Anesthesia Guidelines for Lung Transplants
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Revised 7/25/2019

Introduction:

- When a potential lung donor has been identified, the transplant coordinator will notify the attending cardiac anesthesiologist on call. The senior anesthesia resident on call and the TEE resident should be notified. The recipient patient will be admitted to the CTICU for preoperative preparation. All relevant medical information regarding the recipient should be readily available in the CTICU.
- Most patients presenting for single or double lung transplantation will typically fall into one of the following categories: COPD, pulmonary fibrosis, alpha-1 antitrypsin deficiency, cystic fibrosis, or primary pulmonary hypertension. Preoperatively, important aspects of the patient history include oxygen dependency, history of bronchospastic disease and use of bronchodilators, and positional effects on dyspnea. Sedation should be administered judiciously and with the patient monitored at all times.

Preop Preparation:

- Patient will first be taken to CTICU, for evaluation, blood work and preliminary line placement.
- A peripheral IV and arterial line are placed in the patient in the CTICU. IJ introducer (usually a MAC introducer) and PA line placement may be either in the CTICU preop or in the OR.
- Type and Cross: 6U PRBC's (CMV negative, leukocyte reduced). If the patient is on Coumadin, consult with the Anesthesia attending regarding setting up FFP versus using Kcentra.
- Preop Meds: (Given in CTICU prior to going to OR)
    - Heparin 5000 units sq. If patient already on coumadin, no heparin sq required.
    - Tacrolimus 0.1 mg/kg po before OR
    - Consider giving a dose of Reglan and Pepcid if the patient is not NPO.

- Patient will be brought to the OR when donor lung/lungs are accepted.
- Once the patient is ready in the OR, the patient will be induced at surgeon's request after there is notification from the procurement team of estimated time of arrival.

OR Setup:

- Generally will be done in either room 18 or 19.
- The set-up is similar to any cardiac case with the addition of double lumen endotracheal tubes. Have 35, 37, and 39 Fr left DLETTs in room.
- Ask the circulating RN to bring an OR bronchoscopy cart into the room with adult and pediatric scopes. Should be set up on left side of patient, adjacent to the TEE machine. Move the OR bed distally to make room for this equipment.

- An ICU ventilator should be set up in the room. Contact respiratory therapy to set it up. Position behind Anesthesia machine monitor
- CCO PA catheter.
- TEE machine and probe.
- For single lung transplants, over the body forced air warming is used. For double lung transplants, underbody water circulating pad or forced air warming system will be used.
- IV and transducer setups - 2 for peripheral lines - at least one of these should be on a hot line with blood tubing; 2 lines for MAC introducer, VIP line on mini dripper; triple set for A-line and PA catheter.
- Have Level-One or Belmont available and set up. Discuss with attending.
- Cerebral oximetry.

Drips & Drugs:

- Available Drips: Have epi, vasopressin, and norepi, and insulin spiked. Have phenylephrine, milrinone, and NTG in the room. Also, have Amicar or TXA spiked if CPB planned.
- Will most likely be doing TIVA during at least part of the case. Have propofol drip set up.
- Inhaled epoprostenol will frequently be used, to help reduce PA pressures. Notify the CTICU respiratory therapist to set it up. Will be attached to ICU ventilator.
- Antibiotic:
    - Check with surgeon/ transplant pulmonary docs regarding antibiotic choice. The below antibiotics will be the default antibiotics, but these may be adjusted depending on donor and recipient cultures.
    - Piperacillin/Tazobactam 3.375 gm IV and q 4 hours and Vancomycin 1 gram IV and q 12 hours.
    - If recipient is allergic to penicillin then administer Clindamycin 900 mg and Tobramycin 80 mg IV – but this should be checked with pulmonologists.

Line placement:

- May be done either in the CTICU or in the OR or some combination.
- Arterial line: Radial artery site preferred. The arms will be bent at the elbow for both for single and double lung transplants, potentially making the brachial site problematic. For double lung tx, an alternative is femoral arterial line – you will not have easy access to radial art line site if it becomes problematic.

- Peripheral IVs: Two large bore peripheral lines should be placed. Avoid antecubital IVs since arms will be bent during positioning.
- Central lines: MAC introducer and CCO PA catheter. For single lungs, may be better to place on side that is being operated on. Place PA catheter balloon only 1-2 cm past pulmonic valve – so won't have to be pulled back later.

Induction and Intubation:

- Patient may not be NPO, so consider need for rapid sequence induction and intubation.
- Most anesthesiologists will induce with etomidate or propofol, midazolam, fentanyl. Muscle relaxation is typically with rocuronium (or succinylcholine), followed by vecuronium. Be very careful with induction because many patients will have pulmonary hypertension, and will be prone to right heart decompensation. Induce more like a "heart" than a typical thoracic resection.
- Most of these patients will not tolerate laying flat so anesthetic induction may have to be initiated with the patient in a head-up position.
- The patient is intubated with a Left 2 lumen ETT. The exceptions are the cystic fibrosis patients, who may be first intubated with a single lumen ETT, suctioned and bronchoscoped clean prior to DL tube placement – discuss with surgeon. Typically will use 37 Fr in females and 39 Fr in men, but may vary with patient size.
- Patients with primary pulmonary hypertension are especially prone to crashing on induction. In these patients, it is best to place central lines prior to induction. It may be wise to start inotropes prior to induction, and have surgeon and pump in the room ready to go.

Ventilation Issues:

- Obstructive disease (smoking induced emphysema, alpha-1 antitrypsin deficiency): Issues include air trapping, carbon dioxide retention, and bronchospasm. Use pressure controlled ventilation with I:E ratio 1:3-4. Avoid PEEP.
- Restrictive disease (interstitial fibrosis): Issues include loss of lung elasticity and compliance - thus may need high airway pressures (40s) to generate adequate tidal volumes. Use reduced tidal volumes (6ml/kg) with I:E 1:1-2. PEEP OK to use.
- Cystic fibrosis or bronchiectasis patients have thick copious secretions, and will require frequent suctioning.
- Maintaining baseline hypercarbia is a good goal. However, permissive hypercapnea may be necessary to avoid high airway pressure or air trapping.
- There is frequently a large gradient between arterial and end-tidal CO2 levels.

Positioning:

- Single lung TX: lateral thoracotomy. Hips will be turned to expose a groin for cannulation if needed.
- Double lung transplant: supine, clamshell incision. Arms up in the air, bent at the elbow suspended from ether screen or Monster.

Temperature Management:

- Keep patient warm!
- Bair hugger, warm room, warm fluids.

Fluid Management:

- Maintain on the dry side. (Transplanted lung is prone to pulmonary edema due to lack of lymphatic drainage, re-expansion, and reperfusion injury).
- There is debate about minimally acceptable Hb. Some surgeons prefer Hb > 10 g/dl.

Differential Diagnosis of Hemodynamic Instability:

- COPD induced air-trapping. Consider temporarily disconnecting patient from ventilator to rule out air trapping as a cause.
- RV dysfunction - CVP rises. TEE will show RV dilatation and worsening tricuspid regurgitation.
- Rupture of a bleb – tension pneumothorax. Will see acute decrease in O2 saturation accompanied by increased airway pressures, and hemodynamic instability. Differential diagnosis is air trapping versus mal-positioning of double lumen tube. Transient cessation of ventilation and immediate fiberoptic bronchoscopy is used to rule these out. Needle thoracostomy or surgeon dissection across the mediastinum will be required to mange this situation.

Lung Isolation:

- When one lung ventilation is initiated, beware increases in airway pressure to ventilated lung. If in volume control mode, adjust tidal volume down to maintain reasonable airway pressures to reduce risk of air trapping or pneumothorax. If in pressure control mode, monitor the adequacy of tidal volumes.
- Maintain oxygenation by using 100% FIO2, and using PEEP 5 cm on the ventilated lung. CPAP 5 cm on the non-ventilated lung may also be helpful, but may interfere with surgical exposure.

Preparation for PA clamp:

- Assuming no CPB, heparin 5000 units IV prior to PA cross clamp.
- If patient doesn't oxygenate adequately during 1LV, or develops pulmonary HTN and RV failure with PA clamp, may need to go on CPB or ECMO.
- If PA catheter has been floated well into the PA, may need to pull it back. You may be able to visualize PA catheter position with TEE. Have surgeon palpate for PA catheter prior to clamp. Also, PA catheter would probably occlude during test clamping.
- Sometimes, a test clamping is done to observe for signs of right heart failure and decreasing cardiac output. If this is significant, CPB or ECMO is indicated.

Management of Pulmonary HTN and Right Heart Failure:

- When a pulmonary artery is clamped, the sudden increase in pulmonary vascular resistance can precipitate right heart failure. An increasing CVP and TEE evidence of dilated RV or worsening tricuspid regurgitation are signs of right heart failure.
- RV function is optimized by:
    - Optimizing ventilation & oxygenation.
    - Adding epi to support RV function. Sometimes used in combination with dobutamine. Low dose milrinone may also be helpful, but beware dropping perfusion pressure.
    - Maintaining RV perfusion pressure – vasopressin and/or norepi. (Vasopressin has less pulmonary vasoconstricting effect.)
    - Inhaled epoprostenol can be utilized.
- If patient doesn't oxygenate adequately during 1LV, or develops pulmonary HTN and RV failure with PA clamp, may need to go on CPB or ECMO.

ECMO/Cardiopulmonary Bypass:

- Lung transplant is usually done without ECMO/CPB, however certain patients may require it:
    - Severe pulmonary hypertension (>2/3 systemic pressure).
    - Hemodynamically unstable.
    - Inadequate oxygenation with one lung ventilation.
- If CPB is used, tendency towards more bleeding and coagulopathy.
- Surgeons can alternatively use VA ECMO – with central cannulation or femoral venous and axillary artery cannulation. This requires less heparinization, and may have less coagulopathy associated with it. At the end of transplant, ECMO can be weaned off and the patient can be decannulated, or it can be maintained into the postop ICU course (depending on the patient and degree of reperfusion injury).

ECMO Management Considerations:

- The ECMO flows are not equivalent to complete CPB. The patient is allowed to eject - so this is equivalent to partial bypass. Ventilation is maintained during ECMO, with a low FIO2 (40%), in preparation for reperfusion.

- ECMO oxygen settings should be turned down prior to reperfusion (30-40%?) – with the goal of ***not*** reperfusing with hyper oxygenated blood.
- There is no reservoir in the ECMO circuit, so blood loss must be replaced by the anesthesia team to maintain the patient euvolemic. The volume status is assessed by monitoring CVP and PA pressures, and size of right ventricle on TEE exam. If the patient is not ejecting, then you are hypovolemic.
- There is no vaporizer on the ECMO circuit. Switch to TIVA. (If you are still ventilating with the anesthesia machine, you can use your vaporizer during ECMO, but it is unclear how much inhalation agent the patient will actually be getting since pulmonary blood flow is diminished by ECMO, PA cross clamps, volume status etc.)
- If the patient is successfully weaned off ECMO and the patient is decannulated, the perfusionists will process the ECMO circuit blood through the cell saver and return some of this volume to us.

Preparation for PA clamp release:

- Solumedrol 1000 mg 10-15 minutes before PA reperfusion.

PA Clamp release:

- May see mild, moderate or severe hypotension at reperfusion. Typically is due to vasodilation (vasoactive substances being flushed out of lung?). Vasoconstrict as needed.

Ventilation of New Lung:

- Prior to unclamping pulmonary artery, switch ventilation of old lung to ICU vent and start TIVA.
- Prior to ventilation, perform bronchoscopy to show suture lines to surgeons, and to clean out secretions.
- The pulmonary artery clamp is slowly released over a ten minute period, which limits initial blood flow to the vascular bed of the graft, and may help reduce primary graft dysfunction. To reduce lung reperfusion injury, initial ventilation to the graft should be with a low FiO2 (<30%), TV 3 ml/kg, low peak inspiratory pressures of 15-20 cmH2O and PEEP 10 cmH2O. The respiratory rate is initially set to 15 breaths per minute. (RR will also depend on whether the patient is on ECMO at the same time). Ventilate the new lung with the anesthesia machine (so that you can hand bag if needed), while maintaining ventilation with the other lung on the ICU ventilator. If both lungs are being replaced, this process will be repeated on the other side.
- Once the pulmonary artery clamp is fully released, ventilation settings need to be adjusted to ensure adequate minute ventilation and CO2 removal, and the FiO2 titrated to a safe level of oxygen saturation. Goals are:
    - pH >7.25 with mild permissive hypercapnia acceptable
    - Minimal FiO_2 to maintain $SpO_2 \geq 92\%$
    - PIP<35cm H_2O and Pplateau <25cm H_2O
    - Maintain a PaO_2:FiO_2 ratio >200

- If both lungs have been replaced, can switch both lungs to ICU ventilator with starting setting of 6 ml/kg, 40% FIO2, PEEP 10, rate 15-20. If only one lung replaced, may be better to ventilate each lung independently during the early time after transplant. Use 3ml/kg for each lung.
- Can use either volume control or pressure control. If using PCV:
    - Mode: pressure control (PCV)
    - Set driving pressure to 25 initially with a goal of titrating to target V_T 6 mL/kg *Donor* IBW. (With PCV, PIP equals Pplateau.) (Assuming ventilating both lungs.)
    - FiO_2: 0.3-0.5 weaning to FiO_2 0.3 as tolerated as soon as possible
    - Rate: 12-16
    - PEEP: 10
    - I:E : 1:1
- With single lung transplants the capnograph will often show a biphasic waveform, with the first peak representing exhaled gas from the transplanted lung (with presumably normal compliance and V/Q ratio), and the second peak coming from the native diseased lung (typically representative of V/Q mismatch and compliance differences).

Acid Base/Electrolyte Issues:

- You will likely see some lactic acidosis like we see with heart transplants. However, since many of these patients are CO2 retainers and have high baseline Bicarb levels, it may be less of an issue.
- Glucose climbed will climb, secondary to steroids and inotropes. Insulin drip will be required. Due to insulin and beta agonist cardiac support, KCL supplementation will generally be needed.

Post Protamine Basiliximab:

- Basiliximab will be used in selected patients – should be ordered preop by the transplant team and come to the OR with the patient.
- The dose for adults and children weighing over 35 kg is 20 mg, infused intravenously over 20 to 30 minutes.
- Is generally well-tolerated and does not cause the cytokine release syndrome sometimes seen with its cousins. However, there are rare reports of severe, noncardiogenic pulmonary edema temporally related to the use of basiliximab induction therapy in renal transplant recipients.
- It is used as an adjunct to tacrolimus. Apparently, tacrolimus has significant renal toxicity, so it allows for a reduction in tacrolimus dosing to help decrease this risk.
- Timing: Dose should be given post reperfusion and protamine administration once bleeding is under control. If bleeding is not controlled, delay and may defer first dose to ICU team. (The concern is that inadequate blood levels may be maintained if there is ongoing bleeding and blood replacement).

Dealing With Inadequate Ventilation/Oxygenation Post Transplant:

- If O2 sat < 93%, titrate PEEP to optimize compliance/recruitment:

    - ↑ PEEP by 2 cm H2O keeping DP and PIP constant, stabilize for 6 breaths
        - If exhaled VT ↑, adjust PIP to maintain 6 mL/kg. If SaO2 still < 92%, repeat above steps until PEEP =16.
        - If exhaled VT ↓ s/p incremental 2cm ↑ PEEP, resume previous PEEP and increase FiO2.
- If SaO2 <92% with PEEP ≥ 16 and FiO2 ≥ 0.8, initiate nitric oxide. Other options are independent lung ventilation (see next section), and ECMO.
- Patients with severe COPD have increased lung compliance. The transplanted lung may have decreased compliance depending on the severity of reperfusion injury. In this scenario, more of the tidal volume goes to the non-transplanted lung, and less tidal volume goes to the new lung. If this compliance mismatch leads to hyperinflation and hemodynamic instability, the treatment is to ventilate each lung independently. The donor lung is ventilated as described above, and the native lung is ventilated with low tidal volumes 2-3 ml/kg, rate 2-4/min, and no PEEP.

Potential Surgical Complications:

- Pulmonary venous obstruction: presents as acute persistent pulmonary edema of the transplanted lung. TEE shows narrowed pulmonary venous orifice with turbulent high velocity flow and loss of normal phasic waveform.
- PA anastomotic obstruction: Suspected if PA pressures fails to decrease after reperfusion of the lung graft. The right PA may be able to be visualized with TEE and dopplered, while the left is more difficult to see. If suspected, the surgeon can check pressure gradient by inserting transduced needles on each side of the anastomosis. Alternatively, if the PA catheter is in that side, it can be advanced across the anastomosis to look for a step down in pressure.

End of Case:

- Change to single lumen tube, unless you have a COPD patient that is requiring 2 ventilators. If using tube change, be careful not to pass beyond end of ET tube.
- Bronchoscopy is done to clear secretions, check anastomosis.
- Plan to keep patient sedated on propofol.

Extubation:

- After overnight ventilation, the patients CXR and oxygenation will be assessed.
- Patients may be extubated as soon as 6-12 hrs postop, but more frequently days postop.

Postop Problems:

- Reperfusion injury to new lung - begins immediately, and may take several days to resolve. This typically manifests as pulmonary edema, pulmonary hypertension, hypoxemia, and decreased lung compliance. CXR shows pulmonary edema of new lung. Reperfusion injury is more commonly seen in the postoperative period. Is treated with PEEP. In the worst case scenario, ECMO may become necessary.

- Rejection peaks 3-5 days postop. CXR shows unilateral pulmonary edema. Treated with steroids.
- Pneumonia - can occur if transplanted lung colonized or infected prior to transplant.