(Print pagebreak 449)

CHAPTER 6.4

Heart/Lung Transplantation

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(Print pagebreak 450)

Surgery for Heart Transplantation

Surgical Considerations

Description: Although heart transplantation has been practiced since 1967, it has had its greatest expansion since the early 1980s with the introduction of cyclosporine and its more recently introduced formulations (e.g., Gengraf). Currently, there are approximately 150 transplant centers and 2,200 heart transplant procedures performed yearly in the United States. Indications for heart transplantation range from hypoplastic left heart syndrome (HLHS) in the neonate to cardiomyopathy and ischemic heart disease in the adult. Recipients usually have end-stage heart disease manifested by CHF and a prognosis of less than 1-yr survival. Many patients are on inotropic drugs or on some type of additional mechanical assist, such as the use of an intraaortic balloon pump (IABP) or an implanted LV-assist device. Current immunosuppressive protocols consist of a combination of cyclosporine with prednisone and mycophenolate mofetil. Immunosuppression begins either immediately preop or perioperatively and will continue throughout the life of the patient. Induction immunosuppression is commenced in the operating room after protamine administration with methylprednisolone 500 mg iv and daclizumab 1 mg/kg iv. Current 1-yr survival averages 85% in most centers with 3-yr survival of approximately 80%, and a median survival approaching 10 years.

In **adult heart transplantation,** following median sternotomy, the pericardium is opened with care being taken to preserve the phrenic nerve. The aorta and vena cava are cannulated, the aorta is cross-clamped, and caval tapes (tourniquets to prevent VAE) are applied. The aorta and PA are then transected. This is followed by an incision through the atria, and the recipient heart is removed. The donor heart is prepared by opening the left atrium through the pulmonary veins, separating the aorta and PA. The donor heart is attached by a long, continuous suture line around the left atrium, followed by separate anastomoses to the inferior and superior vena cavae. Alternatively, the donor right atrium is anastomosed to the recipient right atrium with a single long continuous suture. Next, the PA and aorta are anastomosed to their respective recipient vessels. Multiple deairing maneuvers are followed by aortic unclamping and rewarming and resuscitation of the heart. NSR is established and CPB D/C'd. Heparin is reversed, hemostasis is secured, and the chest is closed in a routine manner. Following chest closure, these patients will often have implanted defibrillators that will be removed. An incision is made to access the pacemaker pocket, and the device is explanted. After hemostasis is established, the pocket is closed. (See pp. 336+ for discussion of CPB.)

Neonatal heart transplantation differs in that the PA is cannulated if the ductus arteriosus is patent. Reconstruction of the aortic arch in the patient with HLHS requires CPB with deep hypothermia (< 18°C) and circulatory arrest. The heart is then excised and the transverse aortic arch is opened beyond the ductus arteriosus to minimize risk of late coarctation. The donor heart is prepared, with special attention given to trimming the transverse aortic tissue for subsequent reconstruction. The left and right atrium, PA, and aorta are sutured in place. The new ascending aorta and right atrium are cannulated and CPB with rewarming is reinstituted. Chest closure is routine. (See Pediatric Transplantation p 1428.)

Pediatric heart transplantation has become common place in the past 10 years. Patients often have had previous cardiac surgery, and re-entry and excision of the native heart are complicated by the presence of adhesions and graft material from previous attempts at palliative/corrective surgery. Patients are often highly sensitized and may require intraoperative plasmapheresis while on cardiopulmonary bypass. Preparation for cardiopulmonary bypass is often similar to the adult heart transplant patient and the implantation procedure is also similar. However, provisions should be made for prolonged cross-clamp times necessary for implantation in the setting of abnormal systemic-cardiac or pulmonary-cardiac connections. (See Pediatric Transplantation p. 1438.)

Usual preop diagnosis: Cardiomyopathy; CAD with ischemic cardiomyopathy; CHD (e.g., HLHS or anomalous left coronary artery); end-stage valvular heart disease

Summary of Procedures

	Adult Heart Transplantation	Neonatal/Pediatric Heart Transplantation
Position	Supine	
Incision	Median sternotomy	
Special instrumentation	Ascending aortic, SVC, and IVC cannulae	Ascending aortic and right atrial cannulae
Unique considerations	Due to complete excision of the heart, use of a PA catheter is usually not feasible.	Deep hypothermia with circulatory arrest
Antibiotics	Cefazolin 1–2 g iv	Cefazolin 25–50 mg/kg iv
Surgical time	Cross-clamp: 45–60 min Surgery: 3–4 h	Circulatory arrest: 45–60 min; Cross-clamp: 80–100 minutes Surgery: 4–6 h
Closing considerations	Temporary AV pacing wires are occasionally placed. A PA catheter may be advanced, especially with concerns about residual pulmonary HTN and donor right heart function. An isoproterenol infusion is started intraop to keep HR = 100–110 and help improve right heart function and ↓ PVR. Inhaled NO may be used to further ↓ PVR.	Temporary ventricular pacing wire is usually placed. Temporary transthoracic left atrial line may be placed. Extensive aortic suture line requires avoidance of postop hypertensive episodes.
EBL	500–1,500 mL	50–100 mL
Postop care	Cardiac ICU: 1–2 d of assisted ventilation; 2–3 d stay.	Pediatric ICU × 1–2 d of assisted ventilation; 4–5 d stay, with attention to pulmonary care.
Mortality	< 5%	
Morbidity	Early acute rejection episodes from 10–21 d: 50% Infection, particularly pulmonary: 10% Pulmonary HTN with right heart dysfunction: < 10% Dysrhythmias with nodal rhythms: 5% Bleeding: 2–4% Hyperacute rejection: Rare (< 1%) Intracoronary air emboli	Respiratory problems: 20% Infection: 10% Pulmonary vasospasm with right heart dysfunction: < 10% Bleeding: 2–4%
Pain score	8–10	8–10

(Print pagebreak 451)

Patient Population Characteristics

Age range	18–75+ yr (average 50–55 yr)	1 d–2 mo (neonatal); 2 mo–18 yr (pediatric)
Male:Female	7:3	1:1
Incidence	2,200/yr (United States)	Rare
Etiology	Cardiomyopathy (50%); CAD with multiple pre	No apparent correlation with any specific genetic disorder. Cardiomyopathy (49%); CHD

	vious infarcts (48%); other (2%)	(42%); other (7%)
Associated conditions	CHF	Other congenital anomalies

Anesthetic Considerations

Preoperative

Patients scheduled for heart transplantation are terminally ill, typically with CHF, which is associated with a mortality of > 50% in 2 yr. (Studies have shown that patients with severe CHF have a mortality of 50% in 6 mo.) The progression of cardiovascular disease is usually well documented in these patients. A Hx of recent exacerbation of cardiac dysfunction should be sought and all data should be interpreted in light of interval changes.

(Print pagebreak 452)

Respiratory	The presence of pulmonary HTN and ↑PVR may be disclosed by catheterization. The severity of the abnormality and the responsiveness to specific vasodilators must be determined. **Tests:** Right heart catheterization
Cardiovascular	Indicators to consider include: hemodynamic status; LV EF (mortality is rapid in patients with EF < 10% and is worse for patients with EF of 10–20%, as compared with those with EF > 20%); myocardial structure and morphology, symptoms, and functional capacity; neuroendocrine status; serum sodium; and dysrhythmia. Unfortunately, while these measures show trends with mortality, they are not individually strong enough to predict a particular patient's course. Low maximum O_2 consumption (< 10 mL/kg/min) is associated with poor survival. Normal O_2 consumption is 40 mL/kg/min. In practice, however, this measure is too severe, because many patients awaiting heart transplantation have maximum O_2 consumption of 20 mL/kg/min. Dysrhythmia is a major cause of death; unfortunately electrophysiology studies of these patients may not be helpful because dysrhythmia tends to be noninducible. This phenomenon frustrates efforts to select and test antidysrhythmic drug therapy. The effectiveness of past antidysrhythmic therapy should be reviewed. **Tests:** ECG; cardiac catheterization; ECHO
Hematologic	Patients with dilated cardiomyopathy or previous cardiac surgery are frequently treated with anticoagulants to reduce the risk of thrombus formation, although the efficacy of this therapy has not been studied. Hepatic dysfunction may result from RV failure and may reduce synthetic function. Mild hepatic dysfunction and chronic anticoagulation may contribute to postop bleeding. The anticoagulant effect of warfarin should be reversed with FFP. **Tests:** Hct; PT; PTT; fibrinogen; Plts
Endocrine	Neuroendocrine abnormalities are often present in severe CHF cases. The cardiomyopathy produces low CO → compensatory sympathetic activation and renin-angiotensin activity. The result is excessive vasoconstriction with salt and H_2O retention, which further impair myocardial performance. Markedly worse survival is seen in CHF patients with serum sodium < 130. This may indicate the importance of neuroendocrine pathophysiology or may simply be evidence of the severity of the CHF. It may also simply indicate that patients with more severe CHF are treated with more diuretics. When patients are treated with an angiotensin-converting enzyme inhibitor, such as enalapril, the

serum sodium is normalized and survival chances are improved because of the slowing of the progression of CHF, not from alteration in the incidence of sudden death.
Tests: Electrolytes; Cr

Laboratory

Evidence of renal and hepatic dysfunction should be sought by H&P and lab studies. Hypokalemia is generally not treated in view of the K+ in the graft.

Premedication

Although anxious, these patients are usually well informed and psychologically prepared to undergo heart transplantation. They respond well to the reassurance of the preop visit, and pharmacologic premedication usually is not necessary. O_2therapy should commence prior to transport of the patient to the OR. Reassuring the family of a patient who suffers from rapidly progressive cardiac dysfunction also is valuable. The patient may be at increased risk for pulmonary aspiration of gastric contents because of the unscheduled nature of the surgery and use of oral cyclosporine immediately preop. Ranitidine (50 mg) and metoclopramide (10 mg) may be administered iv, most efficiently accomplished in the OR.

Intraoperative

Anesthetic technique: GETA. After the patient is placed on the operating table, O_2 and noninvasive monitors are applied. Dyspnea (a complication of the supine position) can be treated by raising the back of the table. As infection is a much-feared complication in the immunosuppressed transplant patient, aseptic technique is extremely important. Aseptic technique is used in inserting and securing all vascular catheters. The anesthesia machine should be equipped with a supply of air to control the FiO_2.

(Print pagebreak 453)

Induction

An arterial line for BP and blood gas monitoring should be inserted, using liberal amounts of local anesthetics before induction. There are rare exceptions to this rule, but the presence of real-time BP monitoring can be critical during induction. If infusion drugs (e.g., dopamine) are necessary before insertion of the CVP catheter, they can be infused temporarily through a separate peripheral iv. In patients who have a ↓ EF, it is often helpful to infuse dopamine 3–10 mcg/kg/min during induction to avoid ↓ HR and ↓ CO. Anesthesia is not induced until the team harvesting the graft reports that the donor heart appears to be normal. The patient is denitrogenated (FiO_2= 1.0), and cricoid pressure is applied just before induction. Induction agents include fentanyl (5–10 mcg/kg) or sufentanil (1–4 mcg/kg). Etomidate (0.1–0.2 mg/kg) is useful in permitting rapid control of the airway and for assuring lack of patient awareness. Midazolam also may be used. Vecuronium (0.15 mg/kg), pancuronium (0.1 mg/kg), or a combination of these two agents should be administered immediately to permit airway control.
Care must be taken to avoid bradycardia, which often results in low CO in these patients. Immediate control of the airway is crucial, as hypercarbia and hypoxia must be avoided. The patient can be expected to have a low CO, resulting in a delayed induction of anesthesia, which must be anticipated to avoid anesthetic overdosage. Low CO and a volume-contracted condition make the patient initially very sensitive to anesthetics. Hypotension should be treated promptly with inotropes (bolus and/or infusion). High preload is often necessary, and iv fluid may be administered cautiously to compensate for the vasodilating effect of anesthetic-mediated sympatholysis. Fluid boluses may be poorly tolerated in patients with diminished contractility.
Patient should be ventilated by mask and cricoid pressure released only after the airway has been secured with a cuffed ETT. The usual aids for managing the unexpectedly difficult airway should be readily available. Antibiotics are administered, and additional monitors (urinary catheter with thermistor, nasopharyngeal temperature probe, TEE, or esophageal stethoscope) are set up. If there is a delay in the anticipated arrival of the graft, the recipient should be covered and kept warm and skin prep should be delayed. Additional narcotics should be administered only in immediate anticipation of the commencement of surgery.

Maintenance	Typical cumulative anesthetic doses for the entire intraop course are: fentanyl 20–50 mcg/kg or sufentanil 10–15 mcg/kg; midazolam 0.2 mg/kg; vecuronium 0.3 mg/kg or pancuronium 0.2 mg/kg; scopolamine 0.07 mg/kg. Junctional rhythm is common in the denervated transplanted heart. Isoproterenol 10–75 ng/kg/min or epinephrine 50–105 ng/kg/min may be used to achieve a HR of 100–120 bpm. Isoproterenol is also useful in providing inotropic support and pulmonary vasodilation (see below). Atropine and neostigmine do not affect HR. HTN does not produce reflex bradycardia. The graft atrium produces normally conducted P-waves. The graft-conductive tissue contains adrenergic receptors and responds normally to norepinephrine, epinephrine, and isoproterenol. Inotropic support with dopamine (2–10 mcg/kg/min), isoproterenol (10–150 ng/kg/min), and epinephrine (20–100 ng/kg/min) may be necessary, especially if pulmonary HTN promotes RV failure. Inhaled NO (20–40ppm) may provide selective pulmonary vasodilation. A PA catheter may be helpful in guiding the use of inotropes and vasodilators.
Termination of CPB	After termination of CPB, TEE may be of particular value in assessing RV dysfunction, estimating PA pressures and guiding appropriate fluid therapy, pharmacologic support, and mechanical support as necessary. RV failure may be produced by the presence of air in the RCA. Visual inspection may demonstrate this problem, and one should wait for the passage of the air and the resolution of ischemia before terminating CPB. SNP (0.2–2.0 mcg/kg/min) is used for afterload reduction. NO, prostaglandin E_1 (PGE_1) (20–100 ng/kg/min), and NTG (0.2–2.0 mcg/kg/min) may be used for pulmonary vasodilation, especially if a preop catheterization study demonstrates responsiveness of the pulmonary circulation. Isoproterenol infusion (10–100 ng/kg/min) may provide appropriate pulmonary vasodilation, chronotropy, and inotropy. IV fluid and vasodilators must be given with particular care, as the flow produced by the denervated heart is quite sensitive to preload.
Postbypass hemorrhage	Postbypass bleeding is a common problem brought on by the preop use of anticoagulants, the depressed synthetic function of the liver in chronic heart failure, and the trauma of CPB. Following administration of protamine, infusion of Plts, FFP, and RBCs may be necessary. Cryoprecipitate is needed occasionally, especially for patients with previous chest surgery. The use of aprotinin, epsilon amino caproic acid (EACA), or tranexamic acid may be appropriate in some cases.
Immuno- suppression	Methylprednisolone 500 mg is given after bypass is terminated. Daclizumab 1 mg/kg is also administered after administration of protamine, and hemostasis has been secured.
Diuresis	There may be little urine production, especially if patient received high-dose diuretics preop. Cyclosporine may exacerbate renal dysfunction. Mannitol and furosemide may be needed to induce diuresis.
Transport	A Jackson-Rees system is used in transporting the patient to the ICU.
Blood and fluid requirements	Possible severe bleeding IV: 14–16 ga × 1–2 NS/LR @ 4–6 mL/kg/h Bleeding is often a problem after termination of CPB. A second iv catheter is inserted in patients with previous chest surgery.
Monitoring	Standard monitors (see p. B-1). Arterial line CVP/PA catheter UO Although it may be helpful to have a triple-lumen CVP line before induction for preload monitoring and infusion of potent infusion drugs, it is not essential. This line is usually inserted after the patient is intubated to avoid patient dyspnea and discomfort. A PA catheter is usually not inserted before bypass since it must be removed during surgery. An 8.5-Fr introducer is used in anticipation that a PA catheter may be necessary to manage right heart failure following the transplantation. In some institutions (not Stanford), the left IJ vein is the preferred site of cannulation, which leaves the right IJ unscarred for

		repeated postop endomyocardial biopsy of the transplanted heart.
	TEE	TEE is used to optimize fluid therapy, inotropic agents, vasodilators, and chronotropic agents.
Positioning	and pad pressure points. eyes. Arms padded at sides Chest roll	

(Print pagebreak 454)

Postoperative

Complications	RV dysfunction Pulmonary HTN	RV failure may occur in patients with pulmonary HTN and high RV afterload (see pulmonary HTN, below). Maneuvers which exacerbate pulmonary HTN should be avoided. These include hypoxia, hypercarbia, acidosis, and extremes of lung volume. Inhaled NO can be used to treat pulmonary HTN (20–40 ppm inspired concentration); however, it must be used with caution in patients with severe heart failure. Efforts to treat pulmonary HTN with vasodilator therapy may be complicated by impaired V/Q matching with hypoxemia and by systemic ↓ BP producing poor coronary perfusion and RV ischemia. Inotropic support of the RV may be necessary. Isoproterenol infusion (10–150 ng/kg/min) is attractive because it combines inotropy, pulmonary vasodilation, and chronotropy.
	Oliguria Drug side effects: • Cyclosporine: HTN, nephrotoxicity, hepatotox icity • Corticosteroids: glucose intoler ance, HTN, obesity, hyperlipi demia, aseptic necrosis of hip, bowel perforation, infection	Preexisting impairment may → chronic ↓ UO state. Other renal problems may be related to cyclosporine toxicity, diuretic toxicity, or CPB. Rx by optimizing hemodynamics. Consider reduction or elimination of nephrotoxins and continuing use of diuretics. Cyclosporine nephrotoxicity occurs in most patients. A functional toxicity with ↓ GFR occurs at low dose and is reversible. Tubular toxicity with morphologic changes occurs at high doses and is generally clinically unimportant and reversible. The most serious damage is vascular interstitial toxicity, which occurs over months at high doses and is not reversible.
Pain management	PCA (see p. C-3) after weaning from mechanical ventilation.	
Tests	Cr Hct	

(Print pagebreak 455)

Suggested Readings

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(Print pagebreak 456)

Surgery for Lung and Heart/Lung Transplantation

Surgical Considerations

Description: With the availability of cyclosporine, the ability to successfully transplant the heart and both lungs was proven in monkeys and then successfully applied in a patient in March, 1981. Subsequently, single-lung transplantation was successfully performed in 1984 and an en bloc, double-lung transplant in 1986. Clinical lung transplantation of these various types has increased markedly in the last few years, and, currently, approximately 600 single-lung transplants, 800 bilateral lung transplants, and 30 heart/lung transplants are performed in the United States each year.

Current indications for heart/lung transplantation are primarily those of combined heart and lung disease, including Eisenmenger's syndrome due to a congenital heart defect with irreversible pulmonary HTN. Certain types of diffuse lung disease, such as primary pulmonary HTN with significant right heart failure, are also treated in some centers by heart/lung transplantation. Recipients for single-lung transplant usually have end-stage pulmonary disease without significant sepsis. This includes patients with interstitial fibrosis, emphysema, and lymphangioleiomyomatosis. Some patients with pulmonary vascular disease, such as primary pulmonary HTN or pulmonary HTN associated with an ASD, have undergone single-lung transplantation with or without cardiac repair. Bilateral lung transplantation is now performed usually as a sequential single-lung transplant with the major indications being septic lung disease, such as cystic fibrosis, chronic bronchiectasis, severe bullous emphysema, or pulmonary vascular disease with or without cardiac repair. Current immunosuppressive protocols consist of a combination of tacrolimus with prednisone and myophenolate mofetil, with or without early induction therapy, using a cytolytic agent, such as antithymocyte globulin. Immunosuppression may begin preop and continue throughout the life of the patient. Current 1-yr survival rates average 70% for heart/lung transplants and 80% for lung transplants.

Heart/lung transplants usually are performed through a median sternotomy, although occasionally bilateral, transsternal thoracotomy has been used. **Single-lung transplants** (usually left side) and **bilateral sequential lung transplants** use a lateral thoracotomy or transsternal bilateral thoracotomy. Single- and double-lung transplants are greatly facilitated with OLV, which is essential for these procedures. If this type of ventilation is not feasible, a bronchial-blocker must be inserted through the operative field during pneumonectomy and reimplantation. CPB is routinely used for heart/lung transplantation, and is used for either single- or bilateral-lung transplantation, depending on the stability of the patient during OLV and/or clamping of the PA. Patients with severe pulmonary HTN undergoing single- or double-lung transplantation will almost always require CPB to reduce PA pressure during clamping. For combined transplants, the recipient heart is removed as for standard heart transplantation (see Surgery for Heart Transplantation, p. 450). A portion of the PA near the ligamentum arteriosum, however, is left intact in order to preserve the recurrent laryngeal nerve. Next, each recipient lung is excised and the trachea is transected above the carina. For single-lung transplant, usually the left recipient lung is excised, leaving a bronchial stump and vascular pedicles for the PA and veins (left atrium). For bilateral-lung transplants, both recipient lungs are removed, the trachea transected just above the carina, and the main PA and left atrium prepared for subsequent anastomosis.

Implantation of the grafts involves a tracheal anastomosis, aortic and separate SVC and IVC anastomoses for heart/lung transplants, and a bronchial anastomosis with PA and pulmonary venous anastomosis for single-lung transplantation. **Bilateral sequential lung transplants** are performed as if they were single-lung transplants. CPB requires heparinization and protamine reversal. Prior to closure, extensive exploration for potential bleeding sites within the posterior mediastinum is carried out with placement of right and left pleural and mediastinal drainage. Thoracotomies are closed in standard fashion with routine chest tube drainage.

Usual preop diagnosis: End-stage heart and lung disease, such as Eisenmenger's syndrome; cystic fibrosis; primary pulmonary HTN; emphysema; bronchiectasis; lymphangioleiomyomatosis; interstitial pulmonary fibrosis; sarcoidosis; other unusual forms of lung disease

(Print pagebreak 457)

Summary of Procedures

	Heart/lung Transplantation	Single-Lung Transplantation	Bilateral-Lung Transplantation
Position	Supine	Lateral thoracotomy	Supine
Incision	Median sternotomy, usual; bilateral anterior thoraco tomy, occasionally	Posterolateral thoracotomy	Transsternal bilateral thoracotomy
Special instrumentation	Ascending aortic, SVC, and IVC cannulae	Occasional need for BB to be inserted through the operative field.	± Aortic, SVC, and IVC cannulation; occasional need for BB.
Unique considerations	CPB. If recipient has had previous thoracotomies, mediastinal collaterals may cause troublesome bleeding. Some patients with cystic fibrosis have severe bilateral scarring, requiring extensive dissection to remove the reipient lung.	± CPB. Patient may become severely hypoxic or hypercarbic during OLV, requiring CPB. During right thoracotomy, cannulation can be performed through the thorax, but left thoracotomy may require femoral artery and vein cannulation.	CPB. Thoracotomy usually is performed on left side first, with implantation of lung on this side, followed by completion of right side thoracotomy and right-lung transplantation. If patient becomes unstable, cannulation in the thorax is usually possible to facilitate transplantation.
Antibiotics	Continue specific antibiotic regime. Coverage for pseudomonas is suggested in patients with cystic fibrosis.	Cefazolin 2 g iv then 1g q 4 h	With appropriate coverage for pseudomonas in patients with cystic fibrosis.
Surgical time	4–5 h	2–3 h	5–6 h
Closing considerations	Temporary pacing wire applied and isoproterenol infusion is usually started intraop to keep HR between 100–110, as with a cardiac transplant.	Ventilation with as low an FiO_2 as possible to maintain a PO_2> 90. Minimize iv fluids.	
EBL	500–2,000 mL	< 500 mL (more if CPB is used)	500–2,000 mL
Postop care	Cardiac ICU: 3–7 d; 1–2 d assisted ventilation		
Mortality	10–15%	10%	10–15%
Morbidity	Early acute rejection episodes from 10–21 d: 75% Infection, particularly pulmonary: 30–40% Pulmonary interstitial edema: 20% Return for bleeding: 4–6% Hyperacute rejection: Rare	— Bleeding: 2–4% Bronchial leak or stenosis: 2–4%	—
Pain score	8–10	8–10	8–10

(Print pagebreak 458)

Patient Population Characteristics

	Heart/lung Transplantation	Single-Lung Transplantation	Bilateral-Lung Transplantation
Age range	3 mo–55 yr (average 30–40 yr)	1–65 yr	
Male:Female	1:1		

Incidence	30/yr (United States) 200/yr (worldwide)	600/yr (United States) 1,000/yr (worldwide)	800/yr (United States) 1,200/yr (worldwide)
Etiology	Eisenmenger's syndrome; CHD; cystic fibrosis; pulmonary HTN; other lung diseases	Acquired chronic lung disease; pulmonary HTN	Cystic fibrosis; interstitial fibrosis; emphysema
Associated conditions	Severe cyanosis and polycythemia; diabetes in patients with cystic fibrosis; sinus infections in patients with cystic fibrosis	Right heart dysfunction; pulmonary valve insufficiency and tricuspid valve insufficiency	Diabetes mellitus; sinus infections in patients with cystic fibrosis

Anesthetic Considerations for Heart/Lung Transplantation

Preoperative

Patients scheduled for heart/lung transplantation are terminally ill, although they may still be able to maintain limited activity. Indications include primary pulmonary HTN, Eisenmenger's syndrome, cystic fibrosis, and combined cardiac and pulmonary disease. The standard preanesthetic evaluation is supplemented with considerations particular to these patients. The progression of disease is usually well documented.

Respiratory	Patients with severe pulmonary HTN (80/50 mmHg) have enlarged PAs. Vocal cord dysfunction (Sx: hoarseness, inability to phonate “e”) may occur when the left recurrent laryngeal nerve is stretched by an enlarged PA, making these patients at increased risk for pulmonary aspiration. Appropriate precautions to avoid aspiration should be taken (see Induction, below). **Tests:** ABG; cardiac catheterization
Cardiovascular	Hx of recent exacerbation of symptoms should be sought and cardiac catheterization data interpreted in light of interval changes. The severity of pulmonary HTN and the responsiveness to specific vasodilators during catheterization should be reviewed. **Tests:** ECG; cardiac catheterization; ECHO
Neurological	R → L intracardiac shunting may be present in patients with pulmonary HTN, and Hx of embolic episodes should be sought. Extra care should be used to avoid injection of even small quantities of intravenous air.
Hematologic	The medication schedule should be verified with particular attention to the recent use of anticoagulants. **Tests:** Hct; PTT; PT (special tubes required if severe polycythemia present 2° ↓ plasma volume); Plt count; fibrinogen
Laboratory	Evidence of renal and hepatic dysfunction should be sought by H&P and lab studies. Hypokalemia is generally not treated because the heart/lung graft is preserved with K+ and implantation will reverse hypokalemia.
Premedication	Although anxious, these patients are usually well informed and psychologically prepared. They respond well to the reassurance of the preop visit, and pharmacologic premedication usually is not necessary. O_2therapy should commence prior to transport of patient to the OR. Patient may be at increased risk for pulmonary aspiration of gastric contents because of the unscheduled nature of the surgery, the use of oral cyclosporine immediately preop and the presence of recurrent laryngeal nerve damage. Ranitidine (50 mg) and metoclopramide (10–20 mg) may be administered iv preop.

(Print pagebreak 459)

Intraoperative

Anesthetic technique: GETA. Infection is a much feared complication in the immunosuppressed transplant patient; thus, aseptic technique is important. Aseptic technique is used in inserting and securing all vascular catheters. The anesthesia machine should be equipped with a supply of air to permit control of the FiO_2; and anesthesia is not induced until the team harvesting the graft reports that it appears to be normal to direct inspection.

Induction	In the OR, the patient should be placed on the operating table and O_2 and noninvasive monitors applied. An arterial line for BP and blood gas monitoring should be inserted, using liberal amounts of local anesthetics before induction. There are rare exceptions to this rule, but the presence of real-time BP monitoring can be critical during induction. A patient who is dyspneic in the supine position may be treated by raising the back of the table. Cricoid pressure must be used when the patient is at risk for aspiration of gastric contents. A major goal of anesthetic induction is the avoidance of further increases in PVR by guarding against respiratory acidosis, hypoxia, N_2O, light anesthesia, and extremes of lung volume. When hemodynamically tolerated, fentanyl (5–10 mcg/kg) is useful in blunting the pulmonary vascular response to intubation. Etomidate (0.1–0.2 mg/kg) may be used when hypotension limits administration of narcotics. Vecuronium (0.15 mg/kg), pancuronium (0.1 mg/kg), or a combination of the two, should be administered early to permit rapid airway control. Midazolam and scopolamine produce amnesia. N_2O is not used because it exacerbates pulmonary HTN, reduces FiO_2 and expands intravascular air bubbles. Patient should be ventilated by mask, and cricoid pressure released only after the airway has been secured with a cuffed ETT. Excessive pressure of the cuff on the trachea should be avoided. An ETT of internal diameter of 8.0 mm will facilitate FOB postop.
Maintenance	Typical total anesthetic doses for the *entire* intraop course are: fentanyl 10–50 mcg/kg or sufentanil 10–15 mcg/kg; midazolam 0.2 mg/kg; vecuronium 0.3 mg/kg or pancuronium 0.2 mg/kg; scopolamine 0.07 mg/kg. After tracheal anastomosis is complete, lungs are ventilated with FiO_2 = 0.21 at 5 breaths/min and a TV of 6 mL/kg. When bladder temperature reaches 36°C, ventilation is increased to 10 breaths/min and TV of 12 mL/kg. TV should be adjusted to eliminate atelectasis and to achieve a peak inflation pressure of 25–30 cmH_2O with the chest open. The FiO_2 is increased to 0.4 and may be altered in response to pulse oximetry and blood gas data. FiO_2 is limited in the hope of curtailing free radical injury. PEEP may be used to enhance oxygenation and is adjusted with an appreciation of the effect of lung volume on PVR. Hypoxemia must be avoided. Hyperkalemia may be treated with Ca++ (e.g., 3–5 mL 10% CaCl q 30 min), glucose (50 g), insulin (10 U), and diuresis. Junctional rhythm is common in the denervated transplanted heart. Epinephrine (50–150 ng/kg/min) or isoproterenol (10–75 ng/kg/min) is used to achieve a HR of 100–120. When sinus rhythm is achieved, it is common to see two P-waves if a biatrial anastomosis has been used. The residual atrial tissue produces nonconducting P-waves.
Termination of CPB	Responses mediated by vagal tone will be seen in the rate of the original atrial tissue and have no clinical importance beyond the ease with which the ECG is interpreted. In the denervated heart, atropine and neostigmine will not affect HR, and HTN will not produce reflex bradycardia. The graft atrium produces normally conducted P-waves. The transplanted heart contains adrenergic receptors and responds normally to norepinephrine, epinephrine, and isoproterenol. The CO of the denervated heart is quite sensitive to preload; thus, iv fluid and vasodilators must be given with particular care. SNP is used for afterload reduction. TEE may be of particular value in assessing RV dysfunction and guiding appropriate fluid therapy, pharmacologic support, and mechanical support as necessary. NO, PGE_1 (20–100 ng/kg/min), isoproterenol, and NTG (0.2–2.0 mcg/kg/min) also may be used for pulmonary vasodilation. Inotropic support with dopamine (2–10 mcg/kg/min), isoproterenol, and epinephrine (20–100 ng/kg/min) may be necessary, especially if pulmonary HTN and RV failure occur.
Immuno- suppression	Methylprednisolone 500 mg iv is given after bypass is terminated.

Diuresis

There may be little urine production, especially if patient received high-dose diuretics preop. Cyclosporine may exacerbate renal dysfunction. Mannitol and furosemide may be needed to induce diuresis.

Transport

A sterile, disposable Jackson-Rees system is used in transporting the patient to the ICU.

Blood and fluid requirements

Anticipate large blood loss.
IV: 14–16 ga × 2

Bleeding is often a major problem after termination of CPB. Patients with intracardiac defects are at increased risk for cerebral embolic events. Care must be taken to remove all air bubbles from intravascular lines.

Control of blood loss

Postbypass bleeding is a common problem.

Postbypass bleeding is exacerbated by preop use of anticoagulants, depressed synthetic liver function, trauma of CPB, and/or previous chest therapy.

Coagulation therapy necessary.

Coagulation therapy may include: protamine (30 mg/kg); Plts; FFP; RBCs; EACA (300 mg/kg); DDAVP; aprotinin (500,000 U/h after loading dose).

Possible severe bleeding

Severe bleeding prompts further therapy: cryoprecipitate, factor IX concentrate, Feiba VH (factor 8 inhibitor bypassing activity), and/or recombinant factor 7a.

Monitoring

Standard monitors (see p. B-1).
Arterial line

CVP/PA catheter
UO

Typically, invasive monitors are placed prior to induction; however, if patient is very dyspneic in the supine position, it may be advantageous to insert the CVP catheter following anesthetic induction. An introducer permits the rapid insertion of a PA catheter when necessary. In some centers (not Stanford) the left IJ vein is the preferred site of cannulation, leaving the right IJ unscarred for repeated endomyocardial biopsies of the transplanted heart.

TEE

TEE is used to optimize volume status (LV + RV size), inotropic agents (LV + RV contractility), vasodilators, and chronotropic agents.

(Print pagebreak 460)

Postoperative

Complications

Oliguria
Pulmonary edema
RV dysfunction

Diuresis may be induced with mannitol and furosemide.
Given the lack of lymphatic drainage in the transplanted lung, pulmonary edema may occur. Diuresis and restriction of iv fluid may be required.
RV failure may occur in patients with pulmonary HTN and high RV afterload (see pulmonary HTN Rx, below).
Pulmonary HTN
Rejection
Infection
Drug side effects:

- Cyclosporine: HTN, nephrotoxicity,

Maneuvers which exacerbate pulmonary HTN should be avoided. These include hypoxia, hypercarbia, acidosis, and extremes of lung volume. NO can be used to treat pulmonary HTN (0.1–100 parts per million inspired concentration); however, it must be used with caution in patients with severe heart failure. Efforts to treat pulmonary HTN with vasodilator therapy may be complicated by impaired V/Q matching with hypoxemia and by systemic hypotension, producing poor right coronary perfusion and RV ischemia. Inotropic support of the RV may be necessary. Isoproterenol is attractive because it combines inotropy, pulmonary vasodilation, and chronotropy.
Monitor rejection Sx with

	hepatotoxicity • Corticosteroids: glucose intolerance, HTN, obesity, hyperlipidemia, aseptic necrosis of hip, bowel perforation, infection • Azathioprine: anemia, thrombocytopenia, leukopenia, hepatotoxicity	transvenous endomyocardial biopsy and transbronchial biopsy. Cyclosporine nephrotoxicity occurs in most patients. A functional toxicity with reduced GFR occurs at low dose and is reversible. Tubular toxicity with morphologic changes occurs at high doses and generally is clinically unimportant and reversible. The most serious damage is vascular interstitial toxicity, which occurs over months at high doses and is not reversible.
Pain management	PCA (see p. C-3).	

(Print pagebreak 461)

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Anesthetic Considerations for Lung Transplantation

Preoperative

The patient presenting for lung transplantation typically has end-stage pulmonary fibrosis or emphysema, although other diseases, such as pulmonary HTN, also may be treated by single-lung transplantation. Double-lung *(Print pagebreak 462)* transplantation can be used to treat cystic fibrosis and bronchiectasis. The progression of the disease is usually well documented; however, Hx of recent exacerbation of symptoms should be sought.

Respiratory	Assess the patient's ability to undergo OLV by review of the V/Q scan. If little perfusion of the nonoperative lung is present, anticipate the need for CPB. The extent of the restrictive lung disease and diffusion abnormality must be assessed preop. For example, room-air PaO_2< 45 mmHg predicts the need for CPB. **Tests:** PFT; V/Q scan; ABG
Airway	Patients with severe pulmonary HTN (80/50 mmHg) have enlarged pulmonary arteries. Vocal cord dysfunction (Sx: hoarseness, inability to phonate “e”) may occur when the left recurrent laryngeal nerve is stretched by an enlarged PA, making these patients at increased risk for pulmonary aspiration; therefore, appropriate precautions to avoid aspiration should be taken (see Induction, below).
Cardiovascular	Evidence of RV dysfunction with tricuspid regurgitation should be sought by physical exam, ECHO, and cardiac catheterization. RV ejection fraction (EF) may be estimated with radionuclide ventriculography (normal EF = > 50%). Pulmonary HTN is considered to be severe and may produce RV failure when pressure is > 2/3 of systemic arterial pressure. Note response to specific vasodilators recorded during catheterization. **Tests:** Preview cardiac catheterization data; ECG; mean PAP > 40 mmHg and PVR > 5 mmHg/min/L may predict the need for partial CPB.
Neurological	R→L intracardiac shunting may be present in patients with pulmonary HTN, and Hx of embolic episodes should be sought. Extra care should be used to avoid injection of even small quantities of intravenous air.
Musculoskeletal	Chronic cachexia precludes the procedure.
Hematologic	Polycythemia 2° chronic hypoxemia is common. Autologous blood is collected as CPB is initiated. **Tests:** Hct; coagulation studies require special blood tubes to correct for low plasma volume in patients with severe polycythemia.
Laboratory	Other tests as indicated from H&P.
Premedication	Patients awaiting lung transplantation are generally well informed about the planned perioperative course. These patients respond well to the reassurance of the preop visit, and pharmacologic premedication usually is not necessary. O_2therapy, with the usual home O_2regimen, should commence prior to transport to the OR. Patient may be at ↑ risk for pulmonary aspiration of gastric contents because of the unscheduled nature of the surgery, the use of oral cyclosporin immediately before surgery, and the presence of recurrent laryngeal nerve damage. Ranitidine (50 mg) and metoclopramide (10–20 mg) may be administered iv before surgery.

Intraoperative

Anesthetic technique: GETA. Typically, OLV through a DLT is required for single-lung transplants. Consider ETT/BB in cystic fibrosis patients with tenacious sputum. Infection is a much feared complication in the immunosuppressed transplant patient; thus, the aseptic technique is important. Aseptic technique is used in inserting and securing all vascular catheters.

Induction	An arterial line for BP and blood gas monitoring should be inserted, using liberal amounts of local anesthetics before induction. There are rare exceptions to this rule, but the presence of real-time BP monitoring can be critical during induction. Typically, fentanyl 5–10 mcg/kg (incremental doses) after invasive monitors placed, ± etomidate 0.1–0.2 mg/kg when rapid control of the airway is desirable; vecuronium 0.15 mg/kg or pancuronium 0.1 mg/kg (avoid succinylcholine 2° ↓ HR); midazolam 0.1 mg/kg or scopolamine 0.005 mg/kg for amnesia. Cricoid pressure must be used when the patient is at risk for aspiration because of the unscheduled nature of the surgery, use of preop oral cyclosporin, and possible vocal cord dysfunction associated with stretch injury of the recurrent laryngeal nerve. Avoid further increases in PVR by guarding against hypoxemia, acidosis, hypercarbia, light anesthesia, and extremes of lung volume.
Maintenance	Typically, narcotic/O_2/air/± isoflurane (in absence of hypoxemia and right heart failure). Typical total anesthetic doses for the entire intraop course: fentanyl 20–50 mcg/kg or sufentanil 10–15 mcg/kg, midazolam 0.2 mg/kg, vecuronium 0.3 mg/kg, or pancuronium 0.2 mg/kg, scopolamine 0.07 mg/kg.
Emergence	Before closure of the chest, lungs are inflated to 35 cmH_2O to reinflate atelectatic areas and check adequacy of bronchial closure. At the conclusion of surgery, both lumens of the DLT should be suctioned and the tube replaced with a single-lumen 8.0 mm ETT. The patient is transported to the ICU intubated and ventilated.
Blood and fluid requirements	IV: 14 or 16 ga × 1–2 NS/LR @ 4 mL/kg/h
Monitoring	Standard monitors (see p. B-1). Arterial line PA catheter Urinary catheter with thermistor TEE
OLV	DLT: 41 Fr (men); 39 Fr (women) Use large TV (12–15 mL/kg) during regular and OLV. Frequent suctioning

Patients with intracardiac defects are at increased risk for cerebral embolic events; take care to remove all air bubbles from intravascular lines.

ECG leads should be covered with tape to insure that electrical contact is not degraded by prep solution or blood. Mixed venous oximetry may be desirable during OLV, and with partial CPB. Be careful of air embolization during catheter insertion. Patients who are profoundly dyspneic (→ high negative intrathoracic pressure) are at high risk for VAE; consider inserting the catheter after GA and IPPV have been instituted. Oxygenation must be watched closely. Blood gases are sampled at 10-min intervals.

RV EF measurement may be useful for evaluating RV function (normal EF = 0.5–0.7).

A DLT is inserted in the left mainstem bronchus to permit surgical access. FOB is used to verify proper tube placement. Positioning of the bronchial cuff in the proximal left mainstem bronchus does not interfere with surgical access to the bronchus. The position of the DLT should be verified after the patient is moved to the lateral position. Finally, verify ventilation and proper functioning of the tube, then eliminate volatile anesthetic or vasodilators, which may blunt hypoxic pulmonary vasoconstriction. Apply O_2 with CPAP at 5

		cmH_2O to the nondependent lung. Further adjustment of CPAP may enhance oxygenation. The nondependent lung may be reinflated with O_2 if necessary, to achieve adequate oxygenation. If adequate oxygenation cannot be achieved, CPB should be initiated. Frequent suctioning is necessary in patients with tenacious secretions.
PA clamping	Improve V/Q mismatch. Improve oxygenation. PAP ↑↑→ RV failure	Clamping of the PA will improve V/Q mismatch and oxygenation; however, severe pulmonary HTN and RV failure may develop. Vasodilators, such as NTG (0.2–2 mcg/kg/min), SNP (0.2–10 mcg/kg/min), PGE_1 (20–100 ng/kg/min) or inhaled NO (20–40 ppm) should be used to treat pulmonary HTN and ↓ RV afterload; however, care must be taken to avoid systemic hypotension. Inotropic support for the RV may be necessary (dopamine [2–10 mcg/kg/min] or epinephrine [20–100 ng/kg/min]). The right atrial pressure should be monitored for evidence of tricuspid regurgitation associated with RV dilation.
PA unclamping	PIP: 20–25 cmH_2O O_2sat: 95–100% PEEP: 5–10 mmHg	Temporary unclamping of the PA may be necessary to allow further pharmacologic therapy. If RV failure cannot be controlled pharmacologically, CPB should be initiated. The PA should not be unclamped until ventilation is possible to the transplanted lung. Perfusion without oxygenation of the transplanted lung would produce profound shunt and hypoxemia. TV should be adjusted to eliminate atelectasis and to achieve a PIP of 20–25 cmH_2O with the chest open. The FiO_2 (0.35) is limited in the hope of curtailing free radical injury. PEEP may be used to enhance oxygenation.
Positioning	For single-lung: • Supine to lateral decubitus • Axillary roll • Airplane splint • Avoid arm hyperextension (> 90°). For double-lung: • Supine with arms above head for bilateral subcostal incision and pad pressure points. eyes.	Verify correct position of DLT or BB after moving patient to the lateral position. Difficult access to airway after patient positioned. ***NB:** potential for kinking of iv and arterial lines

(Print pagebreak 463)(Print pagebreak 464)

Postoperative

Complications	Pulmonary edema Infection: bacterial, viral, fungal, or protozoan Side effects of immunosuppressive agents: • Corticosteroids: HTN, osteoporosis, glucose intolerance, hyperlipidemia • Azathioprine: anemia, thrombocytopenia, leukopenia	Given the lack of lymphatic drainage in the transplanted lung, pulmonary edema may occur. Diuresis and restriction of iv fluid may be required. Mannitol and furosemide can be used to induce diuresis. Immunosuppression drugs typically include: tacrolimus, myophenolate mofetil, and corticosteroids. Early induction therapy with a cytolytic agent (e.g. antithymocyte globulin) may be used.
Pain management	Epidural narcotics (see p. C-2) Parenteral narcotics (see p. C-2)	Postop analgesia may be provided by infusion of narcotics through an epidural catheter. If CPB is used, the insertion of the epidural catheter should be delayed until normal coagulation function is documented in the ICU.

(Print pagebreak 465)

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