Cardiopulmonary transplantation

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Abstract

The Registry of the International Society for Heart and Lung Transplantation reported 4196 heart transplants and 3812 lung transplants worldwide in 2015. The 100,000th heart transplant mark has been passed. Heart transplantation is a proven surgical option for selected patients who have advanced heart failure refractory to surgical or medical management. Lung transplantation is the definitive treatment for end-stage lung disease for patients who have failed medical therapy. More than 90% of adult patients presenting for heart transplantation have dilated cardiomyopathy or ischaemic cardiomyopathy. Anaesthetic principles for heart transplantation include full monitoring including transoesophageal echocardiography, cardiostable anaesthesia and cardiac support, and assessment and treatment of pulmonary vascular hypertension. Median survival after cardiac transplantation is 11.9 years. Lung transplantation includes single-lung, double-lung, bilateral sequential single-lung, heart-lung and lobar transplantation. The most common indication is chronic obstructive pulmonary disease, which represents more than one-third of all transplant recipients. Donor criteria are becoming more liberal. Lung transplants may involve cardiopulmonary bypass. Pre-bypass air trapping can compromise cardiac function. Postoperative ventilation management should be guided by pH, not $PaCO_2$. Thoracic epidural provides optimal analgesia without respiratory depression. Five year survival after lung transplantation is approximately 65%.

Keywords Cardiac anaesthesia; end-stage lung disease; heart failure; heart transplantation; lung transplantation; transoesophageal echocardiography

Royal College of Anaesthetists CPD Matrix: 3G00

Learning objectives

After reading this article, you should be able to:

- understand the indications for heart and lung transplantation
- understand the basic pathophysiology before and after transplantation
- list the main specific anaesthetic concerns associated with heart and lung transplantation
- name three of the most common immunosuppressive agents

Introduction

There were over 7000 cardiopulmonary transplants reported in the International Society for Heart-Lung Transplantation (ISHLT) database (www.ishlt.org/registries) in 2015 worldwide across 388 centres (see Further Reading). These included 4196 heart and 3192 lung transplants. The majority of centres perform fewer than 30 cardiopulmonary transplants per year. Heart transplantation is a proven surgical option for selected patients who have advanced heart failure refractory to surgical or medical management. Lung transplantation is the definitive treatment for end-stage lung disease for patients who have failed medical therapy.

Heart transplantation

More than 90% of adult patients presenting for heart transplantation (HTx) have dilated cardiomyopathy (53%) or ischaemic cardiomyopathy (38%). Candidates for HTx typically have symptoms at rest (New York Heart Association class IV), with systolic and diastolic dysfunction. Globally, heart transplantation is limited by the severe shortage of suitable donor hearts. In the UK, less than half of all patients listed for transplantation will receive a transplant even after 3 years. Increased left ventricular (LV) filling pressures lead to increases in pulmonary venous pressures and development of pulmonary vascular congestion and oedema. Sympathetic tone is increased, leading to vasoconstriction, and salt and water retention. High levels of catecholamines lead to catecholamine receptor down-regulation and decreased myocardial norepinephrine stores. After a thorough evaluation of all major organ systems, potential recipients are placed on the transplant waiting list.

Donor hearts are allocated according to the condition of the recipient blood group, body size and waiting time. In adults, ABO matching is mandatory to avoid hyper-acute rejection, but this matching is not necessary in very young children. The main-stay of cardiac transplantation was donor hearts following brain stem death. Recently, there has been development in the use of hearts donated following circulatory determined death. Donor ischaemic time is defined as the time from aortic cross-clamp after harvesting the organ(s) to cross-clamp release following implantation in the recipient. Increasing donor ischaemic time is associated with poor post-transplant outcome and every effort is made to limit this to 4 hours. Traditionally, donor hearts are flushed with cardio-protective preservation solution and then cold stored for transport between donor and recipient sites with a key limiting factor being ischaemic time. However, with advances in ex-situ machine perfusion, transplant teams are able to extend periods of transportation. The currently available platform for ex-situ heart perfusion used a system of normothermic blood based perfusion to limit the ischaemic insult to the heart during transportation. After a thorough evaluation of all major organ systems, potential recipients are placed on the transplant waiting list. Pulmonary hypertension (PHT) is a risk factor for post-transplantation right heart failure; elevated pulmonary vascular resistance (PVR) unresponsive to vasodilators is a

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contraindication to HTx (PVR> 5 Woods units (WU) and a transpulmonary gradient >15 mmHg). The PVR in WU is calculated using the equation:

$$\mathrm{PVR} = \frac{\mathrm{MPAP} - \mathrm{PCWP}}{\mathrm{CO}}$$

where MPAP is mean pulmonary artery pressure, PCWP is pulmonary capillary wedge pressure and CO is cardiac output.

$$\text{Transpulmonary gradient} = \mathrm{MPAP} - \mathrm{PCWP}$$

Many HTx recipients are treated with inotropes (40%) or a mechanical circulatory device (33%) before HTx. The optimal time for HTx after LVAD implantation is unknown.

Denervation of the heart post transplantation does not significantly change cardiac function but it delays the response when increased CO is required. Heart rate increases only slowly with exercise, via circulating catecholamines. Only drugs with direct cardiac effects (such as catecholamines, phosphodiesterase inhibitors or levosimendan) are effective.

Anaesthetic management

Currently, of all DBD hearts that are offered in the UK, only 27% will yield a transplant. In the UK, several studies have shown that focussed donor management may help to increase this yield. This targeted donor management, guided by the use of haemodynamic measurements from a pulmonary artery flotation catheter (PAFC) and transoesophageal echocardiography (TOE) are often carried out by personnel with anaesthetic training. Furthermore, in the use of DCD hearts, Papworth Hospital, in addition to using an ex-situ perfusion platform, use a system of normothermic regional perfusion in the donor to perform a functional assessment of the donor heart in situ which is based on PAFC readings and TOE findings.

The anaesthetic approach for the recipient operation is the same as that for a patient with severely impaired myocardial function. Perioperative bleeding can be increased because of previous cardiac surgery, preoperative anticoagulation, liver dysfunction, prolonged cardiopulmonary bypass (CPB) time and hypothermia. Antibiotics and immunosuppressants are given according to local protocol. Several immunosuppressive agents are used, such as steroids, tacrolimus and mycophenolate. Most cases have induction immunosuppression with polyclonal antilymphocytic antibodies or interleukin-2 receptor antagonists. Nephrotoxicity, hypertension, hepatotoxicity and neurotoxicity are common side effects. Box 1 summarizes the basic anaesthetic principles during HTx.

A complete TOE examination should concentrate on the presence of cardiac thrombi and atheroma of the aorta and aortic arch. TOE is important for assessment of de-airing and biventricular function, when separating from CPB.

Low CO post transplantation may be due to hypovolaemia, inadequate inotropic support, raised PVR, myocardial injury during harvesting or poor preservation, acute rejection, tamponade or sepsis. Immediate therapy should be guided by invasive monitoring, TOE and endomyocardial biopsy. Implantation of temporary ventricular assist device(s) may be necessary.

The transplanted donor heart has no efferent sympathetic and parasympathetic nerves and is dependent on preload (Frank–Starling mechanism) and levels of circulating catecholamines. Resting heart rate is usually higher than normal and rises to a lesser degree during exercise. It does not respond to atropine. Up to 20% of transplanted patients will require a permanent pacemaker.

Specific anaesthetic principles for heart transplantation

- Assess right ventricle function and pulmonary resistance
- Blood products should be made available
- Deactivate implantable cardioverter defibrillator
- External defibrillator pads are required if re-do surgery
- Transoesophageal echocardiography (TOE)
- Administration of immunosuppressants and prophylactic antibiotics, and meticulous attention to sterility
- Monitoring: multi-lead ECG, oxygen saturation (SpO_2), arterial blood pressure, central venous pressure, PAP
- Large-bore venous access, central venous access (some centres prefer left side to preserve the right internal jugular vein for endomyocardial biopsies after heart transplantation), 8F central venous sheath (for pulmonary artery catheter), Foley catheter
- Balanced general anaesthetic with haemodynamic stability
- Antifibrinolytics (e.g. tranexamic acid)
- Transoesophageal echocardiography to provide information about donor heart function
- Left atrial pressure line can be sited intraoperatively for estimation of left ventricular end-diastolic pressure
- Inotropic support is nearly always used, agent varies by institution
- Reduction of pulmonary vascular resistance, e.g. inhaled nitric oxide up to 20 ppm or epoprostenol (prostacyclin (PGI2) 2–50 ng/kg/min), sildenafil

Box 1

Approximately a third of patients undergo at least one episode of rejection during the first year after transplantation, which presents with breathlessness, fatigue and reduced exercise tolerance. Treatment usually consists of high-dose immunosuppression.

Graft failure, malignancy, infection and accelerated coronary atheroma are the main causes of death after the first year of transplantation. Anaesthetists should assume that there is a risk for coronary vasculopathy in any heart transplant recipient beyond the first 2 years post transplantation.

The median survival after cardiac transplantation is 11.9 years.

Lung transplantation

Lung transplantation (LTx) includes single-lung, double-lung, bilateral sequential single-lung (72%), heart–lung and lobar transplantation. The most common indication is chronic obstructive pulmonary disease (COPD), which represents 31% of all transplant recipients. Idiopathic pulmonary fibrosis (25%), cystic fibrosis (16%), α1-antitrypsin deficiency (5%) and primary pulmonary hypertension are other indications for LTx. Primary pulmonary hypertension is the most common indication for LTx in children younger than 5 years. The disease process of

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