Overview of Lung Transplantation, Heart-Lung Transplantation, Liver-Lung Transplantation, and Combined Hematopoietic Stem Cell Transplantation and Lung Transplantation

Shruti Gadre, MD[a], Jason Turowski, MD[a], Marie Budev, DO, MPH[b,*]

KEYWORDS

• Lung transplantation • Heart-lung transplantation • Liver-lung transplantation
• HSCT-lung transplantation • Lobar transplantation

KEY POINTS

- Lung transplantation (LTx) has evolved to represent the therapy of choice for a growing number of patients with end-stage lung diseases. Appropriate candidate selection for LTx is an important determinant of a positive outcome from transplantation.
- Posttransplantation survival has steadily improved, but long-term survival continues to be a challenge with a median survival of 5.8 years.
- Advances in the care of patients with cardiopulmonary dysfunction have decreased the need for combined heart-lung transplantation.
- Simultaneous liver-lung transplantation has been performed successfully in select patients who are not expected to survive either organ transplant alone.
- LTx following hematopoietic stem cell transplantation (HSCT) has been performed in patients who develop end-stage pulmonary complications following HSCT. Experience regarding simultaneous HSCT and LTx is limited to case reports at this time.

Lung transplantation (LTx) is a widely accepted treatment for end-stage lung disease. However, several pulmonary disease states are prone to developing both cardiac and hepatic complications. Simultaneous thoracic transplantation, including heart-lung (HLTx) or combined liver-lung transplantation (LLTx), can be a lifesaving surgery for patients with dual-organ failure. This review focuses on the

Disclosure Statement: The authors have no relationship with a commercial company that has a direct financial interest in subject matter or materials discussed in article or with a company making a competing product. The authors have nothing to disclose.

[a] Pulmonary and Critical Care Medicine, Respiratory Institute, Cleveland Clinic Foundation, A-90, 9500 Euclid Avenue, Cleveland, OH 44195, USA; [b] Lung Transplant and Heart Lung Transplant Program, Pulmonary and Critical Care Medicine, Respiratory Institute, Cleveland Clinic Foundation, A-90, 9500 Euclid Avenue, Cleveland, OH 44195, USA
* Corresponding author.
E-mail address: budevm@ccf.org

Clin Chest Med ■ (2017) ■–■
http://dx.doi.org/10.1016/j.ccm.2017.07.004

indications, candidate selection, listing, the early postoperative management and outcomes in LTx alone, combined dual-organ transplant, including heart and liver transplantation, as well as combined hematopoietic stem cell and LTx.

LUNG TRANSPLANTATION

LTx is an established treatment option for patients who suffer from end-stage lung disease. The origins of LTx were born in the early 1940s with the initial experimental transplantation techniques in canine subjects by Vladimir Demiknov and Dominique Metras.[1] The first human lung transplant was performed by Dr James Hardy in 1963. The initial transplant was successful on minimal immunosuppression available at the time, but the patient eventually died 18 days later, succumbing to multisystem organ failure due to sepsis. Although the patient died shortly after the transplant, the lung allograft did not show any evidence of acute rejection on autopsy.[2] It was not until almost 2 decades later in 1981, that Dr Bruce Reitz and Dr Norman Shumway performed the first successful HLTx in a patient with end-stage primary pulmonary hypertension.[3] A few years later in 1983, Dr Joel Cooper performed the first lung transplant at the University of Toronto that resulted in the recipient surviving for almost 7 years, before dying of renal failure.[4] After the initial experience by the Toronto group in the early 1980s, there was an exponential growth in the number of cadaveric donor lung transplants performed through the 1990s. Over the last 5 decades, 55,700 lung transplant procedures have been performed worldwide according to data from the International Society for Heart and Lung Transplantation.

Indications for Lung Transplantation

The indications for LTx include a diverse array of pulmonary diseases of the airway, parenchyma, and vasculature (**Table 1**). Chronic obstructive pulmonary disease (COPD) represents the leading indication for LTx, accounting for approximately one-third of all transplant procedures performed to date.[5] Transplant for idiopathic pulmonary fibrosis (IPF) has been steadily increasing and, although still second to COPD worldwide, it is now the leading indication for LTx in the United States.[6] Although LTx was once the only available treatment option for idiopathic pulmonary arterial hypertension (IPAH), IPAH now accounts for only 2% of lung transplants performed, reflecting major advances in the medical management of these patients.[5]

There are certain disease states that have center-specific guidelines and limitations and deserve additional mention. LTx of patients with systemic sclerosis–related lung disease remains controversial. Systemic sclerosis is a relative contraindication to LTx at many centers because of esophageal dysmotility and reflux, which may increase the risk for aspiration and accelerated graft loss, leading to chronic lung allograft dysfunction (CLAD). However, a few single-center studies have demonstrated that short-term functional outcomes and survival after transplantation of carefully selected patients with systemic sclerosis are comparable with the nonsystemic sclerosis patient population.[7,8] Candidate selection seems to be extremely important in considering this population, including avoiding patients with bowel or severe skin involvement.

Chronic airway infection is a universal feature of cystic fibrosis (CF). Despite the presence of highly resistant *Pseudomonas aeruginosa*, the effect of the resistance pattern on survival after transplantation seems to be small, and patients

Table 1
Primary indications for adult lung transplantation (transplants 1995–2015)

COPD	
COPD without A1ATD	31.3%
COPD with A1ATD	5.1%
ILD	
IIP	24.5%
ILD, not IIP	5.2%
Bronchiectasis	
CF	15.8%
Non-CF bronchiectasis	2.7%
PAH	
IPAH	2.9%
PH-not IPAH	1.6%
Less common diagnoses	
Sarcoidosis	2.5%
LAM/tuberous sclerosis	1.0%
Obliterative bronchiolitis	0.9%
CTD	0.7%
Cancer	0.1%
Other	1.7%
Retransplantation	4.1%

Abbreviations: A1ATD, α_1-antitrypsin deficiency; CTD, connective tissue disease; IIP, idiopathic interstitial pneumonia; ILD, interstitial lung disease; IPAH, idiopathic pulmonary arterial hypertension; LAM, lymphangioleiomyomatosis; PH, pulmonary hypertension.

Data from Yusen R, Edwards L, Dipchand A, et al. The Registry of the International Society for Heart and Lung Transplantation: thirty-third adult lung and heart-lung transplant report—2016; focus theme: primary diagnostic indications for transplant. J Heart Lung Transplant 2016;35:1170–84.