UCSF Anesthesia Resident Pearls
Lung Transplant

Background

Over the past few decades, lung transplantation has become a viable treatment option for patients with a variety of end stage lung diseases. The first human lung transplant was performed in 1963; the recipient survived 18 days and ultimately succumbed to renal failure and malnutrition.

The number of lung transplants performed worldwide have increased dramatically since 1985, however further increases in these numbers are limited by organ availability. Since May 2005, the priority on the lung transplant waiting list has been based on a Lung Allocation Score (LAS) that was developed to address high waiting list mortality. To meet the challenge of increasing organ availability and improving patient outcomes, a portable lung perfusion system, OCS^{TM} Lung, has been developed. As of 2019, there have been several clinical trials to evaluate the safety and efficacy of the ex vivo lung preservation system—the INSPIRE trial, the VIENNA trial and the EXPAND trial. The first two showed that such system has comparable short-term clinical outcomes, and the EXPAND trial, which UCSF was a participating site, showed that the technology holds promise in expanding the pool of potential donor organs.

According to the 2013 Registry report, the median survival for all adult recipients is 5.6 years. While any patient without history or inclination for chronic pulmonary infection (i.e. cystic fibrosis) or idiopathic pulmonary hypertension can benefit from single lung transplant, bilateral lung recipients appear to have a better median survival (6.9 versus 4.6 years, respectively). Of note, UCSF lung transplant program, which does mostly bilateral transplants, has the highest one-year survival in the nation (96% vs. national average of 84%) between July 2010 and December 2012.

Primary graft dysfunction (PGD), a form of ARDS/diffuse alveolar damage, which occurs in the early hours to days after transplant is the leading cause of death in the first 30 days (~25% of deaths). Chronic allograft rejection or chronic graft dysfunction, which manifests as bronchiolitis obliterans syndrome (BOS), is the leading cause of mortality after the first year (~40% of deaths). This remains the primary obstacle to better long-term outcomes after lung transplantation.

Recipient Selection

Causes of End Stage Pulmonary Diseases

- Obstructive etiologies: COPD, alpha-1 antitrypsin deficiency, etc.
- Restrictive etiologies: idiopathic pulmonary fibrosis, etc.
- Idiopathic pulmonary artery hypertension
- Cystic fibrosis and bronchiectasis
- Pulmonary manifestation of systemic diseases such as sarcoidosis, SLE, etc.
- Congenital heart disease

Indications: Lung transplantation should be considered in patients with advanced lung disease whose clinical status has progressively declined despite maximal medical or surgical therapy. Candidates are usually symptomatic during activities of daily living and have a limited expected survival over the next two years. Other considerations include (developed by American Thoracic Society and the International Society of Heart and Lung Transplantation)

- Age appropriate (used to be ≤ 65 year old, but now trending older)
- Acceptable nutritional status; usually 80-120% of IBW and BMI ≤ 30 to 35 (variable)
- Satisfactory psychosocial profile and support system
- Adequate financial coverage for the procedure and postoperative care

Contraindications

- Non-curable systemic infection (chronic active hepatitis B, hepatitis C, and HIV)
- Malignancy in the last two years (except cutaneous SCC or BCC)
- Significant dysfunction of other vital organs (may consider concurrent transplant of a second organ)
- Significant CAD or heart failure, include congenital cardiomyopathy (may consider combined heart-lung transplant)
- Active tobacco smoking
- Significant psychosocial issues: absence of reliable social support system, ongoing history of substance abuse, history of medical non-compliance, or inability to comply with complex medical regimen and follow up care.
- Advanced age (> 65 years old, but a relative CI)
- Significant chest wall/spinal deformity (relative CI)

Day of Surgery Pre-op Assessment

- Review of prior anesthetic experience/record
- Past medical and surgical history (especially previous thoracic surgery).
- Recent deteriorations in functional status/increase in oxygen or iNO requirement (including ECLS). This is important in IPF patients as it is associated with worsening pulmonary hypertension and these patients classically have crescendo symptoms in the final stages of their disease. Prior echo/PA pressure estimates are often misleading/out-of-date in this setting.
- Labs (hematology including anti-coagulation/anti-platelet therapy, renal and hepatic function)
- Cardiopulmonary studies – ECG, echocardiography, stress test, right and/or left heart catheterization, CXR, PFT, ventilation/perfusion scan
- Allergies
- Medications: especially pulmonary vasodilators such as PDE inhibitors, endothelin receptor inhibitors, and IV epoprostenol ("Flolan"), which should not be missed. "Flolan" is a continuous infusion through a central catheter. Always confirm the infusion rate (fixed) and daily refill schedule with the patient and the nurse. Only 10ICC nurse and nurses on 10 Moffitt have been trained to care for Flolan patients. When in doubt, 10ICC charge nurse can put you in touch with a Flolan nurse. **Backup pump and backup cartridge (from pharmacy, store on ice/fridge) will come with the patient.**
- NPO status (may need RSI if full stomach or significant reflux)

Preoperative Preparation

Machine check, include **iNO** setup with modified circuit with humidifier, injection and sampling lines.

Airway Equipment

- **Left sided DLT**. General recommendation: Men > 6 ft tall: 39 Fr, ≤ 6 ft tall: 37 Fr, women: 35 or 37 Fr.
- Fiberoptic equipment with DLT exchange catheter
- Glidescope
- CPAP setup (for during one lung ventilation, OLV)

Monitors

- Pulse oximeter x2
- Triple transducer: Arterial, CVP, femoral artery
- Cerebral Oximeter x2
- EEG entropy monitor
- TEE
- Temperature

Immunosuppression

- *Basiliximab (Simulect) 20 mg – give slowly as IV infusion over 20 minutes
- *mycophenolate mofetil (Cellcept) 1000 mg – give over 2 hours
- Methylprednisolone (Solu-medrol)– need 500 mg per each graft lung given prior to reperfusion

Antibiotics

- *Vancomycin 1 g q12h over 30-60 minutes
- Ceftriaxone 1-2 g q12h prior to incision

Anti-fibrinolytics (usually only if going on CPB or ECMO)

- Aminocarpoic acid (10 g bolus over 30 minutes then 2 g/hr infusion), OR
- *Tranexamic acid (30 mg/kg bolus over 30 minutes then 10mg/kg/hr)

Bolus drugs

- Induction agents: midazolam, fentanyl, ±propofol/etomidate, NMBAs
- Calcium chloride (100 mg/ml)
- Vasoconstrictors/inotropes
- Nitroglycerin (20 mcg/ml), Esmolol
- Full dose heparin (300 units/kg for CPB, 70-100 units/kg for ECMO)

Infusions (may not need all, discuss with the attending), usually:

- Norepinephrine (mcg/kg/min)
- Epinephrine (mcg/kg/min)
- *Vasopressin (units/min or units/hr): some evidence to suggest low dose vasopressin may have less vasoconstriction effect on the pulmonary (vs. systemic) circulation.
- Dobutamine (mcg/kg/min)
- *Nitroglycerin (mcg/kg/min)
- *Insulin (units/hr)
- Propofol (mcg/kg/min): for IV anesthesia during ECMO and postoperative transport
- Heparine (units/kg/hr): for anti-coagulation on ECMO

Blood products (have prior to incision)

- PRBC (4 units)
- FFP (4 units)
- Platelet, cryoprecipitate (rarely needed)

***** Denotes items that require ordering from pharmacy

- Additionally albumin (2L)

Pre-induction Access/Preparation

- It may be prudent to have anesthesia transport the patient directly to OR, especially those on 1) iNO, 2) ICU, 3) inotropes, and of course 4) ECMO.
- Ideally, baseline cerebral oximeter reading should be at preop oxygen level.
- At least one reliable PIV
- Radial arterial line, preferably on the RUE. In the setting of peripheral (femoral) ECMO, ABG from the right arm is more representative of lung/graft function due to less mixing with the oxygenated ECMO blood (farthest from the femoral arterial cannula).
- ±CVC (Its need prior to induction usually depends on the severity of one's pulmonary hypertension and RV dysfunction, and the likelihood of significant hemodynamic decompensation during induction)
- Wait for final confirmation of the donor organ from the surgeon
- In the future, with the OCS^{TM} system, the organ viability window may be extended to minimize unnecessary trips to the OR for the potential recipients and optimize OR usage.

Induction

Goal: smooth induction of anesthesia, and expedient securing of airway to avoid hypoxia/hypercapnia which may trigger RV failure and cardiovascular collapse.

Co-morbidities of concern

- Pulmonary hypertension and RV dysfunction.
- Underlying lung pathology: COPD, IPF, restrictive disease
- GERD, potential full stomach, difficult airway
- Other systemic manifestation of the underlying lung disease (such as RA and cervical spinal disease, Scleroderma and CREST syndrome, SLE and renal disease, and steroid side effects)

Typically a **balanced induction** of anesthesia with midazolam/fentanyl/propofol vs. etomidate

- Consider preemptive pressor or inotrope infusion to avoid hypotension and RV failure.
- Systemic hypotension and bradycardia are poorly tolerated in those with pulmonary hypertension.

Airway management

- May not tolerate supine (vs. sitting) position while awake.
- Mask ventilation may
  - Require high pressure, low volume and rapid breath if the patient has restrictive disease, OR
  - Need to avoid excessive pressure and "auto-PEEP" if the patient has COPD and blebs.
- Discuss the need for iNO prior to induction.
- Left sided DLT for the procedure (see above for DLT size).
- Desaturation can occurs quickly and is poorly tolerated.
- **Fiberoptic confirmation** of ETT position.
- Backup equipment/plan in case of difficult intubation with DLT.

Post-induction Access

- ±Additional PIVs
- Introducer (PSI or MAC): weigh the slightly higher risk of vascular complication with left IJ access against the desire to preserve the right IJ for post-transplant VV ECMO using a bi-caval dual lumen cannula ("Avalon") in the setting of severe PGD.
- No PA catheter: Remind the surgeons if they wish to directly measure the PA pressure with a needle.
- Femoral arterial line is usually placed concurrently by the surgeon: back-up blood pressure monitoring and potential emergency ECMO access.

Procedure Summary/Special anesthetic consideration

Position is **Supine, with arms abducted at shoulders and forearms elevated.**

- Check arms frequently especially during repositioning of the OR table.
- Foam head rest without any hard/sharp object underneath.

Anesthesia maintenance

- Volatile inhaled anesthetic of your choice – isoflurane/sevoflurane
- Midazolam ≤ 10 mg total unless with known tolerance
- Fentanyl ≤ 10-20 mcg/kg unless with known opiate tolerance
- NMBD as needed – rocuronium, vecuronium, or cisatracurium

Dissection/Exposure and Ventilator Management. Close communication with surgeons regarding blood pressure, pressor/inotropes, oxygenation and one vs. two lung ventilation is paramount.

- For bilateral transplant, an **anterolateral thoracosternotomy incision** ("clam-shell") is performed.
  - The need for **higher PIP and high FiO2** increases the risk of pneumothorax or broncho-pleural fistula (after chest opening) and further injury to the native lungs. This makes ventilation more difficult and can risk surgical field fire. Fortunately, replacements are on the way.
- **Intermittent OLV** is needed during the dissection. Desaturation is nearly inevitable and SaO2 can drop precipitously. Discuss the strategy to maintain saturation during OLV (FiO2, PEEP, CPAP etc.) with the attending. Surgeons are very amendable to go back on two lung ventilation.
- **Suction** may be necessary if there is chronic infection or thick secretion
- **Bronchus, pulmonary veins and PA on each side are dissected and encircled**.
- **Significant hypotension can occur**, usually associated with high intra-thoracic pressure, manipulation of the lung and compression of the heart or great vessels, especially if there is inadequate preload. Remember these patients are likely hypovolemic due to preop diuresis or NPO. It is common to give 2 L or more of fluid (crystalloid or albumin) prior to the completion of dissection.
- **Pericardium is opened**, and purse-string sutures are placed in preparation for possible cannulation
- Ideally all of this is performed prior to the arrival of donor organ to minimize ischemic time (≤6 hr). The decision for the need of CPB or ECMO is finalized, if not earlier.
- During the waiting for the donor organ to arrive, the surgeon typically performs bilateral **cryoablation of intercostal nerves** for postoperative analgesia. This has largely replaced epidural at UCSF.

Decision on whether to perform the transplantation on ECMO, CPB, or off pump depends on the patient's RV function, severity of pulmonary hypertension (will worsen with PA cross clamp), hemodynamic stability and oxygen saturation during dissection on OLV, and any intra-cardiac repair.

- **The advantages of CPB**:
  - Hemodynamic stability, especially if there is significant RV dysfunction.
  - Transfusion via the reservoir is easy in the setting of hemorrhage.
  - Saturation is easily maintained.
  - The first graft organ can be rested while on CPB. It is still ventilated with low pressure and low FiO2, but without receiving excessive flow and risking become hyperemic and edematous.
  - Allows the opportunity to repair any intra-cardiac shunt or tricuspid regurgitation on CPB.
- **The advantages of doing it off CPB**:
  - Avoid exposure to the CPB circuit, post-CPB coagulopathy and bleeding
  - Avoid instrumentation of aorta and vascular complication
- **The majority of bilateral lung transplant at UCSF are now done with central VA ECMO**
  - It can provide gas exchange and hemodynamic stability similar to CPB, but exposes the recipient to much less heparin.
  - Remember that ventilation is still necessary while on ECMO. Venous drainage may be poor and fluid replacement may be necessary.

Graft implantation (assuming without CPB or ECMO)

- **Cross clamp of PA** (after a total 3000-5000 unit of heparin)
  - May need inotropic support for the RV, i.e. epinephrine, dobutamine, etc.
- **Explant** of the recipient organ
- **Bronchial anastomosis**. Upon its completion and at the surgeon's request, a Valsalva maneuver on the graft lung is performed with the anastomosis under water to detect any leak up to 30 cmH2O.
- **Pulmonary vein anastomosis**
- **PA anastomosis**. It is during this period that the surgeon will request the methylprednisolone 500mg to be given, timed to finish prior to the release of PA and reperfusion of the graft organ.
- In preparation of the reperfusion of the graft organ:
  - Inspection of the ETT lumen to confirm that the bronchial anastomosis is intact and there is no excessive intra-lumen blood.
  - Check frequent ABG as the patient may become progressively acidotic. Respiratory acidosis likely due to underlying disease and OLV. But metabolic acidosis is also possible due to low cardiac output, anemia or the use of vasoconstrictors. Consider treating with sodium bicarbonate (if ventilation permits) or THAM (if renal function adequate) to correct the acidosis prior to reperfusion. Calcium and vasopressor/inotropes on standby.
  - **Start iNO** (if not already in use) 20 ppm, and increase the fresh gas flow to match minute ventilation to deliver correct iNO dose and avoid rebreathing/NO2 buildup.
  - **Start ventilation** after discussing the OLV setting for the graft organ with the surgeon usually FiO2 0.4- 0.6, PEEP 5-7 cmH2O, and tidal volume ~3 mL/kg/lung. Make sure to first recruit the graft lung and eliminate atelectasis.

Graft reperfusion is a critical period of the surgery. PGD can occur quickly with onset of pulmonary edema, which can be severe despite suction and may necessitate initiation of ECMO (if done off ECMO). Also, reperfusion of the lung can release metabolites into the circulation causing acidosis and hypotension.

- The surgeon can use fingers on the PA as a partial clamp to control the reperfusion to some extent.
- Pressors, inotropes, calcium as needed.
- Avoid excessive fluid after donor lung implantation due to concern over edema. The donor lung has no functional lymphatics. However, fluid may be necessary if there is significant base deficit.
- **ABG 5 minutes after reperfusion** (if done off ECMO or CPB).

Repeat on the other side

- Any worsening graft dysfunction (hypoxemia or edema) or other instability, can prompt the (re)initiation of ECMO.
- Short of ECMO or CPB, furosemide can be used to treat the pulmonary edema, remember to dose it according to patient's preoperative diuretic exposure to avoid excessive hypovolemia.
- Rarely, PGD or RV dysfunction is so severe that postop ECMO is necessary.
  - Ideally, the patient can be weaned from central ECMO or CPB first, heparin is reversed and hemostasis achieved before the initiation of ECMO.
  - Central VA: CPB aortic and RA cannula can be switched to an ECMO circuit, OR
  - Peripheral VA: separate V-cannulas are inserted via the femoral vessels
  - VV: RIJ access with Avalon cannula, which will require fluoroscopy and TEE guidance.

Consider **Exchange DLT to SLT** while still on ECMO. Oxygenation and hemodynamics are much more stable. However, OLV would not be possible after exchange, so surgical exploration for hemostasis after ECMO will require intermittent apnea which may be poorly tolerated. Discuss with the surgeons. Tube exchange is usually done under direct or video laryngoscopy over a DLT exchange catheter.

Chest closure. Both lungs will be inspected, and wedge resection may be performed for oversized lungs.

- Frequent ABG to assess graft function.
- Exchange DLT for SLT or tracheostomy tube if not done earlier.
- The surgeons will perform a thorough bronchoscopy (through SLT) to assess the degree of pulmonary edema and PGD, so they can compare it to the post-operative bronchoscopic findings.
    - Often this will improve oxygenation.

Transfusion Goals

Always discuss Hct goal and the need to transfuse with the surgeon. Special consideration is paid to the CMV status of the patient and the donor. All UCSF PRBC units are leuko-reduced which is generally considered to be CMV-negative equivalent. However, for lung transplant patients, **if both the recipient and donor are CMV-negative, specific CMV-negative blood should be transfused.**

Coagulopathy is uncommon here at UCSF after ECMO. High risk patients include those that have preoperative coagulopathy, anticoagulant use, prolonged preoperative ECMO support, and re-transplant. Consider checking platelet counts, fibrinogen, and coagulation labs in these patients, and treat accordingly (platelets, cryoprecipitate, prothrombin complex concentrate, and fibrinogen concentrate). Recombinant factor 7 is rarely used in patients on ECMO as it has a high risk of pump thrombosis.

Post-operative Course

ICU transport

- Intubated (SLT) with ICU ETT holder
- **Respiratory therapist will provide the modified transport ventilator equipped with iNO**
- Low dose propofol is usually used for sedation during transport.
- Check ABG (on stable ventilation setting) prior to leaving the OR.

Those patients that have persistent pain despite cryoablation may have **epidural catheter placed** by the pain team after the correction of any coagulopathy, initiation of epidural analgesia, followed by an extubation trial.

- Evidence of possible PGD, RV dysfunction, or the continuing need for ECMO may delay extubation.
- iNO can be continued after extubation using high flow nasal cannula.

Resources

1. https://ishltregistries.org/registries/slides.asp The International Society for Heart and Lung transplantation

2. Yusen RD,Christie JD, Edwards LB, et al. The Registry of the International Society for Heart and Lung Transplantation: Thirtieth Adult Lung and Heart-Lung Transplant Report—2013;focus theme: age. J Heart Lung Transplant 2013;32:965

3. Gries CJ, Mulligan MS, Edelman JD, et al. Lung allocation score for lung transplantation: impact on disease severity and survival. Chest 2007; 132:1954,

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5. Warnecke G, Van Raemdonck D, Smith MA, et al. Normothermic ex-vivo preservation with the portable Organ Care System Lung device for bilateral lung transplantation (INSPIRE): a randomised, open-label, non-inferiority, phase 3 study. *Lancet Respir Med*. 2018;6(5):357-367.

6. Slama A, Schillab L, Barta M, et al. Standard donor lung procurement with normothermic ex vivo lung perfusion: A prospective randomized clinical trial. *J Heart Lung Transplant*. 2017;36(7):744-753

7. Loor G, Warnecke G, Villavicencio MA, et al. Portable normothermic ex-vivo lung perfusion, ventilation, and functional assessment with the Organ Care System on donor lung use for transplantation from extended-criteria donors (EXPAND): a single-arm, pivotal trial. *Lancet Respir Med*. 2019;7(11):975-984.

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