Chapter 18
Lung Transplantation for Idiopathic Pulmonary Fibrosis

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Abstract  Despite advances in the development of novel pharmaceutical agents to treat idiopathic pulmonary fibrosis (IPF), there are no medical therapies known to resolve fibrosis or improve lung function in IPF. Therefore, lung transplantation remains the only life-saving therapy available to treat patients with IPF. However, a shortage of suitable donor organs limits the number of affected individuals who can undergo this procedure, and this shortage highlights the need to allocate donor lungs to those who are in the greatest need of a life-saving therapy yet ensure that those who undergo transplantation will have a reasonable expectation of long-term survival.
Still, outcomes remain relatively poor for many patients after lung transplantation, although a sizable minority of patients can enjoy long-term survival after lung transplantation.

**Keywords** Lung transplantation • Idiopathic pulmonary fibrosis • Lung allocation score • Transplant candidate selection • Deceased donor organ allocation

**Background**

Lung transplantation is a surgical procedure during which one or both diseased lungs are replaced by organs from a deceased organ donor (or, less commonly, by lobes from living donors) (Table 18.1). Although survival time after lung transplantation is typically limited, transplantation can confer substantial benefits, including prolongation of life, to selected candidates with advanced lung diseases such as idiopathic pulmonary fibrosis (IPF) [1]. Between 1988 and 2011, there were 23,652 lung transplant procedures performed in the USA, of which 5,565 (24 %) were performed for IPF [2]. In recent years, the proportion of lung transplant procedures performed for IPF in the USA has increased, and in 2007, IPF surpassed chronic obstructive pulmonary disease as the leading indication for lung transplantation in the USA (Fig. 18.1) [3]. In 2011, 36 % of US lung transplant procedures were performed for IPF [2]. In this chapter, we will review the role of lung transplantation for patients with IPF, including candidate selection criteria, the evaluation process, organ allocation in the USA, and outcomes and complications of transplantation.

| Procedure                          | Description                                                                 | Number performed in the USA in 2010a |
|------------------------------------|-----------------------------------------------------------------------------|--------------------------------------|
| Single lung transplantation        | Replacement of a single lung with a deceased donor lung                      | 539                                  |
| Bilateral sequential lung          | Replacement of both lungs with deceased donor lungs with two main stem      | 1,212                                |
| transplantation                   | bronchial anastomoses                                                       |                                      |
| En bloc bilateral lung             | Replacement of both lungs with deceased donor lungs with a single tracheal  | 19                                   |
| transplantation                   | anastomosis                                                                  |                                      |
| Heart-lung transplantation         | Replacement of both lungs and the heart with deceased donor lungs and heart  | 41                                   |
| Living-donor lung                  | Replacement of both lungs with lobes from two living donors                  | 0                                    |
| transplantation                    |                                                                           |                                      |

*aSource: OPTN data as of May 4, 2012*
Timing of Referral of IPF Patients for Lung Transplant Evaluation

IPF has been estimated to affect as many as 89,000 Americans [4]. Yet, in 2011 only 666 adults underwent lung transplantation for IPF in the USA [2]. While some patients with IPF do not meet criteria for lung transplantation or may be too well for the procedure, the surprisingly small number of patients with IPF undergoing transplantation annually largely reflects the scarcity of suitable lungs from deceased organ donors. While there were in excess of 12,000 deceased donor kidney transplants performed in the USA in 2011, only 3,160 lungs from deceased organ donors were used for transplantation. This discrepancy is largely due to unsuitable pulmonary conditions at the time of death in the majority of donors, such as pneumonia, ARDS, and pulmonary contusion [2].

In the face of this organ shortage, lung transplant providers must not only balance the risks and benefits of lung transplantation for individual patients but must also attempt to allocate deceased donor organs in a fashion that maximizes the overall public good achieved through transplantation (a utilitarian approach to the principle of distributive justice) [5]. Therefore, patients who stand to benefit from transplantation, but who are also at exceedingly high risk of early death after transplantation, should not undergo lung transplantation in geographic regions where a
donor shortage exists. Stated simply, a patient must be “sick enough” to warrant transplantation, but also “well enough” to tolerate the procedure and potentially enjoy many years of additional life after transplantation.

For these reasons, the selection of appropriate candidates for lung transplantation is challenging. In 2006, the International Society for Heart and Lung Transplantation (ISHLT) published guidelines to aid in the selection of candidates for lung transplantation [6]. In general, these guidelines recommend that patients be referred for transplant evaluation when it is estimated that a patient has only a 50% chance of surviving the next 2–3 years or has New York Heart Association class III or IV symptoms [6]. Given the poor prognosis of patients with IPF, the guidelines specifically recommend that patients with IPF be referred for lung transplantation upon identification of “histologic or radiographic evidence of UIP irrespective of vital capacity” [6]. In a joint statement, the American Thoracic Society, the European Respiratory Society, the Japanese Respiratory Society, and the Latin American Thoracic Association have recommended that IPF patients undergo transplant evaluation “at the first sign of objective deterioration,” but details or specific criteria for “deterioration” were not provided in this guideline document [7].

While these recommendations have strong face validity, current evidence suggests that many patients are not referred for subspecialty or transplant care early in the course of their disease. Two prior studies have shown that the median delay between symptom onset and accessing subspecialty pulmonary care (by an ILD expert or transplant pulmonologist) is 2 years [8, 9] and that longer delays are associated with a higher risk of death independent of lung function and age [9].

While some clinicians have used failure of a trial of corticosteroids as an indication for transplant referral (as prior guidelines have suggested [10]), one arm of a recent clinical trial of immunosuppressive therapy for IPF was halted early when an interim efficacy analysis indicated that increased mortality, hospitalizations, and adverse events were observed among study participants allocated to a combination of prednisone, azathioprine, and n-acetylcysteine [11]. In the absence of the availability of an effective medical therapy for IPF, a trial of medical therapy should not delay referral of patients with IPF for transplant evaluation.

One recent study demonstrated that a higher titrated oxygen requirement (TOR) was associated with greater mortality in IPF, independent of forced vital capacity and 6-minute walk test results, with higher TOR values having greater specificity to predict the risk of death [12]. It may be reasonable to include TOR in clinical decision making, but there are insufficient data to support TOR as a sole criterion to delay referral for transplantation.

Early referral for lung transplant evaluation allows sufficient time for a thorough evaluation of the medical, surgical, and psychosocial candidacy of the patient, permits longitudinal evaluation of progression by the transplant team, ensures adequate transplant-specific education, and avoids high-risk emergent transplantation of patients with severe hypoxemic respiratory failure. It is our recommendation that patients with IPF be referred for lung transplantation as soon as the diagnosis is made. In cases in which delayed referral is favored by providers, it is our opinion that referral should occur no later than upon determination that supplemental oxygen is required during ambulation and/or exercise.
Contraindications to Lung Transplantation

ISHLT-recommended contraindications to lung transplantation are listed in Table 18.2 [6]. There is general agreement that malignancy, severe chronic comorbid illness, psychosocial barriers, and the other absolute contraindications in Table 18.2 should prohibit lung transplantation for most candidates. On the other hand, the barrier that each of the relative contraindications listed in Table 18.2 poses to transplantation will vary according to candidate- and center-specific characteristics. These relative contraindications are largely factors reflecting body composition and surgical suitability that increase the risk of complications after lung transplantation.

Older age is associated with shorter survival time after lung transplantation [13]. The median survival time for adults over age 65 is only 3.5 years compared to 6.7 years for those age 35–49 (Fig. 18.2) [14]. Despite this increased risk, the proportion of lung transplants performed for older individuals has increased over time: in 2011, 26 % of all lung transplant procedures in the USA were performed for adults 65 years of age and older [2]. The ISHLT guidelines state that age alone should not be used as the sole criterion to deny lung transplantation, but instead should be considered as one of the many factors when determining suitability for transplantation.

Obesity, defined as a body mass index (BMI) >30 kg/m², is an independent risk factor for increased early mortality and primary graft dysfunction after lung

| Table 18.2 | Contraindications to lung transplantation |
|------------|------------------------------------------|
| Absolute contraindications | |
| • Malignancy in the last 2 years, with the exception of cutaneous squamous and basal cell tumors. In general, a 5-year disease-free interval is prudent | |
| • Untreatable advanced dysfunction of another major organ system (e.g., heart, liver, or kidney) | |
| • Non-curable chronic extrapulmonary infection including chronic active viral hepatitis B, hepatitis C, and human immunodeficiency virus | |
| • Significant chest wall or spinal deformity | |
| • Documented nonadherence or inability to follow through with medical therapy or office follow-up, or both | |
| • Untreatable psychiatric or psychological condition associated with the inability to cooperate or comply with medical therapy | |
| • Absence of a consistent or reliable social support system | |
| • Substance addiction (e.g., alcohol, tobacco, or narcotics) that is either active or within the last 6 months | |
| Relative contraindications | |
| • Age older than 65 years | |
| • Critical or unstable clinical condition (e.g., shock, mechanical ventilation, or extracorporeal membrane oxygenation) | |
| • Severely limited functional status with poor rehabilitation potential | |
| • Colonization with highly resistant or highly virulent bacteria, fungi, or mycobacteria | |
| • Obesity defined as a body mass index (BMI) exceeding 30 kg/m² | |
| • Severe or symptomatic osteoporosis | |
| • Mechanical ventilation | |
| • Suboptimal treatment of other medical conditions that have not resulted in end-stage organ damage, such as diabetes mellitus, systemic hypertension, peptic ulcer disease, or gastroesophageal reflux | |

Table created with data from [6]
transplantation in IPF [15, 16]. The mechanisms underlying these findings are not yet clear, but may involve secretion of pro-inflammatory mediators from macrophages in adipose tissue [17]. The magnitude of harm from obesity in IPF may be substantial, with an estimated twofold increased risk of primary graft dysfunction and a 30% increased risk of death, and it appears that obesity might account for as many as 20% of all deaths in the first year after transplantation for IPF [15, 16]. Based on these risks, mild elevations in BMI should not prohibit lung transplantation in all candidates, but instead the risks associated with obesity should be balanced with other risk factors and the potential benefit of transplantation for each individual candidate. In some cases, it may be reasonable to withhold lung transplantation from obese candidates (particularly with severe forms of obesity) until weight loss has been achieved. Healthcare providers should provide counseling, and, when indicated, interventions in order to achieve a healthy weight for all patients with IPF should be recommended, regardless of disease severity. For a discussion of the impact of age and obesity in lung transplantation, we refer the reader to a recent review on this topic [18].

Candidate Evaluation and Timing of Listing for Lung Transplantation

Once referred for lung transplant evaluation, patients with IPF should undergo a thorough evaluation to determine if they are suitable candidates for lung transplantation based on the selection criteria described above and in Table 18.2. There are
few published descriptions of the required elements of the evaluation of a lung
transplant candidate, making the evaluation largely center specific. Candidate eval-
uation typically begins with a review of medical records to determine if any abso-
lute contraindications exist. If none are identifi-
ced, the candidate meets with a
transplant pulmonologist, thoracic surgeon, and/or a transplant coordinator during
which an extensive history and physical examination is performed, and the patient
and his or her family are educated about the evaluation process, the transplant pro-
cedure, postoperative expectations, complications, post-transplant lifestyle changes,
and survival statistics. In addition, this opportunity is taken to individualize the
discussion of risks and benefi-
cTs of transplantation and to discuss the patient’s spe-
cific barriers to transplantation (such as obesity, underweight, poor functional sta-
tus, and comorbidities), and recommendations to improve candidacy are made.

Following the initial consultation, patients typically undergo an extensive evalua-
tion to determine their suitability for lung transplantation (Table 18.3). Once the
evaluation has been completed, the patient’s case is discussed at a multidisciplinary
team selection meeting. If deemed a suitable candidate for transplantation, the patient
is placed on the active waiting list for transplantation. Commonly, patients will not be
deemed candidates until they complete miss components of the evaluation, achieve
strict health-related goals (such as weight loss and participation in pulmonary

### Table 18.3  Suggested evaluation of lung transplant candidates

| Radiologic and functional studies | Consultations |
|----------------------------------|---------------|
| Chest radiograph and high-resolution chest computed tomography scan | Psychosocial evaluation is completed by a transplant social worker and, if deemed necessary, supplemented by psychiatric evaluation |
| Quantitative ventilation/perfusion lung scan | Rehabilitation medicine |
| Complete pulmonary function tests with arterial blood gas | Nutritionist, if deemed necessary on the initial nutritional screening |
| Cardiopulmonary exercise testing (if deemed necessary) | Dental evaluation |
| 6-minute walk test | Ophthalmologic evaluation |
| Echocardiogram and electrocardiogram | Age- and gender-appropriate cancer screening |
| Right heart catheterization | |
Table 18.4  ISHLT recommendations for the timing of listing for lung transplantation in IPF

| Condition                                      |
|------------------------------------------------|
| Diffusing capacity of carbon monoxide of less than 39% predicted |
| A 10 % or greater decrement in forced vital capacity during 6 months of follow-up |
| A decrease in pulse oximetry below 88 % during 6-minute walk testing |
| Honeycombing on HRCT (fibrosis score of >2) |

Table created with data from [6]

rehabilitation), or until additional follow-up shows signs of disease progression. The timing of listing for lung transplantation is based largely on the estimated risk of respiratory failure and death for patients with IPF. Table 18.4 shows known predictors of an increased risk of death in IPF that are recommended by the ISHLT as thresholds for listing patients with IPF for lung transplantation [6]. In addition to these criteria, patients with IPF who have an interval increase in oxygen requirements or develop pulmonary hypertension should also be considered for active listing for lung transplantation. Additional factors that might favor earlier listing for lung transplantation (depending on local donor availability) include pre-sensitization to human leukocyte antigens, need for bilateral transplantation, and short stature.

Deceased Donor Lung Allocation in the USA

Prior to 2005, allocation of deceased donor lungs in the USA was based on waiting time, with the highest priority given to those with the longest waiting time. Aside from a 90-day credit for patients with IPF, disease severity was not a factor in determining waiting list priority. In 1999, the US Department of Health and Human Services issued the “Final Rule,” which requires that deceased organ allocation systems de-emphasize waiting time and instead allocate organs based on “objective and measurable medical criteria… ordered from most to least medically urgent…” [19]. In response, UNOS/OPTN and the SRTR developed the Lung Allocation Score (LAS) system, which was put into place on May 4, 2005 [20]. The LAS system prioritizes waiting list candidates based on two criteria: medical urgency (the predicted risk of dying within 1 year) and estimated transplant benefit (the number of additional days of life expected from lung transplantation during the next year). Transplant benefit is calculated as the difference between expected survival time after lung transplantation and expected waiting list survival time (medical urgency). Medical urgency and expected survival after lung transplantation are estimated from multivariable regression models that contain the predictors given in Table 18.5. The LAS, which varies from 0 to 100, is then derived from output of these models. Those with the greater medical urgency and expected transplant benefit receive higher LAS scores. After accounting for other criteria (geographic proximity to the donor, pediatric age, and blood type), deceased donor lungs are offered first to those with higher LAS scores. The LAS has been updated since its inception to include
the addition of the partial pressure of carbon dioxide in arterial blood, and the addition of serum bilirubin is planned (to aid the estimation of medical urgency for those with right heart failure due to pulmonary arterial hypertension). In addition, extensive modifications to the LAS calculation are currently undergoing public comment and will likely be instituted in the near future.

The LAS system has had a number of notable consequences overall and for patients with IPF in particular. First, the transplantation rate for actively listed patients has increased dramatically with the greatest increase observed among those with IPF (Fig. 18.3), leading to IPF becoming the leading indication for lung transplantation in the USA (see Fig. 18.1) [3]. Second, waiting list mortality rates, which were decreasing prior to institution of the LAS system, have begun to increase, particularly for patients with IPF (Fig. 18.4) [3]. Whether this increase in waiting list mortality is due to removal of healthier patients from the waiting list, due to listing of more severely affected patients, and/or an inadequate number of donors remains to be determined. Third, as discussed above, older patients are now being considered more commonly for transplantation, opening up this treatment modality to a wider pool of patients with IPF.

While the LAS score appears to have increased the availability of transplantation for patients with IPF, concern remains that the scoring system—by preferentially emphasizing pre-transplant urgency—may be prioritizing those at highest risk for poor post-transplant outcomes. Indeed, one study suggested there might be higher rates of primary graft dysfunction and longer intensive care unit stays under the LAS system [21]. Two studies have also suggested that higher LAS scores are associated with higher mortality rates after lung transplantation [22, 23]. These studies raise questions about the utility of a system that grants organs to the sickest patients, increasing the likelihood of performing “futile” transplantation (i.e., transplantation of a donor organ without a consequent prolongation of life). Development of innovative methods to predict perioperative and post-transplant risk is under way and may ultimately lead to improved allocation methods and may aid in optimizing the timing of lung transplantation.

Table 18.5 Variables included in the LAS calculation

| Category                | Waiting list urgency       | Post-transplant survival |
|-------------------------|----------------------------|--------------------------|
| Disease severity        | Forced vital capacity      | Forced vital capacity    |
|                         | Mechanical ventilation     | Mechanical ventilation   |
|                         | Diagnosis                  | Diagnosis                |
|                         | Oxygen requirement         | Pulmonary capillary wedge pressure |
|                         | Pulmonary artery pressure  |                          |
|                         | Partial pressure of carbon dioxide in arterial blood |                          |
| Physiologic reserve     | Age                        | Age                      |
|                         | Functional status          | Functional status        |
|                         | Diabetes mellitus          | Serum creatinine         |
|                         | Body mass index            |                          |
|                         | 6-minute walk distance     |                          |
**Fig. 18.3** Rate of lung transplantation for waiting list candidates in the USA stratified by LAS diagnostic group, 1998–2009. *Group A*, obstructive lung disease. *Group B*, pulmonary vascular disease. *Group C*, cystic fibrosis. *Group D*, restrictive lung disease including IPF. Adapted from Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN/SRTR 2010 Annual Data Report. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation; 2011. Available at [http://srtr.transplant.hrsa.gov/annual_reports/2010/chapter_index.htm](http://srtr.transplant.hrsa.gov/annual_reports/2010/chapter_index.htm). Accessed 31 May 2012

**Fig. 18.4** Mortality rate of adults on the lung transplant waiting list, by LAS diagnosis group, 1998–2009. *Group A*, obstructive lung disease. *Group B*, pulmonary vascular disease. *Group C*, cystic fibrosis. *Group D*, restrictive lung disease including IPF. Adapted from Organ Procurement and Transplantation Network (OPTN) and Scientific Registry of Transplant Recipients (SRTR). OPTN/SRTR 2010 Annual Data Report. Rockville, MD: Department of Health and Human Services, Health Resources and Services Administration, Healthcare Systems Bureau, Division of Transplantation; 2011. Available at [http://srtr.transplant.hrsa.gov/annual_reports/2010/chapter_index.htm](http://srtr.transplant.hrsa.gov/annual_reports/2010/chapter_index.htm). Accessed 31 May 2012
Types of Transplant Procedures

While five different lung transplant procedures have been developed (see Table 18.1), the vast majority of lung transplant procedures performed in the modern era are either bilateral sequential lung transplantation or single lung transplantation. In general, bilateral lung transplantation is indicated for patients with septic lung disease (such as bronchiectasis) and is preferred in patients with moderate-to-severe pulmonary hypertension. In IPF, many patients are candidates for either a bilateral or single lung transplant procedure, and there are advantages to each procedure: bilateral transplantation confers greater improvement in lung mechanics and avoids native lung complications (such as malignancy), while single lung transplantation is a simpler, shorter operation with a shorter waiting time that leaves the recipient with native lung function that may aid gas exchange during allograft complications, such as primary graft dysfunction [24].

The first isolated lung transplant procedures were single lung transplant procedures for IPF and other interstitial lung diseases [25, 26]. Over time, bilateral lung transplantation has become the preferred procedure for IPF in the USA (Fig. 18.5) [27], yet controversy remains regarding whether one procedure confers a survival benefit over the other. The earliest report comparing single to bilateral lung transplantation came from Washington University and found that among 45 patients with IPF who underwent lung transplantation between 1988 and 1998, single lung transplantation was associated with longer survival time than bilateral lung transplantation [28]. An analysis of OPTN data comprising 821 patients with IPF who underwent lung transplantation between 1994 and 2000 also found that single lung transplantation was associated with improved survival compared to double lung transplantation only among patients younger than 50 (which may reflect a population enriched for ILDs other than IPF) [29]. In contrast, a report from Cleveland of

![Fig. 18.5](image-url) Distribution of single and bilateral lung transplantation for IPF in the USA, 1998–2010. Data from the Organ Procurement and Transplantation Network
82 patients with IPF transplanted between 1990 and 2005 suggested that bilateral lung transplantation was associated with improved survival compared to single lung transplantation [30]. ISHLT registry data suggest that patients who have undergone single or bilateral lung transplantation for IPF have fared similarly over the first 2 years after lung transplantation, but that single lung transplant recipients have had higher risks of death after that time period [14].

Observational studies of treatments are typically confounded by the indication for the treatment itself [31], making interpretation of these studies problematic. One group attempted to overcome this issue by performing an observational comparative effective study of single versus bilateral lung transplantation for IPF using OPTN data [27]. In propensity-matched analyses, single and bilateral lung transplant recipients with IPF fared equally well, suggesting that earlier studies did not adequately take confounding factors (such as disease severity) into account. The authors did note a small increase in early mortality among bilateral recipients (perhaps related to surgical factors) and a small increase in late mortality (perhaps related to malignancy) among single recipients.

In clinical practice, the decision to offer single or bilateral lung transplantation to patients with IPF is often informed by the presence of pulmonary hypertension and the candidate’s perceived surgical suitability for one procedure or the other. For candidates thought to be eligible for either procedure, single lung transplantation should be preferred, since the other lung could be used to transplant a second candidate, and available data suggest that overall outcomes are similar between procedures. Indeed, patients with IPF listed for single lung transplantation have higher transplantation rates and lower waiting list mortality rates than those listed for bilateral lung transplantation [32].

Outcomes and Complications of Lung Transplantation

Overall survival after lung transplantation has improved over time, with the median survival time improving from 4.7 years in the 1988 to 1994 ISHLT cohort to 5.9 years in the 2000–2009 ISHLT cohort [14]. For patients with IPF, the historical median survival time is 4.5 years (see Fig. 18.2), and unfortunately patients with IPF have the lowest 5- and 10-year survival rates compared to patients with other diagnoses [14]. Risk factors for 1-year mortality after lung transplantation for patients with IPF include older age, mechanical ventilation or hospitalization at the time of listing, prior pregnancy, elevated bilirubin, and elevated creatinine [14]. Despite these risks, observational studies suggest that, on average, lung transplantation prolongs life for patients with IPF [1, 33].

Most lung transplant recipients have improved functional status, with over 80% of surviving lung transplant recipients having no activity limitation at 1, 3, or 5 years after transplantation, and approximately 50% of 5-year survivors work full or part time (or are retired) [14], suggesting a significant personal benefit of lung transplantation to many recipients.
Despite these benefits, lung transplantation carries significant risk. During the first post-transplant year, approximately 30% of lung transplant recipients experience an episode of acute rejection and 60% are re-hospitalized, most commonly for infection or rejection [14]. Metabolic and cardiovascular complications are also common, with 54% developing systemic hypertension, 24% developing chronic kidney disease, 29% developing hyperlipidemia, and 30% developing diabetes within 1 year of lung transplantation [14]. The leading causes of death in the first year after transplantation are graft failure and non-CMV infection [14].

The most feared complication of lung transplantation is bronchiolitis obliterans syndrome (BOS), a disorder recognized clinically as an irreversible reduction in FEV$_1$ below the post-transplant baseline (Table 18.6) that occurs in approximately 50% of lung transplant recipients by 5 years and 75% by 10 years [14, 34]. BOS is often due to obliterative bronchiolitis and manifests as airflow obstruction, but alternative causes have been described [35] and a restrictive allograft syndrome without airflow obstruction is increasingly recognized [36]. BOS is likely a final common pathway of multiple causes of airway injury, including alloimmune-mediated inflammation, infection, and gastroesophageal reflux [37], suggesting a variety of methods to potentially prevent BOS. Nevertheless, once BOS is present, there are (by definition) no known methods to improve lung function. BOS is often progressive and is the leading cause of death after the first year of transplantation [14].

### Summary

Lung transplantation is an effective therapy for highly selected patients with advanced IPF. Early referral to a lung transplant program should be considered for all patients with IPF. Because selection criteria continue to evolve, referring clinicians should consider referral of patients who may not have been candidates in past years, such as adults over the age of 70 and those with acute illness.

| BOS stage | FEV$_1$ criterion | FEF25-75 criterion |
|-----------|------------------|-------------------|
| BOS 0     | 90% or more of baseline | >75% of baseline |
| BOS 0-p   | 81–90% of baseline | ≤75% of baseline |
| BOS 1     | 66–80% of baseline | Any |
| BOS 2     | 51–65% of baseline | Any |
| BOS 3     | ≤50% of baseline | Any |

Adapted from The Journal of Heart and Lung Transplantation, 21/3, Estenne M, Maurer JR, Boehler A, Egan JJ, Frost A, Hertz M, et al., Bronchiolitis obliterans syndrome 2001: an update of the diagnostic criteria, 297–310, 2002, with permission from Elsevier.
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