Pulmonary Thromboendarterectomy Guidelines

Pulmonary Thromboendarterectomy (PTE) is the gold standard treatment for chronic thromboembolic pulmonary hypertension (CTEPH) and includes bilateral endarterectomies of the pulmonary arteries to relieve obstruction, decrease pulmonary hypertension, improve blood flow through the pulmonary arteries, and improve right heart dysfunction.

I. Surgical Considerations
   General Considerations:
   - Chronic thromboembolic pulmonary hypertension (CTEPH) represents secondary, WHO class IV PH, and is defined as PH in the presence of an organized chronic thrombus within the pulmonary vascular bed that persists at least 3 months after the onset of anticoagulant therapy. While the thrombus resolves, an inflammatory infiltrative process results in intimal thickening and obstruction. Pulmonary hypertension is a result of obstructed perfusion beds and secondary vasculopathy in the perfused beds as a result of the elevated flow and wall stress. The disease is progressive, ultimately resulting in right heart failure as pulmonary vascular resistance remains elevated. While acute pulmonary embolism (PE) is relatively common with an incidence of 1 in 1,000 patients, CTEPH is relatively rare. Best estimates predict CTEPH developing in 3-5% of patients with PE, producing an estimated 3,000-15,000 cases per year. Patients most commonly present with exertional dyspnea. As the disease progresses, patients develop progressively limited exercise tolerance, hypoxia and ultimately worsening symptoms of right heart failure. Atypical chest pain, a nonproductive cough, and episodic hemoptysis are observed less frequently. Because of the insidious onset and large differential for early symptoms, diagnosis is frequently delayed and patients present with advanced symptoms.
   - Pathobiology: The natural history of pulmonary embolism is resolution of emboli and restoration of normal blood flow through the pulmonary arteries. A subset of patients, however, do not undergo normal restoration of blood flow, are left with residual clot adherent to the pulmonary artery, and over time the embolic material progressively becomes organized and forms fibrous obstructions, further inhibiting pulmonary blood flow. Though CTEPH is a late sequel of venous thromboembolism, 40% of patients with CTEPH have no known history of symptomatic pulmonary embolism. Assessment of pathophysiology is a challenge since patients are often diagnosed at a median age of 63 years, and they often have concomitant cardiovascular disease or lung disease.

   We do know that CTEPH is a dual vascular disorder. Stenoses, webs, and occlusions predominate in large and medium-sized pulmonary arteries at the sites of previous pulmonary emboli. A secondary vasculopathy resembling the pulmonary arteriopathy that are encountered in other forms of pulmonary hypertension predominates in low-resistance vessels. Anastomoses between bronchial artery branches and precapillary pulmonary arterioles appear during evolution of the disease. Other acquired vascular connections between bronchial arteries and pulmonary veins may trigger venous remodeling.

   Patients that develop pulmonary embolism (PE) are at risk for CTEPH. These include patients with hyperactive coagulation (e.g., high coagulation factor VIII, combined coagulation defects, dysfibrinogenemias), however, the majority of patients that develop CTEPH do not have an identifiable coagulation defect. Inflammatory conditions such as chronic infection, the presence of anti-phospholipid antibody or lupus anticoagulant increase the risk. Other risk facts for CTEPH include insufficient anticoagulation after PE, non-O blood groups, and misguided thrombus resolution.
   - Indications: CTEPH is an insidious disease that may result in progressive right heart failure and, ultimately, death. At a mean pulmonary arterial pressure above 30 mmHg, 5-year mortality risk is 50%. Above 40 mmHg, 3-year survival is 50%; above 50 mmHg, 2-year survival is only 20%. Early intervention is necessary to reduce pulmonary vascular resistance and avoid the secondary vasculopathy that results
from long-standing hypertension. Although the majority of patients with significant CTEPH will benefit from PTE surgery, the selection of a patient remains quite subjective and is typically based on:

- Extent and level of obstruction with chronic thromboembolic disease based on high-quality imaging via multiple modalities
- Correlation of severity of the pulmonary hypertension versus the degree of obstruction
- Individual patient comorbidities.
- Existence of any technical challenges for the procedure (previous surgeries).
- An assessment of risk/benefit ratio, based on the patient’s individual expectation and acceptance of the risks.
- Importantly, the degree of right heart dysfunction and severity of pulmonary hypertension is not a contraindication for surgery. Severity of PH and worsening preoperative right heart function increases the risk of surgery, but does not preclude an operation. Rather, the surgical accessibility and correctability of the disease is the critical factor in determining whether a patient is an appropriate candidate.

- **Diagnostic Work Up:** The diagnostic evaluation is used to: confirm CTEPH diagnosis, determine surgical accessibility of the disease, and determine the likelihood of symptomatic and hemodynamic benefit from surgical resection.
  - Chest radiographs may suggest pulmonary hypertension, but are neither sensitive nor specific for the diagnosis. Ventilation–perfusion (VQ) scanning is 97% sensitive for detecting CTEPH, making it a valuable screening study. Conventional catheter-based pulmonary angiography retains an important role in establishing the presence and extent of chronic thromboembolic disease and remains the gold standard. On pulmonary arteriogram, characteristic findings of CTEPH include: vascular webs, band-like narrowing, intimal irregularities, and abrupt narrowing of pulmonary arteries. Innovative technologies such as dual-energy computed tomography, dynamic contrast–enhanced magnetic resonance imaging, and optical coherence tomography show promise for contributing diagnostic information and assisting in the preoperative characterization of patients with CTEPH.
  - Echocardiography is important to assess the structural changes in the heart and assess for the presence of patent foramen ovale (PFO) that, if present, may need closure as part of the procedure. The majority of patients with significant pulmonary hypertension and right ventricular dilation have a significant degree of tricuspid regurgitation. Tricuspid valve repair at the time of PTE is somewhat controversial. At our institution tricuspid repair is generally avoided as the right ventricle undergoes significant postoperative remodeling in the setting of successful PTE and rigid fixation may impair subsequent annular remodeling. It is essential to proceed with right heart catheterization to define how severe is the disease and prepare appropriately during the surgery. It is controversial to consider placement of a temporary inferior vena cava (IVC) filter. However, it is preferred and considered standard at our institution, primarily to provide additional protection in the perioperative period should full anticoagulation be contraindicated for a variety of reasons.

- **Critical Components of PTE:** The key steps of a successful PTE have been laid out by the University of California San Diego (UCSD), who have performed over 3500 operations to date and lead the nation in volume at approximately 200 operations per year. The critical components to a successful PTE are a full, bilateral operation done in the appropriate endarterectomy plane. The operation requires a bloodless field to maintain the correct dissection plane in the distal vessel, thus deep hypothermic circulatory arrest is utilized to avoid any back-bleeding from bronchial collaterals.

**II. Preoperative Considerations:**

- Review the degree of pulmonary hypertension and right heart dysfunction prior to surgery to assess tolerance of anesthesia.
- Review the cause for the hypercoagulable state – states such as cold agglutinin disease or sickle cell disease may need altered intraoperative management due to induction of hypothermic circulatory arrest, making these disease states hypercoagulable.
III. Case Setup

• Set up:
  a. Cardiac drug tray: Standard cardiac drug tray (includes epinephrine and phenylephrine) plus milrinone
  b. Amicar for anti-fibrinolytic (10gm bolus and 1gram/hour infusion)
  c. Fluid warmer with blood tubing set up
  d. Triple transducer setup: A-line, CVP, PA catheter
  e. TEE probe, machine, and probe holder
  f. Ensure current type and screen, order blood: 2U PRBC
  g. Call respiratory therapy on 7W for iNO/Veletri for post-CPB

IV. Monitoring

a. Arterial line (either right or left)
b. LIJ MAC with PA catheter (floated pre-CPB)
c. TEE

V. Intraoperative Considerations

• Prior to induction of anesthesia:
  a. Preoperatively: Evaluate allergies, current medications, cardiopulmonary status and NPO status
  b. If the patient is on intravenous pulmonary vasodilators, ensure these are continuously infusing
  c. Heparin infusion should be continued during the preoperative/early intraoperative period.
  d. Preinduction: place arterial line and large bore peripheral IV placement under local anesthesia. Avoid benzodiazepines or opiates pre-induction to prevent hypoxemia/hypercarbia, unless specifically discussed with attending anesthesiologist.
  e. Place Kimberly Clark warming devices on patient prior to induction of anesthesia

• Anesthetic Considerations: Induction of Anesthesia to Incision
  a. Goals for induction:
     i. Avoidance of myocardial depression (especially right heart)
     ii. Avoidance of hypoxemia and/or hypercarbia leading to worsening of pulmonary hypertension and right heart dysfunction
  b. Airway:
     i. Single lumen endotracheal tube
     ii. Consider availability of video laryngoscope in case of difficult airway.
  c. Anesthetic maintenance: Balanced technique using opiates, volatile anesthetics and neuromuscular blockade.
  d. Venous access: Left IJ MAC. Peripheral IVs should ideally be placed in the forearms to avoid kinks and poor flow after positioning. Left IJ is preferred over Right IJ central line due to possible need for VV-ECMO in the event of severe reperfusion injury. *Note that this is a preference but not a requirement in the event of difficult access.
  e. PA catheter: A CCO swan should be placed through the MAC and floated into the PA. *Please note that the PA catheter should be floated prior to the operation regardless of the history of pulmonary embolus (this is in fact going to be removed during the operation).
  f. Foley Catheter: To be placed by OR Nursing after induction of anesthesia.
  g. Temperature: Nasal and bladder temperature probes placed
  h. Antibiotics:
     i. Ancef infusion protocol
  i. Positioning: supine with both arms tucked at the side.
j. Steroids:
   i. Ensure that Solumedrol 1gm was given prior to the patient’s arrival to the operating room. If this has not been administered previously, administer now.

**From Incision to Initiation of CPB**

a. Heparin: CPB dose of heparin prepared in case of emergent need for CPB.
   b. TEE performed
   c. Heparinization 300-400 units/kg with goal ACT >500 given. Since these patients have a propensity for clotting, ACTs should be targeted higher than usual.
   d. Amicar bolus and infusion started after heparinization.
   e. Be prepared for major blood transfusion in case of injury to major vascular or cardiac structures (blood products prepared, hot line primed and connected).

**Anesthetic Considerations: From Institution of CPB to Circulatory Arrest**

a. After institution of CPB, the patient will undergo deep hypothermia (20°C) and ultimately circulatory arrest. Antegrade cerebral perfusion is typically not performed on these patients as the circulatory arrest time is typically <20 minutes per side and antegrade or retrograde cerebral perfusion may result in back-bleeding through the bronchial collaterals.

b. After institution of CPB and cooling, please apply local cooling to the head. To do this, take one surgical towel (green towel) and place this under the head. Ask anesthesia tech for 4 zip-lock bags of ice. Apply bag of ice to each side of head (right, left, front, top). Secure these in place with surgical towel (may need clamp to secure towel). May desire to place one towel on top of the head to ensure no direct contact from ice onto skin – avoiding injury from ice.

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| **Institution of CPB** | • Sternotomy performed  
• Cannulation for CPB: Arterial-ascending aorta. Venous-bicaval cannulation (SVC/IVC). SVC cannulation will be performed and CPB will be instituted. While on CPB, IVC cannulation will be performed.  
• Heparinize fully, give antifibrinolytic (Amicar), go on CPB  
• Aortic cross-clamp not typically used unless significant aortic insufficiency is present. Myocardial protection is performed by deep hypothermia and limited circulatory arrest intervals.  
• While on CPB, keep ACT >500, assist perfusionist with maintenance of the MAP 60-80 with the addition of vasoconstrictor (Phenylephrine/Norepi) or vasodilators (clevidipine)  
• Correct anemia, hyperglycemia.  
• Patient cooled gradually to 18°C (takes 60-90 minutes to cool).  
• LV vent placed |
| **Endarterectomy** | • SVC is freed from the right main PA. Right main PA is dissected distally.  
• Main PA is freed from the aorta and left PA is dissected out.  
• Right main PA is opened. The endarterectomy is performed with the dissection plane started proximally, regardless of where the disease is located. The dissection plane is extended distally and circumferentially until visualization becomes problematic, then circulatory arrest is performed.  
• **Circulatory arrest:** BIS should be 0, patient temp 18°C. CPB pump turned off, and the perfusionist exsanguinates the patient. The anesthesiologist should then hand-bag the lungs several times to empty the bronchial circulation. |
• During circulatory arrest, the dissection is continued distally until segmental branches are encountered. Each segmental branch is dissected separately. The PA arteriotomy is then closed (sometimes performed while on circulatory arrest)
• The procedure is repeated on the left side.
• The endarterectomy is, on occasion, more difficult and requires an extended period of circulatory arrest. The arrest period is typically limited to 20 consecutive minutes, followed by a 5 minute period of reperfusion before resumption of circulatory arrest.

**Rewarming**

• After the endarterectomy, rewarming is instituted following a 5 minute perfusion washout period
• Rewarming is gradual and takes 60-120 minutes
• Remove ice packing from head upon rewarming
• Once patient temperature 26-27°C, volume is left in the heart and defibrillation is performed if necessary
• Aggressively treat hypokalemia and hypocalcemia during this time, goal K >3.5 when coming off CPB
• Atrial and Ventricular pacing wires typically not implanted unless significant arrhythmia present (most commonly sinus bradycardia). If used, connect and check thresholds. Document underlying rhythm.
• Once ventilation is instituted, start iNO at 20ppm or iVeletri at 50 ng/kg/min IBW
• Once heart is rhythmically beating, start inotropes (confirm agents/dosing with attending)
• Send coagulation labs at 32°C bladder temperature.
• Once patient is 32-33°C, SVC cannula will be turned towards heart and IVC cannula will be clamped and removed.
• Separate from CPB when >35°C

**Prior to Weaning from Cardiopulmonary Bypass:**
   a. Ventilate with 30% FiO₂ and inhaled NO/Veletri
   b. Re-zero transducers
   c. Ensure patient is not hypokalemic or hypocalcemic (K > 3.5 and Ca > 1.1). May need to aggressively treat hypokalemia.
   d. Initiate medium dose of epinephrine (0.04-0.06 mcg/kg/min) once heart is rhythmically beating; if RV dysfunction is severe, discuss increasing the inotropy with attending
   e. Discuss with the perfusionist the amount of volume available in the venous reservoir, which should be enough to allow slow separation from CPB. If Hb marginal (approx. 8g/dl) and volume in the venous reservoir low, discuss administration of PRBC prior to separation from CPB.

**Coming off Cardiopulmonary Bypass:**
   a. Maintain a MAP >70 mmHg
   b. Maintain a CVP <15 mmHg
   c. Do not decrease inotropy (if hypertensive, initiate afterload reduction)
   d. Ventilate with 30% FiO₂ and inhaled NO/Veletri – assess oxygenation after separation from CPB. Goal paO₂ >60. If FiO₂ increases, inform anesthesiologist and surgeon

**Maintenance after Cardiopulmonary Bypass**
   a. After anesthesiologist and surgeon approve of hemodynamic profile and RV function, give test dose of protamine (2 mL) and evaluate for significant hemodynamic instability.
b. After confirming with surgeon, proceed with protamine reversal. After 1/3 in, announce to surgeon and perfusionist and confirm perfusionist has turned off the “pump suckers.”

c. Start collecting CCO data from PA catheter

d. These patients have a propensity for clotting, administration of coagulation factors (platelets, cryoprecipitate, FFP) should be performed only if the labs show abnormalities AND the patient is bleeding after separation from CPB. This evaluation must be performed by direct communication between the anesthesia and surgical team.
   o While transfusion of plasma is rare, these patients may develop thrombocytopenia or hypofibrinogenemia that necessitates transfusion of platelets or cryoprecipitate. Communicate all abnormal lab values with anesthesiologist and surgical team.
   o If the platelet count is <80k, prepare platelets, but do not transfuse unless the patient is bleeding
   o Do not empirically prepare cryoprecipitate, consider doing so after discussion with team in presence of significant hypofibrinogenemia

e. Draw arterial blood gases q30 min to ensure metabolic acidosis is corrected and all labs normalized.

f. Be careful with volume administration, constantly assess RV function and volume status.

• **Management of Hemodynamics:**
  a. Epinephrine is initial inotrope of choice
  b. Dopamine may be needed if bradycardia present and pacing wires not placed (Dopamine 2-5 mcg/kg/min)
  c. Milrinone may be used if additional inotropy needed and HTN present (Milrinone 0.125-0.25 mcg/kg/min)

• **TEE Exam:**
  Prebypass: perform a complete examination (see Duke TEE Imaging Protocol)
  Provide special attention to:
  RV function
  Aortic insufficiency
  Presence of patent foramen ovale
  Severity of TR
  Thrombus in main/right PAs

  Postbypass evaluation: perform a complete examination (see Duke TEE Imaging Protocol)
  Provide special attention to:
  RV function
  Aortic insufficiency
  Presence of patent foramen ovale
  Severity of TR
  Assessment of laminar flow in PAs

• **End of surgery**
  a. Ensure pacemaker in synchronous mode (if applicable)
  b. Bronchoscopy performed by surgical team
  c. Pulmonary hemorrhage or significant pulmonary edema remains a possibility due to reperfusion injury (and may be present even in the setting of a good endarterectomy result based on the amount of lung reperfused). This will be evaluated by bronchoscopy and ability to ventilate. If severe, may require VV-ECMO until resolves.
  d. In the event of surgically uncorrected persistent pulmonary hypertension, right heart dysfunction may necessitate VA-ECMO as a bridge to recovery.

**VI. Postoperative Considerations**
a. Call respiratory therapy to help transport the nitric oxide/Veletri back to the unit. (385-2636)
b. Place transport monitors and ventilate patient with the transport ventilator
c. Ensure safe handover to the ICU team
d. Management in the ICU includes
e. Weaning of inotropes and pressors, nitric oxide, and continued resuscitation
f. Extubation on POD 1, if possible
g. Early ambulation and diuresis

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