Lung Transplantation for Cystic Fibrosis

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KEYWORDS

• Lung transplantation • Cystic fibrosis • Advanced lung disease • Respiratory failure
• *Burkholderia cepacia* • Nontuberculous mycobacteria

KEY POINTS

- Lung transplantation is a good option for many patients with advanced lung disease due to cystic fibrosis (CF), including patients with comorbidities, resistant pathogens, prior thoracic procedures, and liver disease.
- Early referral is critical for patient education and intervention for comorbidities, such as malnutrition, poorly controlled diabetes, and atypical infections that may increase the risk of posttransplant complications.
- Criteria for lung transplant for patients with CF vary significantly among transplant centers; thus, referral to multiple centers may be necessary to maximize opportunities for individual patients.
- Patients with CF and respiratory failure requiring mechanical support with ventilation and/or extracorporeal membrane oxygenation may remain viable candidates for transplant with outcomes comparable with other patients with CF.

BACKGROUND

Lung transplantation is a viable option for many patients with end-stage lung disease. Since inception, more than 47,000 adult lung transplantations have been performed worldwide, according to the most recent International Society of Heart and Lung Transplantation report.[1] Despite the development of newer cystic fibrosis (CF) therapies and improved delivery of care, which has resulted in improved median survival for patients with CF,[2] lung transplantation provides an additional management option for patients with end-stage pulmonary disease from CF. In 1983 the first lung transplant for CF was performed, and CF now accounts for almost 17% of all pretransplant diagnoses.[1,3] Despite refinements in lung allocation practices, a proportion of patients with CF die while waiting for lung transplantation. Historically, the forced expiratory volume in 1 second (FEV_1) has been the most often used functional variable to predict prognosis, with early reports of a FEV_1 less than 30% predicted being associated with a 2-year mortality of 50%.[4] Other variables associated with a high risk of death from CF are hypoxia, hypercapnia, pulmonary hypertension, reduced 6-minute walk distance, and female sex.[4,5] From these variables, a few predictive models of survival in patients with CF have been developed; however, predicting survival for patients with CF is imprecise at best.[6–8] The goal of lung transplantation in patients with CF is to not only extend survival but also to improve quality of life. In comparison with other patients with end-stage lung disease, individuals with CF

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face unique challenges when considering lung transplantation, yet the median survival for individuals with CF after transplant exceeds those of individuals who underwent a transplant for other end-stage lung diseases.[1]

GUIDELINES FOR REFERRAL AND EVALUATION

Listing for lung transplantation should be considered at a time when survival from respiratory-related complications from CF is considered to be less than survival after lung transplantation. To date, there are no prospective, randomized, well-powered studies that define the optimal timing of transplant referral and listing. Early referral to a lung transplant center, before the anticipated need for listing, is highly encouraged to initiate patient and family education and to identify and correct potential barriers to lung transplantation (eg, malnutrition, substance abuse, poor psychosocial support). The decision to list patients with CF is complex and should take into account the rate of decline in pulmonary function, frequency of exacerbations, and the development of baseline hypercapnia and pulmonary hypertension. Current recommendations from the International Society of Heart and Lung Transplantation are based on small studies and expert opinion consensus (**Box 1**). To determine the severity of disease and appropriateness for lung transplantation, several studies are performed during the evaluation process (**Box 2**).

Box 1
Criteria for listing for lung transplantation in patients with CF

- FEV_1 less than 30% predicted or rapidly declining lung function
- Frequent exacerbations requiring antimicrobial therapy
- Recent exacerbation requiring mechanical ventilation
- Increasing oxygen requirements
- Recurrent hemoptysis despite embolization procedures
- Refractory or recurrent pneumothorax
- Baseline hypercapnia (P_{CO_2} >50 mm Hg)
- Pulmonary hypertension
- Ongoing weight loss despite aggressive nutritional supplementation

Box 2
Studies performed during lung transplant evaluation for CF

- Chest radiograph
- Computed tomography of the chest
- Complete pulmonary function tests
- 6-minute walk
- Quantitative ventilation/perfusion scan
- Barium swallow
- Electrocardiogram
- Transthoracic echocardiogram
- Right +/− left heart catheterization
- Bone densitometry
- Age-appropriate health maintenance examinations
- Complete blood count
- Renal function panel
- Hepatic function panel
- Arterial blood gas
- Sputum culture, including fungal and AFB
- 24-hour urine for creatinine clearance
- Thrombosis risk panel
- HLA molecular typing
- HLA antibody screen
- Blood group type
- Hemoglobin A1C
- Urinalysis
- PPD/Quantiferon Gold TB test
- Serologies
  - HIV
  - Hepatitis B
  - Hepatitis C
  - Syphilis
  - Herpes simplex virus
  - Varicella-zoster virus
  - Cytomegalovirus
  - Epstein-Barr virus
  - Toxoplasmosis

Abbreviations: AFB, acid fast bacilli; HIV, human immunodeficiency virus; PPD, purified protein derivative; TB, tuberculosis.

SELECTION OF CANDIDATES FOR LUNG TRANSPLANTATION

Lung transplantation should be considered for patients whose clinical status has progressively