all isolated lung transplantations performed for "primary pulmonary hypertension (PPH)" has decreased from 13% in 1990 to 3% in 2004, the actual number of PPH transplantatons has fallen by only 25%, averaging 64 per year from 1990 to 1995 and 48 per year from 1996 to 2004.[4] This suggests a modest reduction because of effective medical therapy (epoprostenol was FDA approved in 1996). There is little doubt that currently available agents can delay or eliminate the need for transplantation for some patients, particularly those with IPAH.[5] Once medical therapy has failed, transplantation continues to be the only alternative to prolong survival. As of May 18, 2007, 46 patients with PPH (IPAH) and 20 with other types of PAH were on the active United Network of Organ Sharing (UNOS) lung transplant waiting list, representing 6.4% of all active candidates in the United States.[6] In 2006, 53 PAH patients received a lung transplant, representing 3.7% of the total. Highlighting the urgency of this procedure is the 30% waitlist mortality among IPAH patients.[7]

In addition to the impact of medical therapy, two other factors have altered the landscape of lung transplantation for PAH in recent years. For all diagnoses, post-transplant survival has risen in this decade, largely as a result of reduced early mortality,[4] reflecting refinements in surgical techniques and early postoperative care. Since the reduced post-transplant survival of IPAH recipients relative to other diagnoses is entirely accounted for by higher perioperative mortality, further advances in this area are likely to translate into improved outcomes. Second, the allocation system for donor lungs in the United States was drastically altered in May 2005.[7] While this system has rapidly led to the more efficient utilization of donor organs and reduced waiting time in general, it may have the unintended consequence of reducing the availability of transplantation for PAH patients.

Selection Criteria and Timing of Lung Transplantation

Decisions regarding who should be listed for lung transplantation and when are among the most difficult in clinical medicine. This is especially true for PAH patients given, on the one hand, potentially effective medical therapy that continues to evolve at a fairly rapid pace and, on the other, historical 1- and 3-year post-transplantation survival rates of 66% and 57%, respectively.[4] Recipients should have a prognosis sufficiently poor to warrant the risk of transplantation. However, extremely ill patients with advanced right heart failure are less likely to be able to withstand the multiple insults associated with transplantation.

Indications for Transplantation

A reasonably sized body of literature now exists regarding prognostic determinants in IPAH or PPH. An ACCP evidence-based clinical practice guideline gave a grade A recommendation[2] to the following parameters:

Key Words—Idiopathic PAH; lung transplantation; contraindications; primary graft dysfunction; UNOS Lung Allocation System.

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- Advanced NYHA functional class
- Low 6-minute walk distance
- Presence of pericardial effusion
- Elevated right atrial pressure
- Reduced cardiac index
- Persistence of NYHA functional class III or IV after at least 3 months of therapy with epoprostenol

Other factors considered to have potential importance include low mixed venous oxygen saturation, persistently elevated B-type natriuretic peptide (BNP) or pro-BNP levels, echocardiographic assessments of right ventricular function, a history of right heart failure, and hemoptysis.

Few data are available regarding the prognosis of other types of PAH. Patients with Eisenmenger syndrome typically have preserved right ventricular function relative to IPAH despite higher pulmonary artery pressures. In one report, 3-year survival on the lung transplant waiting list was 77% compared with 35% for IPAH.[8] Combined with the high perioperative mortality for Eisenmenger syndrome, studies have failed to demonstrate a transplant survival benefit.[9,10] In contrast, PAH associated with scleroderma tends to be less responsive to medical therapy and has higher mortality than IPAH.[11-14]

A recent ISHLT consensus report provides the following guidelines for transplantation in PAH patients:

- Persistent NYHA class III or IV with maximal medical therapy
- Low (less than 350 meters) or declining 6-minute walk distance
- Failing therapy with intravenous epoprostenol, or equivalent
- Cardiac index of less than 2 L/min/m^2
- Right atrial pressure exceeding 15 mmHg

We would also consider an episode of massive hemoptysis as an indication for transplantation.

Contraindications

The complex nature of lung transplantation, the attendant high complication rate, and the limited donor supply mandate that only carefully screened individuals with a reasonable likelihood of a successful outcome be selected. **Table 1** lists the major contraindications outlined by the ISHLT consensus report.[15] Of particular relevance to PAH and timing is the presence of renal or hepatic dysfunction, which may be the result of advanced right heart failure. Azotemia[16] and hyperbilirubinemia[4] have been identified as risk factors for 1-year mortality among all diagnostic groups. In the early Stanford experience, 8 of 14 PAH patients with preoperative bilirubin levels greater than 2 mg/dL died early after heart-lung transplantation.[17]

Certain associated conditions preclude transplant consideration, eg, HIV, myeloproliferative disorders, and hemoglobinopathies. Portopulmonary hypertension cases may be suitable for combined lung-liver transplantation at selected centers. Connective tissue diseases are often accompanied by extrapulmonary involvement that could jeopardize the success of a lung transplant. These include nephropathy, myositis, vasculitis, neurologic disease, and disabling arthritis.

Table 1: Contraindications to Lung Transplantation

Absolute Contraindications

- Recent malignancy
- Advanced dysfunction in other major organs (eg, heart, liver, or kidney)
- Noncurable chronic extrapulmonary infection, including chronic active viral hepatitis B, hepatitis C, and human immunodeficiency virus
- Significant chest wall/spinal deformity
- Documented noncompliance
- Severe psychological condition associated with inability to cooperate or comply with medical therapy
- Absence of consistent or reliable social support system
- Substance addiction (eg, alcohol, tobacco, or narcotics) within last 6 months

Relative Contraindications

- Age older than 65 years
- Critical or unstable clinical condition
- Severely limited functional status with poor rehabilitation potential
- Colonization with highly resistant or highly virulent bacteria, fungi, or mycobacteria
- Obesity (body mass index exceeding 30 kg/m^2)
- Severe or symptomatic osteoporosis
- Other conditions (eg, gastroesophageal reflux or poorly controlled diabetes)

Gastrointestinal involvement is of particular concern in scleroderma, where esophageal dysmotility is a nearly universal finding.[18] Surgical vagal injury and the effects of immunosuppressive therapy on gastric peristalsis can induce further derangements in gastroesophageal motility after transplantation. While clinical aspiration is uncommon in scleroderma, its occurrence in the lung allograft could be catastrophic. Gastroesophageal reflux, even asymptomatic, has been increasingly linked to the development of bronchiolitis obliterans syndrome (chronic allograft rejection),[19] the major cause of long-term mortality after lung transplantation. Many transplantation centers have considered these risks too great. However, it appears that more programs are evaluating these patients on a case-by-case basis, as evidenced by UNOS data showing 23 scleroderma patients undergoing transplantation in 2006 alone.[6] A report of a two-center experience of 29 recipients found survival rates comparable to IPAH and idiopathic pulmonary fibrosis.[20]

Timing of Referral

Prior to institution of the new lung allocation system, median time to transplantation on the waitlist was over 2 years[21] and thus early referral and listing to accrue time was critical to allow survival to transplantation. If patients stabilized or improved with therapy, they could be inactivated as they approached the top of the list. In 2005, after institution of

the allocation system, median waiting time fell to a 10-year low of 202 days.[21] Moreover, early listing simply to accrue time is no longer of value, since priority for donor organs is based on the allocation system score and not waiting time. Thus, currently, referral to a transplant center can be reserved for patients meeting the guidelines delineated above as well as those with advanced (NYHA class IV and/or right heart failure refractory to diuretics) or rapidly progressive disease, irrespective of ongoing therapy. Earlier referral affords the opportunity to provide patient education and identify correctible comorbidities and factors that could prolong waiting time (such as short stature, blood type, and anti-HLA antibodies).

Transplantation Procedure and Outcomes

Type of Operation

Heart-Lung vs Lung Transplantation

In the early years, the prevailing opinion was that the right heart dysfunction of PAH required a combined heart-lung procedure (HLTx). Once isolated lung transplantation (LTx) was introduced for parenchymal lung disease, it was observed that the right ventricular remodeling changes of cor pulmonale regressed. This led to the application of LTx for IPAH as well as Eisenmenger syndrome, combined with repair of the congenital defect for the latter.[22] In the absence of complications, pulmonary artery pressure and vascular resistance fall to near normal values within 24 hours after either single (SLTx) or bilateral (BLTx) transplant.[23] Right ventricular dilatation and dysfunction resolve gradually over days to weeks,[24] likely contributing to the common occurrence of postoperative hemodynamic instability and increased early mortality. Importantly, there is no clear survival advantage for HLTx vs LTx in IPAH. For Eisenmenger syndrome on the other hand, HLTx appears to be superior with 30-day and 1-year survival of 81% and 70%, respectively, compared with 68% and 55% with LTx. This benefit was, however, largely restricted to recipients with ventricular septal defect.[25]

Thus, current practice at most centers is to restrict HLTx to PAH associated with ventricular septal defect or multiple congenital defects and concomitant acquired heart conditions or left ventricular dysfunction. Nevertheless, HLTx continues to be applied for many IPAH patients and accounted for 25% of all lung transplantations for this diagnosis in the United States in 2006.[6] Some cardiac transplant surgeons may prefer an HLTx, particularly if profound right ventricular dysfunction is present. The operation is more technically demanding and requires longer cardiopulmonary bypass time. Other drawbacks are the potential for cardiac allograft complications, a longer waiting time, and less efficient utilization of donor organs, which are scarce. For critically ill patients hospitalized and treated with intravenous inotropes, listing for HLTx places them in the status 1B or 1A category for cardiac allografts. In this scenario, allocation of a suitable heart-lung block would take precedence over any recipient awaiting lungs only.

Single vs Bilateral Lung Transplantation

Both SLTx and BLTx result in excellent hemodynamic results. Whereas LTx can typically be accomplished with single lung ventilation (sequentially in the case of BLTx) in non-PAH recipients, cardiopulmonary bypass is generally required for PAH patients. The Washington University group reported nearly identical mean pulmonary artery pressure and vascular resistance (averaging 22 ± 6 mmHg and 2.1 ± 0.9 Wood units) at 24 hours (compared with preoperative values of 66 mmHg and 15.8 units, respectively) among 51 BLTx and 39 SLTx for IPAH and PAH associated with congenital heart disease.[23] Short- and long-term survival rates were also comparable. A similar series from Pittsburgh[26] suggested slightly increased pulmonary artery pressures after SLTx compared with BLTx without significant differences in early postoperative oxygenation, duration of mechanical ventilation, hospital stay, or survival.

Advantages of SLTx include a shorter procedure with consequently lessened ischemic and cardiopulmonary bypass times and the ability to provide organs to a larger number of recipients. The potential for long-term regression of vascular remodeling in the native lung[27] and subsequent transplant pneumonectomy[21] offers an additional, albeit remote, theoretical benefit to SLTx. The major drawback, unique to PAH is the inability of the native lung to accommodate a significant proportion of pulmonary blood flow. After SLTx for obstructive or restrictive lung disease, ventilation and perfusion shift concordantly to the allograft, both averaging roughly 75%.[29] With PAH, where the mechanical properties of the lung are not deranged, ventilation is distributed equally among native and transplanted lungs. Perfusion, however, shifts almost completely to the allograft. In the absence of complications affecting ventilation (eg, edema, airways disease), the alveolar-arterial oxygen gradient remains sufficiently narrow (range: 18 to 37 mmHg) to allow adequate gas exchange. In the setting of acute lung injury or bronchiolitis obliterans, ventilation shifts away from the allograft. Perfusion cannot shift as readily to the native lung because of the high vascular resistance, resulting in severe hypoxemia. Abnormalities in matching perfusion to ventilation within the allograft may further alter gas exchange.[29]

As a result of the potential for ventilation-perfusion mismatching and more immediate hemodynamic improvement, the overwhelming majority (over 90%) of lung transplantations performed in recent years for PAH are bilateral.[4] While there is no evidence that primary graft dysfunction (see below) occurs more frequently in SLTx vs BLTx,[30] most clinicians feel that its management is less complex in the latter, particularly in the setting of PAH. In our experience, survival after BLTx is distinctly better, in large part the result of fewer postoperative deaths.[31] Moreover, a weak survival trend ($P = .18$) in favor of BLTx relative to SLTx for IPAH is now evident in the ISHLT registry data.[4]

Outcomes and Complications

Uncomplicated Cases

A successful heart-lung or lung transplantation for PAH leads to sustained normalization of pulmonary hemodynamics and cardiac function with no reports of recurrent pulmonary vascular disease. Regardless of transplant type, functional capacity is excellent, with 6-minute walk distance

Table 2—Complications after Lung Transplantation

Perioperative (30 days)
- Primary graft dysfunction
- Hemorrhage
- Technical: anastomotic stenosis
- Pleural complications
- Acute renal failure
- Phrenic nerve injury
- Bacterial pneumonia
- Systemic embolism

Early (1 to 6 months)
- Infections: bacterial, viral, fungal
- Acute Rejection
- Gastrointestinal
- Hepatobiliary
- Bronchial stenosis
- Venous thromboembolism
- Medication related

Late (more than 6 months)
- Bronchiolitis obliterans syndrome
- Chronic renal failure
- Malignancy
- Osteoporotic fractures
- Cardiac (coronary artery disease in HLTx)
- Diabetes mellitus
- Hypertension

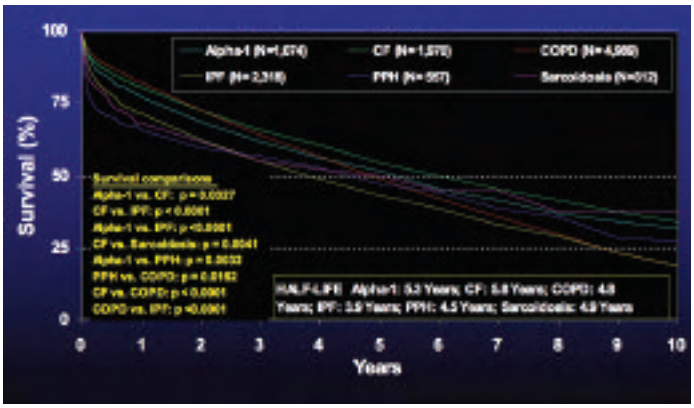

Fig. 1a—Kaplan-Meier survival by diagnosis (transplants: January 1994 – June 2004).

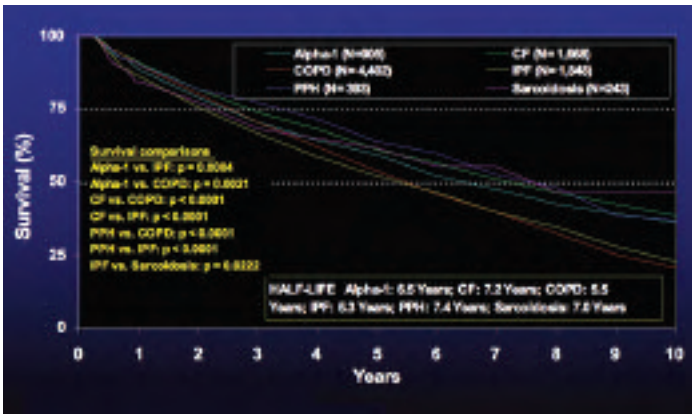

Fig. 1b—Survival to 3 months (transplants: January 1994 – June 2004).

averaging over 500 meters at 1 year.[32] Quality of life is also improved[33] and can approach levels of normal healthy individuals.[34] Despite normal cardiopulmonary function, maximal oxygen consumption is typically reduced to 40% to 60% of predicted due to an apparent defect in peripheral oxygen utilization that may be related to deconditioning and/or the effects of immunosuppressive medications (specifically calcineurin inhibitors).[29]

Complications

Unfortunately, a plethora of complications can lead to a poor outcome **(Table 2).** Among the most potentially devastating is primary graft dysfunction (PGD). PGD likely represents a form of ischemia-reperfusion injury resulting in diffuse alveolar damage manifesting as pulmonary edema and hypoxemia within 72 hours, not attributable to other factors such as left heart failure, venous obstruction, or infection.[35] Severe or grade 3 PGD, defined as a PaO_2/FiO_2 ratio below 200, occurs in 10% of all recipients, is associated with a 30-day mortality of 42%, and accounts for 44% of all early postoperative deaths.[36] One year mortality is increased more than threefold with severe PGD (65% vs 20%).

The pathogenesis of PGD remains poorly understood. Several risk factors have been postulated, including donor, recipient and procedure related.[37,38] The most consistent risk factor has been a recipient diagnosis of IPAH,[38] where the incidence of severe PGD has been as high as 63%.[39] The basis for this dramatically increased risk is not clear, but may be related to right ventricular dysfunction, the requirement for cardiopulmonary bypass, and/or circulating factors such reactive oxygen species and hypercoagulability and inflammatory mediators.[38] Hemorrhage may further increase the risk of PGD and can be particularly problematic in Eisenmenger syndrome, in which systemic-pulmonary collaterals are often prominent.[40]

Survival

As a result of the increased early mortality associated with PGD and other perioperative complications, 1-year post-transplant survival is significantly lower for PAH patients (66%) compared with other diagnostic groups (82% for COPD).[4] By 5 years, survival is 47%, comparable to all other groups as bronchiolitis obliterans syndrome, the main long-term cause of death, occurs with equal frequency **(Figure 1a).** Excluding deaths within the first 90 days, IPAH recipients have the highest 5-year survival (64%) among all diagnoses **(Figure 1b).** This may be explained by the generally younger age and lesser comorbidity in this group. The impact of early mortality on long-term survival is also evident after heart-lung transplantation, where 10-year survival conditional upon 1-year survival is roughly 50% for both IPAH and Eisenmenger syndrome **(Figures 2a** and **2b).**

Strategies to Improve Transplant Outcomes

Reducing early postoperative mortality is an urgent priority for improving the outcome of PAH recipients after lung

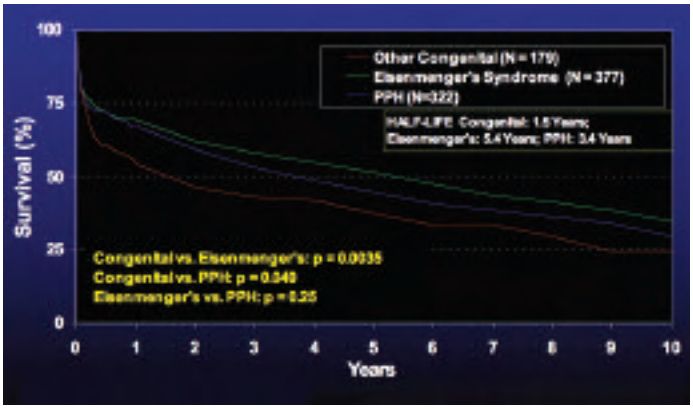

Fig. 2a—Kaplan-Meier survival by diagnosis (transplants: January 1990 – June 2004).

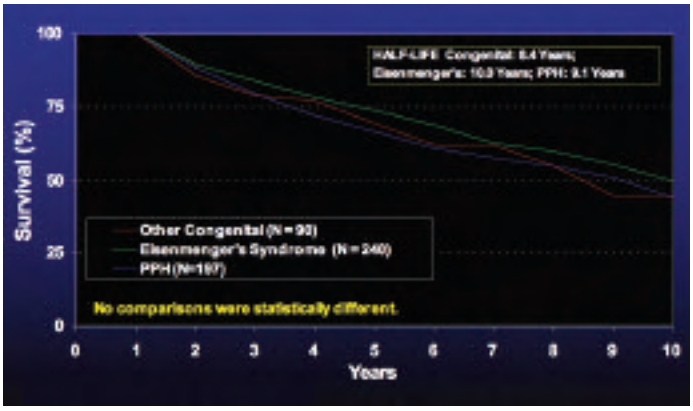

Fig. 2b—Kaplan-Meier survival by diagnosis conditional on survival to 1 year (transplants: January 1990 – June 2004).

transplantation. Appropriate donor selection may be important. Adequate oxygenation (PaO_2/FiO_2 above 300) and the absence of infection or contusion should be ensured. Increasing donor age is a continuous risk factor for 1-year mortality[4] and, along with a donor history of smoking, may be a risk factor for PGD.[37,39] The impact of ischemic time is controversial, but most experts recommend keeping this to a minimum for a PAH recipient, preferably less than 4 hours. For donor lung preservation, most centers currently employ a low-potassium dextran solution (extracellular) such as Perfadex, which may reduce the incidence of severe PGD compared with intracellular solutions (eg, Euro-Collins).[41] Cardiopulmonary bypass may be a risk factor for PGD,[38] but this is not a modifiable factor in PAH. Controlled, gradual reperfusion of the allograft may reduce the severity of PGD. The UCLA group has recently described a modified reperfusion technique whereby recipient blood is depleted of leukocytes and mixed in a 4:1 ratio with a buffered reperfusate solution supplemented with nitroglycerin, aspartate, glutamate, and dextrose. The mixture is then perfused into the pulmonary artery for 10 minutes prior to weaning of cardiopulmonary bypass.[42] While only 2 of 100 patients (5 with PAH) developed severe PGD, both had PAH. Thus, the ability of this technique to reduce PGD in PAH remains to be determined.

We recommend mechanical ventilation in the pressure control mode with distending pressures of 16 to 22 cm H_2O to limit alveolar distension and 8 to 10 cm H_2O of positive end-expiratory pressure to reduce intra-alveolar fluid accumulation. FiO_2 is kept to a minimum, preferably 0.21, to maintain oxygen saturation of 88% or greater while avoiding potential oxygen toxicity. Adequate ventilation must be ensured to avoid hypercapnia and acidosis. There is no evidence that inhaled nitric oxide reduces the incidence or severity of PGD,[43] although some reports suggest its utility in treating established disease.[44] Central hemodynamic monitoring is useful during the early post-operative period. If PGD is present, loop diuretics are administered, while care is taken to avoid hypoperfusion. Inotropic and/or pressor support is frequently required in PAH recipients. However, some authors have described the occurrence of right ventricular outflow tract obstruction in the setting of hypovolemia and hypercontractility of the thickened right ventricle.[45]

The early use of extracorporeal membrane oxygenation (ECMO) has proved to be an effective strategy for severe, life-threatening PGD. If circulatory function is adequate, we prefer the venovenous approach with a heparin-bonded circuit, thereby avoiding the need for systemic anticoagulation.[46] The achievement of adequate gas exchange with ECMO allows reduction in ventilating pressures that often leads to improved hemodynamics and provides time for the acute lung injury to resolve. The group in Vienna has described the use of prophylactic venoarterial ECMO started in the operating room as a replacement for cardiopulmonary bypass and extended into the early postoperative period in high-risk cases or with deteriorating graft function after reperfusion.[47] With this approach, the 3-month survival rate was 85% compared with 93% among recipients not requiring any support. A critical point to the successful use of ECMO is to apply it early, preferably within 24 hours.[48] The likelihood of survival when initiated after 3 days is extremely low.

UNOS Lung Allocation System

The new UNOS lung allocation system was developed to allocate organs based primarily on medical urgency, while avoiding futile transplants.[7] The allocation score is calculated by subtracting a waitlist urgency measure multiplied by two from the 1-year post-transplant survival measure. These are derived from a complex mathematical model incorporating several clinical variables **(Table 3)** predictive of 1-year waitlist and post-transplant survival among listed candidates and recipients, respectively. Diagnosis is an important predictor of both measures. PAH lowers predicted post-transplant survival relative to all other groups. The other parameters are weighted differently depending on the underlying diagnosis.[16] For example, the oxygen requirement reduces predicted waitlist survival considerably more for restrictive and obstructive lung diseases compared with PAH. Pulmonary artery systolic pressure is a strong predictor of waitlist survival among all groups except PAH.

The determinants of post-transplant survival in IPAH patients are poorly defined and more research in this area is urgently needed. While IPAH patients have the lowest 1-year survival rates, the 5-year survival rates are comparable to other diagnostic categories. The median survival is 4.3 years, compared with 3.7 for idiopathic pulmonary fibrosis.

Table 3—Clinical Variables Used to Derive Lung Allocation System Score

Variables for Prediction of Waitlist Survival
- Diagnosis
- Age
- Body mass index
- Diabetes
- NYHA functional class
- Forced vital capacity (% predicted)
- Oxygen requirement at rest
- Continuous mechanical ventilation
- Pulmonary artery systolic pressure (for all groups except PAH)
- 6-minute walk distance < 150 feet

Variables for Prediction of Post-transplant Survival
- Diagnosis
- Age
- Creatinine
- NYHA functional class
- Forced vital capacity (PAH and ILD groups only)
- Pulmonary capillary wedge pressure ≥ 20 mmHg (ILD group only)
- Continuous mechanical ventilation

ILD = interstitial lung disease; NYHA = New York Heart Association; PAH = pulmonary arterial hypertension

It can be argued that the goal of lung transplantation is to extend survival for considerably more than 1 year and therefore using predicted survival after 2 years or longer may be more appropriate.

Because the waitlist urgency measure is counted twice in deriving the lung allocation system score, it is vital that this parameter reliably estimate the severity of disease. The finding that candidates who die on the waitlist in non-PAH groups have higher scores compared to survivors, whereas the score is similar among PAH survivors vs nonsurvivors, indicates that disease severity is not adequately assessed in PAH (UNOS personal communication). While the median calculated score for IPAH patients listed in 2003 was comparable to that of idiopathic pulmonary fibrosis and cystic fibrosis, the 75% and 95% upper range was considerably narrower.[7] This reflects the absence of reliable measures of disease severity in this group. Conspicuously absent from the waitlist survival model for PAH are hemodynamics, particularly cardiac output and right atrial pressure, measures that have been strongly associated with mortality in several studies.[49,50] Missing data may have contributed to the failure of the UNOS analysis to detect an impact on survival since submission of hemodynamics was not mandatory and continues to be optional. Moreover, since the common practice was to list patients early to accrue time, right heart function may have deteriorated considerably between the time of hemodynamic assessment and death. The most consistent prognostic variables in IPAH, NYHA class and 6-minute walk distance, are included in the lung allocation system model, but they have a minimal impact on the score. The 6-minute walk distance is a bivariate factor: < or ≥ 150 *feet*. It is likely that reduced exercise capacity is a continuous variable related to survival and that distances considerably in excess of 150 feet reflect advanced disease. Patients unable to walk this distance are moribund and would have a high post-transplant mortality. This is indicated by the effect of NYHA class IV status, which reduces the post-transplant survival estimate relative to all other classes. NYHA class III or IV status reduces waitlist survival relative to class I or II, but paradoxically, class IV yields a slightly better survival than class III.

Despite the presence of advanced disease, the lung allocation system score varies little in IPAH. This makes it difficult for a patient in need of a transplant to obtain a sufficiently high score relative to other candidates. Fortunately, as a result of discussions with the UNOS Thoracic Organ Committee by a PHA-sponsored panel, guidelines for considering appeals were instituted in November 2006 whereby PAH patients deteriorating with optimal therapy with right atrial pressure above 15 mmHg and cardiac index below 1.8 L/min/m^2 will have their allocation score increased to the 90th percentile among all candidates nationwide. Meanwhile, as part of the plan when the lung allocation system was instituted, continued review of waitlist and post-transplant outcomes is ongoing in order to refine the model.

Summary

Despite remarkable advances in the medical therapy for PAH, a significant proportion of patients will still require lung transplantation for the foreseeable future. According to UNOS, 1-year posttransplant survival for IPAH has improved from 57% in 1996 to 73% in 2004.[21] More research into the prevention and treatment of primary graft failure will, it is hoped, lead to further improvements in short-term outcomes. Advances in immunosuppression along with development of effective strategies to prevent and treat bronchiolitis obliterans may ultimately yield long-term survival comparable to current outcomes for other solid organ transplantations. Ongoing data collection and analysis will be required to refine the current UNOS lung allocation system in order to optimize the equitable distribution of lung allografts. ■

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