Lung transplantation: state of the art and current practice

Karen L Booth

John H Dark

Abstract

This article is a reflection of the present status of lung transplantation in the UK and worldwide and its transformation of end-stage lung disease. In its infancy, it was swept along by the determination and drive of surgical pioneers. Amongst them the names Demikhov, Hardy, Schumway, Cooley, Reitz, Cooper and Patterson have exemplified the surgeons' drive to bring lung transplantation to clinical fruition. With long-term survivors of heart–lung transplantation (HLTx) from 1981, single lung transplantation (SLT) from 1983 and bilateral lung transplantation (BLTx) from 1986, this decade saw the true genesis of clinical lung transplant programmes. In the modern era, research into donor organ regeneration with ex vivo lung perfusion (EVLP) and retrieval of lungs from non-brain dead donors (DCD transplantation), drug improvements in immunosuppression, technique improvements with ECMO and off-pump surgery have constantly pushed the boundaries and consistently seen a rise in lung transplantation year on year and it now exceeds cardiac transplant activity despite falling numbers of organ donors.

Keywords Immunosuppression; lung; surgical technique; transplantation

Indications for lung transplantation

Indications for lung transplantation include in general terms, obstructive, septic, restrictive and vascular pulmonary diseases, with the majority of transplants being operated on for chronic obstructive pulmonary disease (COPD), cystic fibrosis (CF) and interstitial lung disease.[1] The decision to place a patient on the waiting list for a lung transplant is complex, reflecting consideration not only of clinical and psychosocial characteristics of the individual patient but also program-specific factors and regional considerations (such as the use of a lung allocation score).

The ISHLT International Registry for Heart and Lung Transplantation was established to provide on-going up-to-date information on the thoracic organ transplant experience around the world. Collected statistical information includes outcome data, survival data and risk factor data segregated into subgroups according to various demographic criteria as well as the type of transplant (heart/heart-lung/lung). Reviewing the latest data on indication for transplantation shows the majority of lung transplants are carried out for COPD without alpha 1 antitrypsin deficiency, Idiopathic interstitial pneumonia (IIP) and CF (http://www.ishlt.org/downloadables/slides/2016/lung_adult.pptx).

ISHLT data also shows that in the year 2014–2015 the number of lung transplants carried out around the world and being reported to ISHLT was 3651, making a total of 58,043 since data collection on lung transplantation started in 1990. The trend over time has been a steady incline in lung transplantation despite the falling number of organ donors throughout the world, which is testament to the ongoing research and clinical improvements being made.[2]

General candidacy considerations

Lung transplantation should be considered for adults with chronic, end-stage lung disease who meet all the following (see Box 1).

Contraindications

Because lung transplantation is a complex therapy with a significant risk of perioperative morbidity and mortality, it is important to consider the overall sum of contraindications and comorbidities. The following lists are not intended to include all possible clinical scenarios, but rather to highlight common areas of concern.

Absolute contraindications are listed in Box 2. Other relative contraindications are outlined in Box 3.

'Bridging' to transplantation

It is well recognized that patients 'listed' for transplantation can deteriorate quite rapidly, for example the patient with interstitial lung disease can rapidly deteriorate without an infective trigger. Results when patients are mechanically ventilated before transplant are poor. But the use of extra corporeal life support (ECLS) or extra corporeal membrane oxygenation (ECMO) is suitable for young patients in which there is an absence of multiple organ dysfunction and who have a good potential for rehabilitation.

In such cases, it is appropriate to use a bridge such as venovenous ECMO and change their status to 'urgent' to ensure they receive the next available organ. Essentially the intention is to prolong the pre-transplant life expectancy of patients, increase the chances to receive a lung transplant, and to improve the likelihood of a successful post-transplant outcome by improving pre-transplant clinical stability.[3–5] It allows the patient to still have oral intake and improved nutrition and also

General criteria for consideration of lung transplantation

- High (>50%) risk of death from lung disease within 2 years if lung transplantation is not performed
- High (>80%) likelihood of surviving at least 90 days after lung transplantation
- High (>80%) likelihood of 5-year post-transplant survival from a general medical perspective provided there is adequate graft function

Box 1

Karen L Booth *MSc FRCS CTh is a Specialist Registrar in Cardiothoracic Surgery at The Freeman Hospital, Newcastle Upon Tyne, UK. Conflicts of interest: none declared.*

John H Dark *FRCS is Professor of Cardiothoracic Surgery at Newcastle University and The Freeman Hospital, Newcastle Upon Tyne, UK. Conflicts of interest: none declared.*

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Absolute contraindications to lung transplantation

- Lung transplantation should not be offered to adults with a recent history of malignancy
- Untreatable significant dysfunction of another major organ system (e.g., heart, liver, kidney, or brain) unless combined organ transplantation can be performed
- Uncorrected atherosclerotic disease with suspected or confirmed end-organ ischaemia or dysfunction and/or coronary artery disease not amenable to revascularization
- Acute medical instability, including, but not limited to myocardial infarction and liver failure
- Chronic infection with highly virulent and/or resistant microbes poorly controlled
- Evidence of active *Mycobacterium tuberculosis* infection
- Significant chest wall or spinal deformity expected to cause severe restriction after transplantation
- Body mass index (BMI) >35
- Current non-adherence to medical therapy or a history of repeated or prolonged episodes of non-adherence to medical therapy
- Psychiatric or psychologic conditions associated with the inability to cooperate with the medical/allied health care team and/or adhere with complex medical therapy
- Absence of an adequate or reliable social support system
- Severely limited functional status with poor rehabilitation potential
- Substance abuse or dependence (e.g., alcohol, tobacco, marijuana, or other illicit substances)

Box 2

Relative contraindications to lung transplantation

- Age ≥65 years in association with low physiologic reserve and/or other relative contraindications. Although there cannot be endorsement of an upper age limit as an absolute contraindication, adults ≥75 years old are unlikely to be candidates for lung transplantation in most cases
- Class I obesity (BMI 30.0–34.9 kg/m particularly truncal (central) obesity
- Progressive or severe malnutrition
- Severe, symptomatic osteoporosis
- Extensive prior chest surgery with lung resection
- Mechanical ventilation and/or extracorporeal life support (ECLS).
- Colonization or infection with highly resistant or highly virulent bacteria, fungi, and certain strains of mycobacteria
- For patients infected with hepatitis B and/or C, a lung transplant can be considered in patients without significant signs of cirrhosis or portal hypertension. Lung transplantation in candidates with hepatitis B and/or C should be performed in centres with experienced hepatology units
- For patients infected with human immunodeficiency virus (HIV), a lung transplant can be considered in patients with controlled disease with undetectable HIVRNA, and compliant on combined anti-retroviral therapy
- Infection with *Burkholderia cenocepacia*, *Burkholderia gladioli*, and multi-drug–resistant *Mycobacterium abscessus* if the infection is sufficiently treated preoperatively and there is a reasonable expectation for adequate control postoperatively
- Atherosclerotic disease burden sufficient to put the candidate at risk for end-organ disease after lung transplantation

Special surgical considerations

- Previous surgery is not a contraindication to lung transplantation
- Pleurodesis is the most troublesome situation but is not a contraindication
- Pneumothorax in a patient who may become a future transplant recipient should be given the best immediate management

Box 3

carry out physiotherapy whilst reducing their work of breathing and allowing them to regain some physical conditioning. When used in these situations on the right candidate it does not increase postoperative mortality as the technology with use of bicaval venous cannulas has improved significantly over time and it can now be carried out with relative ease and without much need for blood transfusion (see Figure 1). However, it still has significant resource implications with the need for intensive care support.

Donor and recipient matching

Typically donor–recipient matching takes place on the basis of blood group and predicted and measured total lung capacity. Some recipients also have pre-existing antibodies to HLA antigens and the prospective donor should be screened for antigens where there are antibodies with high activity in the recipient.

Predicted and measured total lung capacity is a measure of the height and sex of the donor (predicted) and recipient (matched). The two are 'matched' as best possible with a predicted lung capacity being predicted for the donor based on height and sex. Lung function is carried out for all recipients listed and this lung capacity is accurate. This is simply to ensure the lungs fit into the chest cavity of the recipient. When deciding whether a donor is acceptable, much research has taken place into this. The standard criteria are shown in Box 4, but many donors fall outside these rather strict criteria.

Allocation of donated lungs on the basis of time spent waiting on the transplant list is inefficient and biased against those who deteriorate fastest and therefore are at highest risk of dying before transplant. In 2005, the system for allocation of deceased donor lungs for transplant in the United States changed from allocation based on waiting time to allocation based on the lung allocation score (LAS). This score looks at various factors such as the diagnosis of the patient, their age, BMI, presence of diabetes, ability to function (using NYHA score), percentage of predicted forced vital capacity (FVC), systolic pressure of the pulmonary artery, pulmonary capillary wedge pressure, flow rate of supplemental oxygen required at rest, distance able to walk in 6 minutes, need or lack of continuous mechanical ventilation and creatinine levels in the blood. The higher the score, the greater the need for transplantation. Allocating lungs for transplant based on urgency and benefit instead of waiting time was associated with fewer waitlist deaths, more transplants performed, and a change in distribution of recipient diagnoses to patients

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