Pulmonary Endarterectomy: Assessment of Operability, Surgical Description, and Post-op Care

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Chronic thromboembolic pulmonary hypertension (CTEPH) is defined as a mean pulmonary artery pressure ≥25 mm Hg and pulmonary artery wedge pressure ≤15 mm Hg in the presence of occlusive thrombi within the pulmonary arteries. Surgical pulmonary thromboendarterectomy (PTE) is considered the best treatment option for CTEPH.

PTE is a technically difficult procedure that requires careful patient selection, surgical experience, and high level of postoperative care to be successful. We have used published literature in tandem with our experience to review operability assessment criteria, detail some specifics of PTE surgical technique, and offer considerations for postoperative care.

Surgical PTE remains the top treatment for CTEPH. Once a diagnosis of CTEPH is made, it must be determined whether the patient will benefit from PTE surgery and if the benefits will outweigh the associated risks. All CTEPH patients should be considered for surgery, and no patient should be turned down without consultation with an experienced center. The success of the surgery owes as much to appropriate patient selection as it does to surgical technique and postoperative management. No level of pulmonary hypertension or degree of right heart failure is a contraindication to surgery, and excellent short- and long-term results can be achieved with adherence to established surgical principles.

Chronic thromboembolic pulmonary hypertension (CTEPH), currently categorized as World Health Organization (WHO) Group 4,1 is defined as a mean pulmonary artery pressure ≥25 mm Hg and pulmonary artery wedge pressure ≤15 mm Hg in the presence of occlusive thrombi within the pulmonary arteries. Surgical pulmonary thromboendarterectomy (PTE) remains the gold standard treatment for CTEPH. Patients who undergo PTE have improved 3-year survival (89% vs 70%)2 compared with nonoperated patients treated with medical therapy. Surgery typically results in a greater mean reduction in pulmonary vascular resistance (PVR) than can be achieved with medical therapy. PTE is a technically difficult procedure that requires careful patient selection, surgical experience, and high level of postoperative care to be successful.

ASSESSMENT OF OPERABILITY

Once a diagnosis of CTEPH is made, the crucial decision, and often the most difficult, is determining if the specific patient will benefit from PTE surgery and if the benefits will outweigh the associated risks. PTE is the only treatment with a potential cure and therefore the treatment of choice for CTEPH. All CTEPH patients should be considered for surgery, and no patient should be turned down without consultation with an experienced center. Much has been learned over the past decade and has improved the operative safety of PTE surgery, which is now considered a relatively safe procedure with an experienced team, with in-hospital mortality rates of 2.2%3 (at a single US referral center) and 4.7%4 (across multiple European centers performing PTE). The success of the surgery owes as much to appropriate patient selection as it does to surgical technique and postoperative management. The determination of operability relies on 3 key assessments:

1. Does the clot burden observed on imaging correlate with the degree of hemodynamic impairment observed during right heart catheterization?
2. Are the diseased vessels surgically accessible?
3. Does the patient have comorbidities that would prohibit PTE surgery?

Correlating clot burden with hemodynamic impairment can be difficult. This is particularly true for patients with Type III disease (segmental level disease) and advanced right heart failure. When considering operability, the goal is to identify sufficient accessible disease so PTE surgery results in a reduction of PVR near or within the normal range. In large series published from the United States and Europe, the mean and median improvements in PVR typically achieve a postoperative PVR <300 dynes·s·cm⁻⁵.3,4

While centers have reported higher mortality in patients with preoperative PVR >1200 dynes·s·cm⁻⁵,5 this finding is not a contraindication to PTE and should not limit referral to a CTEPH.

Key Words—chronic thromboembolic pulmonary hypertension, CTEPH, pulmonary endarterectomy, PTE, operability, post-op, outcome, complications, bleeding, reperfusion edema, persistent pulmonary hypertension

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center for surgical evaluation. In fact, this is the group of patients that requires particular care during evaluation and should be referred to an experienced CTEPH center. Under the care of a team with expertise in CTEPH, with correct patient selection, patients with preoperative PVR >1200 dyne·s·cm⁻² can be operated with good outcomes. Recent data from the University of California San Diego (UCSD) demonstrated a mortality of 4.1% for patients with preoperative PVR >1000 dyne·s·cm⁻² compared with 1.6% for PVR <1000 dyne·s·cm⁻². Persistent pulmonary hypertension (PH) following PTE has a much more dramatic influence on operative and 1-year mortality than elevated preoperative PVR. In 500 consecutive cases performed at UCSD, mortality was 10.3% for patients with a postoperative PVR >500 dyne·s·cm⁻² compared with 0.9% for patients with a postoperative PVR <500 dyne·s·cm⁻². All efforts should be made to perform complete endarterectomy to avoid persistent PH.

Distal location of thrombotic material and thus surgical accessibility plays a significant role in determining operability. Type III disease, where thrombi are located at the segmental and subsegmental level, is increasingly considered operable but requires a particularly high level of surgical expertise. At UCSD, among a series of 121 consecutive type III disease cases, the mean postoperative PVR was 286 dyne·s·cm⁻² and hospital mortality 1.7%.

Based on data from the European CTEPH registry, coronary artery disease increases in the hospital and 1-year mortality associated with the surgery from 2.1% to 10% and 5.1% to 15% respectively. Other factors that make the surgery technically more difficult but have not been shown to increase mortality include elevated body mass index (BMI), taller patient height, and the presence of prior sternotomy.

Surgical Technique
There are 3 guiding principles for the operation:

I. The endarterectomy should be bilateral, performed via a median sternotomy.

II. Cardiopulmonary bypass is essential to ensure cardiovascular stability when the operation is performed and to cool the patient to allow circulatory arrest.

III. A bloodless field is required to define an adequate endarterectomy plane and to then follow the pulmonary endarterectomy specimen deep into the subsegmental vessels. Bronchial blood flow can be copious in these cases, and therefore periods of circulatory arrest are necessary to ensure optimal visibility. The circulatory arrest periods are limited to 20 minutes, with restoration of flow between each arrest for a minimum of 10 minutes.

Figure 1: Surgical Exposure.
Much of the preoperative preparation is common to any open-heart procedure. Following median sternotomy, expect to find an enlarged right heart with a tense right atrium. After full heparinization, wire-reinforced flexible cannulas are used for high ascending aortic and bicaval cannulation and institution of full cardiopulmonary bypass. Temporary pulmonary artery and left atrial vents are placed. In addition to cooling the blood via the heater-cooler, surface cooling with both a head ice-jacket and a cooling blanket is initiated. Gradual cooling with a 10°C gradient ensures uniform tissue cooling and generally takes 45 to 60 minutes. At a core temperature of 20°C, the aorta is cross-clamped and a single dose (1 L) of cold blood cardioplegic solution is administered. A cooling jacket wrapped around the heart offers additional myocardial protection.

The superior vena cava is circumferentially mobilized. The approach to the right pulmonary artery is made medial to the superior vena cava. All dissection of the pulmonary arteries is carried out intra-pericardially. An incision is made in the right pulmonary artery under the superior vena cava and entering the lower lobe branch. When blood obscures direct vision, circulatory arrest is initiated, and the patient is exsanguinated (Figure 1).

Dissection in the correct plane is critical, as dissection too deep will result in vessel perforation and consequent airway bleeding. Dissection that is too superficial will result in failure to remove all thrombotic material. Once the plane is correctly developed, the endarterectomy is performed with an eversion technique. It is important that each sub-segmental branch is followed and freed individually until it ends in a tail beyond which there is no further obstruction.

Jamieson classified pulmonary occlusive disease into 4 types (Figure 2):

I. Type I disease refers to major vessel clot present and readily visible upon opening the pulmonary arteries.
II. Type II disease findings are: thickened intima, webs, and bands. Here, the endarterectomy plane is raised in the main, lobar, or segmental vessels.
III. Type III disease is very distal and confined to the segmental and sub-segmental branches.
IV. Type IV disease affects intrinsic small vessels and is inoperable, although secondary thrombus can occur as a result of stasis.

Once the right-sided endarterectomy is completed, circulation is restarted, and the arteriotomy is repaired. It is important that this suture line is hemostatic because visualization is extremely difficult once the patient is weaned from bypass.

For the left endarterectomy, the heart is retracted to an inferior-medial position with the aid of a heart net while still keeping the heart wrapped in the cooling jacket. The left-sided dissection and repair are analogous to that accomplished on the right.

After the endarterectomy is completed, cardiopulmonary bypass is re instituted and warming is commenced. Methylprednisolone (500 mg) and mannitol (12.5 g) are administered to minimize capillary leak following prolonged cardiopulmonary bypass. If other cardiac procedures are required, these are conveniently performed during the rewarming period. Weaning from bypass and wound closure is routine.

POSTOPERATIVE CARE

Standard Care

Much of the postoperative care is similar to that of other open-heart surgery patients, with focus on hemodynamic support, volume management, and optimizing oxygenation. Patients remain on mechanical ventilation until postoperative day 1 when assessments for extubation are performed. The additional time spent on mechanical ventilation allows additional time to monitor for bleeding, and most importantly early reperfusion pulmonary edema.

Pneumatic compression devices are used for venous thrombosis prophylaxis immediately following surgery. Anticoagulation is initiated a few hours following surgery once chest tube drainage and bleeding is at a minimum. The patient’s risk for rethrombosis dictates the agent used for anticoagulation and the therapeutic target.

For patients considered low risk for rethrombosis, heparin at venous thrombosis prophylaxis levels is used until the pacing wires are removed. The majority of patients immediately post-op are placed on heparin subcutaneously at doses that are usually used for deep venous thrombosis (DVT) prophylaxis. The subcutaneous heparin is started once
chest tube output drainage has slowed. A typical starting point for subcutaneous heparin administration is when the output is <25 mL/hr for 4 hours. The typical dose is heparin 5,000 units subcutaneously for 8 hours, and is sometimes adjusted up or down if patients are very small or very large, but this adjustment is aimed at achieving DVT prophylaxis levels of drug. For patients who are at higher risk of post-operative rethrombosis, intravenous heparin is used instead of subcutaneous heparin, and the target partial thromboplastin time (PTT) or XA levels are those used for DVT/pulmonary embolism (PE) treatment (PTT 60-80).

There is some “artistry” in the choice of PTT target and method of heparin titration. Once the pacing wires are removed and chest tube drainage is at a minimum, warfarin is initiated. For patients taking aspirin in addition to warfarin, the target international normalized ratio (INR) is typically 2-3, and a higher target of 2.5-3.5 is encouraged for all other patients. Currently warfarin- or heparin-based anticoagulation is recommended for the first 6 months following surgery. Newer oral direct thrombin inhibitors may be used after 6 months, but experience with these agents in CTEPH is currently limited.

Patients with intracardiac thrombi, complete obstruction of a main pulmonary artery, unilateral occlusion, and high titer lupus anticoagulant antibodies are at higher risk for early rethrombosis. These patients are anticoagulated more aggressively. The choice of anticoagulant and target PTT varies. Choosing a therapeutic target can be particularly challenging in patients with significantly abnormal baseline PTT values.

Hypoxia is common following PTE. This is due largely to 2 phenomena: atelectasis and impaired ventilation-perfusion (V/Q) matching. Atelectasis is common secondary to prolonged surgery, splinting, and in some cases diaphragm dysfunction. V/Q mismatch occurs in areas of endarterectomy lung where autoregulation is disturbed. The lower resistance, endarterectomized vessels can “steal” blood flow from other areas of lung. It can take weeks to months before autoregulation is completely restored and perfusion imaging shows a more homogeneous distribution of blood flow (Figure 3). Hypoxia usually improves within 1-8 weeks following surgery.

**PERSISTENT PH AND REPERRUSION PULMONARY EDEMA**

The 2 postoperative complications that account for the majority of morbidity and mortality associated with PTE surgery are persistent PH and reperfusion pulmonary edema (RPE). They are often present in combination.

RPE is a syndrome that occurs following reinstitution of pulmonary blood flow to areas of lung that have undergone endarterectomy. It is defined by a PaO2/FiO2 ratio <300, opacity on chest radiograph in a region of reperfused lung with no alternative explanation such as pneumonia or atelectasis (Figure 4). Depending on the definition used, this is seen in 10% to 40% of patients following PTE.7-9 RPE is most common immediately following surgery (50%), with the remainder occurring in the first 48 hours following surgery (30%).10 A minority of RPE (10%) occurs >48 hours following PTE.

Standard approaches to the management of RPE include diuretics to reduce lung water and supportive care with oxygen and positive end expiratory...
pressure (PEEP). A single-center study examined the role of perioperative steroids to minimize RPE and found no difference between groups. In a study of 47 patients, a strategy of low tidal volume (<8 mL/kg) and avoidance of inotropes and vasodilators has been suggested to reduce the incidence of RPE. Another study performed at UCSD examined the impact of different tidal volume strategies to reduce the incidence of RPE and did not demonstrate a difference. In the setting of severe RPE and elevated cardiac index (>3 L/min/m²) following PTE, cardiac output suppression with pressors may reduce capillary leak and lessen the severity of RPE. The effect of this strategy has not been prospectively studied.

In cases of persistent PH following PTE and/or hemodynamic impairment refractory to inotropic and pressor support, venoarterial extracorporeal membrane oxygenation (ECMO) (va-ECMO) has been used. In a report of 7 patients with persistent PH and hemodynamic instability at the time of PTE surgery, central va-ECMO was used as a salvage. Four of the 7 patients (57%) survived to hospital discharge. In a series of 20 patients requiring vv-ECMO 30.0% vs 94.2% mortality was 100% for the 7 patients who initiated ECMO >120 hours after surgery. Based on these experiences, guidelines from the fifth World Symposium on Pulmonary Hypertension recommend that centers performing PTE have the capability of salvage ECMO therapy.

**POSTOPERATIVE BLEEDING**

The most common locations for postoperative bleeding complications to develop following PTE are the pericardium and the airway. Airway bleeding is usually observed immediately following PTE and can present significant management challenges. Pericardial bleeding can be observed early, while mediastinal drainage tubes are still present or late. Reported rates of pericardial bleeding complications have varied widely and occur in anywhere from 0.6% to 17% of patients. The development of late pericardial effusions following PTE has made echocardiogram following chest tube and pacer wire removal a routine part of postoperative care. Pericardial bleeding is managed in the standard fashion. Early bleeding requires return to the operating room for control of the bleeding site, and late effusions require temporarily holding anticoagulation and placement of pericardial drains.

**Airway Bleeding Post-PTE Surgery**

Airway bleeding following PTE can present significant challenges. Early diagnosis and prompt isolation of affected lung segments is essential. The surgeon is in a unique position to aid in this early diagnosis and management by anticipating airway bleeding. Suspicion should be high if the endarterectomy denuded the vessel and only a thin layer of adventitia remains or if a vascular injury was observed during PTE. In contrast, severe early reperfusion pulmonary edema is more expected if bronchoscopy identifies frank, dark, pulsatile blood in the airway upon weaning from bypass. Surgical repair or occlusion of that segmental pulmonary artery branch can be attempted. This repair or occlusion may require that cardiac and circulatory arrest be reinstalled. In contrast, severe early reperfusion pulmonary edema is more likely if bronchoscopy reveals diffuse, pink, frothy material in the airways, and no attempt at vascular repair should be undertaken. The area should be isolated with a bronchial blocker followed by separation from cardiopulmonary bypass (CPB), reversal of heparin, and correction of coagulopathies. Effective isolation is critical to prevent blood from contaminating nonaffected lung and to successfully wean from CPB. Immediately prior to separation from CPB, the PCO₂ should be lowered and the PO₂ increased, as gas exchange may be suboptimal during the period when heparin is being reversed and coagulopathies corrected. If inadequate gas exchange persists, as evidenced by an ongoing drop in SpO₂, the bronchial blocker can be deflated, and if no bleeding is observed the isolated lung segment can be recruited for gas exchange.

Should inadequate gas exchange be an ongoing or recurring problem, vv-ECMO can be instituted; vv-ECMO without anticoagulation may be advantageous in the bleeding post-PTE patient by facilitating clot formation and allowing increased clot strength, which...
ultimately aids in the resolution of airway bleeding. Even though some components of the ECMO circuit might not be heparin coated, we believe that the risk posed to the patient by ongoing airway bleeding outweighs the risk of clot formation in the cannula(s) or oxygenator. In fact, the oxygenator has a large reserve in function and will continue to supply adequate gas exchange despite some clot formation. Furthermore, clot(s) predominantly form on the inflow side of the oxygenator and therefore do not pose an embolic risk to the patient. If clot formation does impact oxygenator function, replacement of the oxygenator can be accomplished in a short time with little impact on gas exchange.

**Arrhythmias**

Arrhythmias are a common and expected complication following PTE. Functional arrhythmias dominate in the early postoperative period and atrial arrhythmias, in particular atrial fibrillation, can occur later. Epicardial pacing wires placed as a routine part of PTE surgery are removed once intrinsic cardiac conduction recoveries.

**Neurologic Complications**

Neurologic disorders related to deep hypothermia have been observed following PTE surgery. The most common neurologic manifestation is delirium, which typically resolves with time.

The impact of PTE surgery on cognitive function was addressed by the PEACOG study performed in the United Kingdom. They examined cognitive function in patients undergoing PTE surgery and randomized 35 patients to traditional surgical technique with deep hypothermic circulatory arrest and compared them with 39 patients who received antegrade cerebral perfusion during PTE. While antegrade cerebral perfusion was safe, no differences in cognitive function were detected between the groups. Additionally, both groups showed improvement in cognitive function testing at 12 and 52 weeks after surgery. The improvement in cognitive function following PTE is speculated to be secondary to improvements in quality of life and oxygen delivery.

**OUTCOME**

**Long-Term Survival**

Long-term survival following PTE is excellent. For patients who survive to hospital discharge, survival rates of 92.5% at 5 years and 88.3% at 10 years have been reported in the United Kingdom. More recent data from the same center showed similar results with a 5-year survival rate of 90.0%. Other centers have demonstrated similar long-term survival results with reports from the Netherlands demonstrating 1-, 3-, and 5-year survival rates of 93.1%, 91.2%, and 88.7% respectively.

**Functional and Hemodynamic Effects**

PTE performed at experienced centers results in an immediate and sustained improvement in hemodynamics. The most recent series of patients published from UCSD resulted in a reduction of PVR from 719 ± 383.2 dyne-secm⁻⁵ to 253.4 ± 148.6 dyne-secm⁻⁵. Mean pulmonary arterial pressure improved from 45.5 ± 11 mm Hg to 26.0 ± 8.4 mm Hg, and cardiac output improved from 4.3 ± 1.4 L/min to 5.6 ± 1.4 L/min³ Data published from CTEPH centers around the world have reported similar improvements in hemodynamics.¹⁴

Most importantly, the improvement in hemodynamics is sustained on long-term follow-up. Data from the United Kingdom have shown sustained improvement in WHO functional class following PTE. Prior to PTE, 66% of patients were WHO functional class III or IV and 88% of patients had improved to WHO functional class I or II at 12 months following PTE.²⁰ Mean improvement in 6-minute walk test following PTE of 103 ± 22.7 m was also sustained at 12-month follow-up. Data from Italy have shown similar results with a sustained functional improvement over a 4-year period, with 97% of patients NYHA III or IV prior to PTE and 74% improved to functional class I at 4-year follow-up.²¹ Other standard endpoints in the treatment of PH have shown sustained improvement following PTE. Patients from the Netherlands had sustained an improvement in NT-pro BNP following PTE from a mean of 1527 ng/L to 160 ng/L following PTE.²²

**Persistent PH Following PTE**

A uniform definition of persistent PH following PTE has not been established, and rates vary depending on the definition used. As previously mentioned, persistent PH and refractory right heart failure following PTE are some of the major contributors to early mortality.

There are 2 distinct groups of patients with persistent PH following PTE: patients who achieve minimal or no hemodynamic improvement following PTE and patients who improve following PTE but continue to meet a hemodynamic definition of PH. For patients in the first group, early institution of advanced PH therapies including prostacyclins, endothelin antagonists, phosphodiesterase type 5 (PDE5) inhibitors and stimulators of guanylate cyclase, may be necessary as rescue. Consideration for lung transplantation in this group is appropriate. For the second group, consideration for additional medical therapy can usually be deferred until patients recover from surgery. Using a mean pulmonary arterial pressure ≥ 25 mm Hg or PVR > 240 dyne-secm⁻⁵ up to 35% of patients had persistent PH following PTE based on data from the United Kingdom.²⁰ Despite meeting hemodynamic criteria for PH, 3-year survival for this group was 94% and 82% of patients remained functional class I or II.

**CONCLUSION**

PTE is and will remain the treatment of choice for CTEPH. Multiple factors are involved in determining candidacy for surgery, but no level of PH or degree of right heart failure is a contraindication to surgery. Excellent short- and long-term results can be achieved with adherence to established surgical principles.

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