

Recent advances in anaesthesia for pulmonary endarterectomy

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Abstract

Chronic thromboembolic pulmonary hypertension (CTEPH) is a form of pulmonary hypertension (PH) that is rapidly gaining importance. The disease is associated with acute or recurrent pulmonary thromboembolism leading to chronic vascular obliteration. The result is increased pulmonary vascular resistance, the development of PH and progressive right heart failure. There have been significant advances in the diagnosis and treatment of this debilitating condition. Therapeutic options include medical therapy, lung transplantation and pulmonary endarterectomy (PEA). By the removal of obstructive material from the pulmonary arterial system, PEA improves functional status and survival for patients with CTEPH. The procedure is now considered the treatment of choice for this condition and recently there has been an expansion in the number of centres performing PEA. Success depends on a high volume of cases and a coordinated multidisciplinary team comprising physicians, radiologists, surgeons, anaesthetists and intensivists.

Key words: chronic thromboembolic pulmonary hypertension, pulmonary endarterectomy, anaesthesia, intensive care.

Introduction

In 1973, Moser and Braunwald reported the first successful surgical intervention for chronic thromboembolic pulmonary hypertension (CTEPH) at the University of California, San Diego (UCSD) [1]. Several thousand patients have now undergone pulmonary endarterectomy (PEA) at an increasing number of centres worldwide [2]. Ongoing improvements in surgical and anaesthetic techniques have resulted in a reduced mortality rate to less than 5% at UCSD [3]. PEA was first performed at Papworth Hospital in 1994 and our programme has expanded since then.

Perioperative care for these patients has developed significantly during this period and we will discuss the current practice of anaesthesia for PEA at our centre.

Epidemiology

Most survivors of acute pulmonary embolism will not develop CTEPH. However, in some patients, pulmonary thromboemboli do not undergo complete resolution by the fibrinolytic system and chronic pulmonary arterial obstruction ensues. The incidence and prevalence of CTEPH are not well described. It appears that the disease is being diagnosed more frequently and that its incidence may be greater than suggested by previous reports [4]. Patients with untreated CTEPH invariably develop right heart failure and have a poor long-term survival.

Pathogenesis

The pathogenesis of CTEPH is complex and has not yet been fully established [5]. There is evidence to suggest that initial pulmonary embolism, either overt or subclinical, triggers a series of pathophysiological events resulting in progressive symptomatic deterioration. Organisation and fibrosis of unresolved thrombi in proximal vessels causes vascular occlusion and PH. Histopathological examination reveals fibrous thickening of the vessel wall and luminal obliteration. Other mechanisms may contribute to the development of widespread pulmonary vasculopathy and PH: recurrent thromboembolism, distal vessel arteriopathy in both non-occluded and occluded vascular regions, and in-situ thrombosis in pulmonary vessels. CTEPH is associated with various abnormalities of the coagulation and fibrinolytic systems as well as a number of immunological and haematological disorders [6]. However, the precise mechanisms responsible for the increased prothrombotic and anti-fibrinolytic tendencies of these patients have so far not been elucidated.

Diagnosis

The clinical presentation of CTEPH is often insidious and difficult to recognise. Patients with CTEPH may remain asymptomatic for a prolonged period of time before presenting with symptoms of right heart dysfunction including

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dyspnoea, fatigue, chest pain and pre-syncope. Patients may or may not have a history of previous pulmonary embolism or lower limb venous thrombosis. Physical examination may detect signs of right heart failure such as elevated jugular venous pressure, hepatomegaly and peripheral oedema.

The diagnostic evaluation of patients with CTEPH involves detection of pulmonary hypertension, confirmation of the diagnosis of CTEPH, assessment of disease severity and determination of suitability for surgical management [7]. Thrombophilia screening is performed to detect the presence of underlying coagulation and fibrinolytic disorders. Features of right ventricular hypertrophy and right atrial dilatation should be sought on the electrocardiograph. Chest radiography may reveal central pulmonary artery enlargement, right ventricular enlargement and pulmonary oligoemia. Transthoracic echocardiography will often demonstrate evidence of right ventricular dysfunction including right ventricular hypertrophy and dilatation, right atrial dilatation, abnormal movement of the interventricular septum and tricuspid regurgitation. Secondary effects of right-sided dysfunction, including left ventricular diastolic dysfunction and right-to-left shunting through a patent foramen ovale, may also be identified. Pulmonary function testing may show mildly restrictive pulmonary mechanics and will also determine the presence of underlying airway or parenchymal pulmonary disease. Exercise testing is useful to establish the degree of functional impairment. Nuclear ventilation-perfusion imaging is an essential investigation to distinguish between CTEPH and other causes of PH. The presence of multiple bilateral perfusion defects suggests that CTEPH may be the cause of PH. Computed tomography and magnetic resonance imaging are being increasingly used to delineate the location and extent of obstructive lesions in the pulmonary arterial system. Right heart catheterisation and pulmonary angiography are presently regarded as the definitive investigations for the evaluation of CTEPH. Calculation of the pulmonary vascular resistance (PVR) and assessment of the anatomical pattern of disease will influence the feasibility of surgical clearance. Patients with distal small-vessel disease, suggested by a disproportionately high PVR relative to the extent of proximal large-vessel disease, may have a poorer outcome after PEA [6].

Therapy

The therapeutic options for patients with CTEPH include medical treatment, lung transplantation and PEA. All patients should receive continuous anticoagulation to prevent recurrent thromboembolic events. Medical treatment with pulmonary vasodilator therapy is being extensively investigated and new pharmacological therapies are emerging [8]. The indications for medical therapy include preoperative treatment prior to PEA, long-term management of patients not suitable for surgery, and postoperative treatment of residual pulmonary hypertension following PEA. Lung transplantation is associated with a low donation rate, a significant perioperative mortality rate, the complications of chronic immunosuppression, and the risk of organ rejection.

PEA is a major surgical procedure that is performed through a median sternotomy. Cardiopulmonary bypass (CPB) is required for PEA and deep hypothermic circulatory arrest (DHCA) is used at most centres. In comparison with lung transplantation, PEA is associated with lower perioperative mortality, requires only long-term anticoagulation therapy and results in a significant haemodynamic and symptomatic improvement. At present, suitable patients with CTEPH should undergo PEA.

Preoperative care before pulmonary endarterectomy

In accordance with the practice of other large centres, patients scheduled for PEA at our centre undergo insertion of an inferior vena cava filter to prevent recurrent venous thromboembolism [3]. In the immediate preoperative period, all medical therapy, including pulmonary vasodilator therapy and anticoagulation, should be continued prior to anaesthesia. Pre-anaesthesia assessment requires a thorough review of the diagnostic investigations. Corticosteroids may be useful in order to reduce the incidence of postoperative reperfusion pulmonary oedema. At our centre we prescribe prednisolone on the night before surgery. Sedative pre-medication can be administered, along with supplemental oxygen, according to the need and clinical condition of each individual patient. In general, our practice is to avoid preoperative sedation prior to PEA and ensure our patients receive adequate psychological preparation.

Intraoperative management for pulmonary endarterectomy

Induction of anaesthesia

The goal of intraoperative management prior to CPB is primarily to support right ventricular function. Physiological factors that increase PVR should be avoided. Invasive haemodynamic monitoring may be inserted before or after induction of general anaesthesia: we prefer the latter approach. Induction of anaesthesia can be hazardous but may be safely accomplished using a variety of techniques. We use a combination of midazolam, fentanyl and pancuronium for induction, followed by continuous administration of propofol for maintenance of anaesthesia. Following intubation and commencement of mechanical ventilation, vasopressors (e.g. metaraminol or phenylephrine) and inotropic support (e.g. dopamine or adrenaline) are commonly required to treat systemic hypotension. We routinely start a low-dose dopamine infusion to maintain haemodynamic stability prior to CPB. The intraoperative mechanical ventilation strategy should seek to limit plateau airway pressures and maintain satisfactory oxygenation by a combination of tidal volume of 6-8 ml/kg and positive end-expiratory pressure (PEEP) of 5-10 mmHg.

Intraoperative monitoring

Our practice is to insert both right radial and right femoral arterial catheters. This is necessary because me-

asurement of radial and femoral arterial pressures is required during selective antegrade cerebral perfusion (SACP). Femoral arterial catheterisation is also useful to provide access for insertion of an intra-aortic balloon counter-pulsation device if required following separation from CPB. Radial arterial pressure may significantly underestimate the systemic arterial pressure following prolonged hypothermic CPB [9]. We routinely measure femoral arterial pressure following PEA in intensive care at our centre. Central venous and pulmonary artery catheterisation are both performed, usually through the right internal jugular vein. Placement of the pulmonary artery catheter may be difficult because of tricuspid regurgitation and dilatation of the right-sided cardiac chambers. Insufflation of the pulmonary artery catheter balloon is contraindicated after endarterectomy because of the risk of vessel rupture. We avoid obtaining a pulmonary artery wedge pressure before or after surgery and instead use a default value of 10 mmHg for the purpose of haemodynamic calculations. The pre-CPB pulmonary artery pressures, cardiac output and PVR are recorded. Intraoperative transoesophageal echocardiography (TOE) is used to assess right and left ventricular function, to detect the presence of a patent foramen ovale, and to identify proximal pulmonary artery obstruction. TOE may also be useful to guide pulmonary artery catheterisation. Temperature should be measured in at least two locations in order to monitor brain temperature (e.g. nasopharynx or tympanic membrane) and core temperature (e.g. bladder or rectum). We use a nasopharyngeal temperature probe to reflect brain temperature and a urethral catheter with a temperature sensor in order to measure urine output and to indicate core temperature. Temperature control is assisted by the use of a water mattress underneath the patient, and a sterile forced air blanket placed over the abdomen and lower limbs. Neurological monitoring may be employed using electroencephalography, jugular venous bulb oximetry or transcranial cerebral oximetry. At our centre, we routinely use transcranial cerebral oximetry to assess the adequacy of regional cerebral perfusion [10]. Care should be taken to ensure safe positioning of the patient in preparation for prolonged surgery. Areas at risk of pressure sore formation should be protected appropriately. Special attention should be given to protection of the eyes in order to avoid direct contact with ice packs during deep hypothermia. Long extensions to vascular lines are necessary to allow access to administration and monitoring ports while ice packs are in place around the head and neck.

Pre-cardiopulmonary bypass

Antibiotic prophylaxis should be given according to local protocol. At our centre we administer both cefuroxime and vancomycin before and after CPB. Our practice is to routinely reverse the effect of preoperative vitamin K inhibitor-induced anticoagulation with parenteral vitamin K. We use aprotinin to reduce blood loss in all patients undergoing PEA. We administer a loading dose of 2 million units and add 2 million units to the CPB circuit prime. An infusion

of 500,000 units per hour is continued until the end of surgery. Methylprednisolone 1g is given for putative neuroprotection prior to the start of CPB. Strict glycaemic control should be commenced with the use of an insulin infusion. We aim to maintain blood glucose at 6-10 mmol/L.

Establishment of CPB

The surgical approach for PEA involves median sternotomy, pericardiotomy and commencement of CPB. Systemic anticoagulation is achieved using unfractionated heparin 400 IU/kg. Bicaval venous drainage is performed by two-stage cannulation of the right atrium and right-angled cannulation of the superior vena cava. Arterial return is to the ascending aorta. As well as the use of aprotinin, other blood conservation strategies at our centre include the use of acute normovolaemic haemodilution and cell salvage. Acute normovolaemic haemodilution is performed via the CPB circuit: autologous blood is collected for later re-infusion and replaced with human albumin solution. Cell salvage occurs throughout the operation and can be continued postoperatively in the intensive care unit if required.

Cooling

On initiation of CPB, systemic cooling is commenced to a temperature of 20°C controlled by the CPB circuit. A cooling jacket is positioned around the right ventricle. Ice packs are placed around the head and neck, carefully avoiding direct contact with the eyes. A circulating cold water cooling helmet placed around the head has been recommended as an alternative to ice packs [3]. This device may provide better surface cooling of the head, particularly the posterior aspect, than the application of ice packs. In order to achieve an even distribution of cooling, a gradient of no more than 5°C is maintained between the CPB arterial blood temperature and the nasopharyngeal and bladder temperatures. Haemodilution to a haematocrit of approximately 24% reduces blood viscosity and optimises blood flow. During the hypothermic period, our practice is to use pH stat arterial blood gas analysis in order to increase cerebral blood flow and promote uniform brain cooling and rewarming. We continuously monitor carbon dioxide partial pressure during CPB by connecting the gas analysis line from the CPB oxygenator to the capnograph on the anaesthetic machine. Complete cooling to a sustained brain and core temperature of 20°C usually requires up to 60 minutes.

Deep hypothermia

The operation involves endarterectomy of first the right and then the left pulmonary artery during deep hypothermia. On each side, the pulmonary artery is exposed and opened and the tip of the pulmonary artery catheter is lifted out of whichever vessel it has floated into. The dissection plane for the endarterectomy is established and continued until bronchial circulation backflow impairs visualisation. At this point, the ascending aorta is cross-clamped and antegrade cardioplegia is delivered into the aortic root. At our

centre selective antegrade cerebral perfusion (SACP) during deep hypothermia is used routinely in preference to complete circulatory arrest. The effect of SACP during PEA on neurological outcome has not yet been conclusively defined [11]. Isolation of the cerebral circulation for SACP is initiated by the application of a cross-clamp to the aortic arch distal to the origin of the left common carotid artery and proximal to the left subclavian artery. During SACP, right radial arterial pressure reflects cerebral arterial pressure, and femoral arterial pressure reflects arterial pressure distal to the aortic cross-clamp. In our practice, transcranial cerebral oximetry has proven useful to detect regional cerebral hypoxaemia due to misplacement of the distal aortic cross-clamp. Blood flow is delivered to the cerebral circulation at approximately 1.0-1.5 L/min and the right radial arterial pressure is maintained at 40-60 mmHg. Collateral blood flow to the spinal cord, abdominal organs and lower limbs results in a right femoral arterial pressure of 10-20 mmHg. If blood from the bronchial circulation continues to obscure the surgical field, periods of DHCA are limited to 20 minutes at 20°C with 10-minute periods of reperfusion. The physiological targets during deep hypothermia include haematocrit 24%, acid-base neutrality, normocarbia, potassium 5.0-6.0 mmol/L and glucose 6-10 mmol/L. Thromboelastography is performed during deep hypothermia to identify developing coagulopathy. When bilateral endarterectomies are complete and both vessels are closed, rewarming is commenced.

Rewarming

During rewarming to normothermia, the operating theatre ambient temperature is increased and the temperature-controlled water mattress and forced air blanket are set to normothermia. Again a gradient of no more than 5°C is maintained between the CPB arterial blood temperature and the nasopharyngeal and bladder temperatures.

Hyperthermia must be avoided and the perfusate temperature is maintained at less than 37.5°C. In order to avoid excessive filling pressures, aggressive diuresis is commenced using mannitol and furosemide. Haemofiltration is performed via the CPB machine to raise the haemocrit, and harvested autologous blood is transfused.

Defibrillation may be necessary if sinus rhythm is not restored spontaneously during rewarming. Mechanical ventilation with a low fractional inspired oxygen concentration is commenced using a mobile intensive care ventilator. Complete rewarming may require up to 120 minutes and during this time other cardiac or thoracic surgical procedures may be performed.

Separation from CPB

Prior to separation from CPB, a low dose dopamine infusion is recommenced and temporary pacing is usually started via epicardial leads applied to the right atrium and right ventricle. Protection of the lungs from barotrauma and oxygen-induced absorption atelectasis is crucial during this period. Mechanical ventilation is continued with a mo-

derate fractional inspired concentration of oxygen, PEEP of 5-10 mmHg and limited plateau airway pressures. Addition of further inotropic support may be necessary during separation from CPB and the use of TOE is helpful to guide therapy. Our preference is a combination of enoximone and noradrenaline to support right ventricular function, and the use of adrenaline if left ventricular function is impaired. Inhaled nitric oxide and nebulised iloprost may be necessary to aid separation from CPB by inducing pulmonary vasodilation. We advocate the early use of intra-aortic balloon counter-pulsation in the setting of haemodynamic instability. Protamine is given to reverse heparin-mediated anticoagulation and blood remaining in the CPB machine is processed by cell salvage. At our centre the use of crystalloid is avoided following CPB and instead we opt for albumin solution for fluid replacement.

Post-cardiopulmonary bypass

The post-CPB pulmonary artery pressures, cardiac output and PVR are recorded. An immediate and sustained decrease in pulmonary artery pressures should be combined with an increase in cardiac output and decrease in PVR compared to preoperative values [3]. The endotracheal tube should be checked for the presence of blood that may indicate acute pulmonary haemorrhage or the presence of frothy tracheal secretions secondary to acute pulmonary oedema due to reperfusion injury. Pulmonary haemorrhage may require fiberoptic bronchoscopy, lung isolation manoeuvres, application of PEEP, endobronchial administration of vasoconstrictor agents and control of pulmonary hypertension prior to definitive surgical management [12]. The management of reperfusion pulmonary oedema is primarily supportive but severe cases may require extracorporeal membrane oxygenation.

If mediastinal haemorrhage is difficult to control following CPB, blood product administration should be based on contemporaneous thromboelastography and laboratory coagulation studies. Once haemostasis is secured, thoracic drains are placed and the sternotomy is closed. During transfer to the intensive care unit, our practice includes the continuation of mechanical ventilation without disconnection of the ventilator and the use of portable monitoring.

Intensive care management after pulmonary endarterectomy

After PEA, patients at our centre receive propofol by continuous infusion for sedation and mechanical ventilation is continued in intensive care. The avoidance of large tidal volumes and high airway pressures may reduce postoperative complications [13]. Ventilatory support is gradually weaned and most patients are extubated within 12-24 hours. Temporary epicardial pacing and inotropic support are continued during this period. Fluid is replaced with albumin solution and haemoglobin is maintained above 10 g/dL. A negative overall fluid balance is maintained with regular doses of mannitol and furosemide. Antibiotic prophylaxis

is continued for 24 hours. Anticoagulation with low-molecular-weight heparin is commenced prior to restarting oral anticoagulation.

Specific complications following PEA that contribute to the early morbidity and mortality include residual postoperative pulmonary hypertension, reperfusion pulmonary oedema, pulmonary haemorrhage and acute neurological dysfunction [15]. Patients with residual pulmonary hypertension may benefit from inhaled nitric oxide, intravenous epoprostenol or nebulised iloprost [8]. The incidence of reperfusion pulmonary oedema may be reduced by treatment with a selectin-antagonist [15]. Patients with residual pulmonary hypertension and reperfusion pulmonary oedema may benefit from recruitment manoeuvres and high PEEP to improve oxygenation [16]. Acute neurological dysfunction may be manifested by delirium, seizure activity or focal neurological deficits. These patients usually improve with appropriate intensive care management.

Conclusion

Anaesthetists play a vital role in the perioperative management of patients with CTEPH undergoing PEA. Adequate preoperative evaluation, meticulous intraoperative management and skilled multidisciplinary care are essential for a successful PEA programme.

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