Surgical Management of Pulmonary Embolus

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Abstract

There is mounting evidence to guide the clinician in the management of both the acute presentation of pulmonary embolus and its chronic state. In this article we will review the role of surgery in both. Its role in acute presentation is not so clear despite 85 years passing since the first reported case of surgical pulmonary embolectomy. Pulmonary embolus is a particularly life-threatening complication when combined with shock, hypotension or right ventricular dysfunction. Essentially, surgical embolectomy has been reserved for high-risk patients. The current survival rate is around 70%. The treatment of choice for most patients with symptomatic chronic thromboembolic pulmonary hypertension is surgical disobliteration by pulmonary endarterectomy, a comparatively novel surgical procedure. This is the only treatment proved to offer significant symptomatic and prognostic benefit and should be distinguished from pulmonary embolectomy for acute embolus. The in-hospital survival rate (95%) for pulmonary endarterectomy in specialist centres is excellent, and patients enjoy a significant reduction in symptoms and increased life expectancy.

Keywords

Pulmonary embolus, venous thromboembolism, pulmonary embolectomy, thrombolysis, chronic thromboembolic pulmonary hypertension, pulmonary endarterectomy

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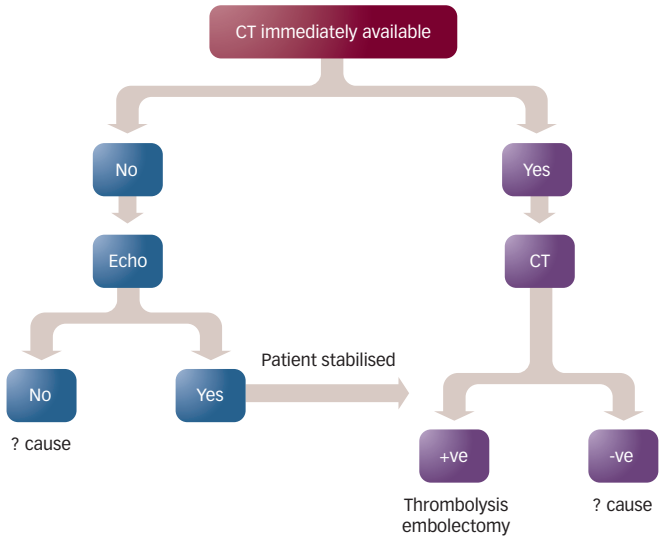
There is emerging clarity in the management of pulmonary embolism (PE) as information has been collated to form guidelines addressing its diagnosis and management.[1] This is appropriate as PE is common, and was observed in 18% of all autopsies in a recent Swedish study,[1] with an incidence in hospital patients of 0.4%. It has a mortality rate of 7–11%,[1] killing up to 10% of patients within the first hour of formation. There is a mounting body of evidence to guide the clinician in the management of both the acute presentation of PE and its chronic state. We will review the role of surgery in both. Surgery has gained an early and authoritative foothold in the management of chronic thromboembolic pulmonary hypertension (CTEPH). Its role in acute presentation is not so clear, despite 85 years passing since the first reported case of surgical pulmonary embolectomy.[2] This article addresses PE as a complication of deep vein thrombosis (DVT). We direct the reader elsewhere for the management of non-thromboembolic PE (septic, amniotic fluid, systemic venous air, fat and foreign body embolus).

Pulmonary emboli suddenly obstruct pulmonary arteries as a complication of DVT, forming the clinical spectrum of venous thromboembolism (VTE). PE is a particularly life-threatening complication when combined with shock, hypotension or right ventricular dysfunction. VTE is recognised in all surgical disciplines but appears to most commonly complicate orthopaedic procedures. Treatment is life-saving and begins with avoidance of DVT through appropriate prophylaxis. Surprisingly, a recent survey showed only 40% of surgical patients to be receiving VTE prophylaxis in the peri-operative period. A substantial volume of the pulmonary vascular bed has to be lost (≥50%) to cause haemodynamic upset or right ventricular dysfunction. However, smaller thrombi may affect the peripheral lung vasculature giving a different clinical picture characterised by pulmonary infarction, pleuritic chest pain and haemoptysis. Many emboli no doubt impact without symptoms, making recognition difficult and treatment more so. To help with recognition of PE a number of diagnostic scoring systems have evolved (e.g. Geneva and Wells) of which the Wells[1] is perhaps the simplest (see *Table 1*), resting as it does so heavily on clinical suspicion. Imaging confirms the diagnosis, probably most commonly involving spiral chest computerised tomography (spiral CT). Confusion arises through a lack of an agreed nomenclature. With this in mind recent guidelines offer a language for PE that is based on risk: high and non-high (intermediate and low non-high) (see *Table 2*). High-risk PE appears to have a frequency of 5–10% of all PEs with 50% of all cases showing evidence of right ventricular dysfunction. High-risk PE is often fatal, with a mortality of approximately 50%. When present, right ventricular dysfunction appears to double mortality from PE.[1] Treatment follows three clear steps, and is elegantly summarised in *Figure 1*:

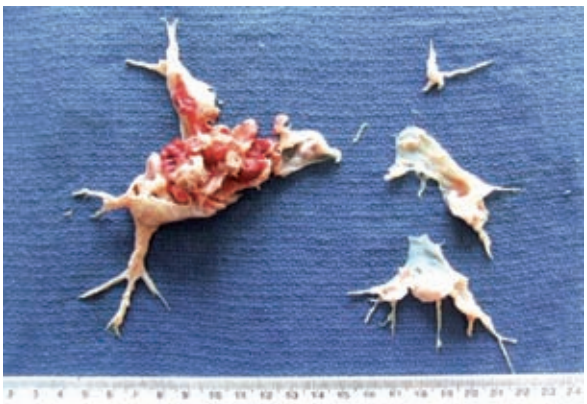
- prompt treatment with intravenous heparin as soon as PE is suspected and before diagnosis is confirmed;
- supportive therapy made up of oxygen therapy, pressor (noradrenaline) and/or inotrope (adrenaline) and pulmonary vasodilators (nitric oxide, sildenafil); and
- first-line treatment is thrombolysis.

Figure 1: Investigation and Treatment for Presence of High-risk Pulmonary Embolism



CT = computed tomography; ECHO = echocardiogram. Source: European Heart Journal, *with kind permission.*

Figure 2: Pulmonary Endarterectomy Specimen



Treatment is effective (reducing fatality to 9.4% from 19% with heparin alone in high-risk cases[3]) and is relatively safe with a cumulative major bleeding rate of 13%. Overall, 1.8% suffer intracranial or fatal haemorrhage.[3] Pulmonary embolectomy is undertaken when there is a failure of or contraindication to thrombolysis (see *Table 3*). Some groups recommend surgical embolectomy in the presence of a free-floating clot within the right atrium or ventricle or when a clot is lodged in a persistent foramen ovale, threatening to become a paradoxical embolus.[4]

Clearly, recommendations for embolectomy are relative and should be modified to fit the risks of the case in hand, aiming for survival benefit. It is probable that, with cardiac surgery available, a patient who has arrested will proceed directly to open surgical embolectomy. The following report illustrates the role of surgery for acute PE. Meneveau and colleagues reported the outcome of all patients treated with thrombolysis for PEs in their hospital. In the 10 years to 2005 this group treated 488 patients. Forty patients (8.2%) showed no sign of improvement after 36 hours and were treated by either repeat thrombolysis (26/40) or surgical embolectomy (14/40), not randomly but with individual surgeon's preference. One patient died following surgery but 10 died after repeat thrombolysis

Table 1: The Wells Scoring System[1]

		Points
Predisposing factor	Previous DVT/PE	1.5
	Recent surgery/immobilisation	1.5
	Cancer	1
Symptoms	Haemoptysis	1
Clinical signs	Tachycardia >100 beats/minute	1.5
	Clinical impression of PE	3
Clinical judgement	Alternative diagnosis less likely than PE	3
Total		12.5

Probability of pulmonary embolism (PE) is low if Wells score is 0–1, intermediate if 2–6 and high if ≥7. DVT = deep-vein thrombosis. Source: European Heart Journal, *with kind permission.*

Table 2: Classification of Pulmonary Embolism

PE Early Mortality Risk	Clinical Markers			Treatment Implications
	Shock/Haemod. Upset	RVD	MI	
High (>15%)	+	+	NA	Thrombolysis/ PE
Non-high/ intermediate (1–14%)	–	+	+	Thrombolysis/ anticoagulation
	–	+	+	
	–	–	+	
Low (<1%)	–	–	±	Thrombolysis/ anticoagulation

PE = pulmonary embolism; Haemod. = haemodynamic; NA = no influence on outcome; RVD = right ventricular dysfunction MI = myocardial injury. Source: European Heart Journal, *with kind permission.*

Table 3: Contraindications for Thrombolysis

Absolute Contraindications
Haemorrhagic stroke or stroke of unknown origin at any time
Ischaemic stroke in preceding six months
Central nervous system damage or neoplasms
Recent major trauma/surgery/head injury (within preceding three weeks)
Gastrointestinal bleeding within the last month
Known bleeding
Relative Contraindications
Transient ischaemic attack in preceding six months
Oral anticoagulant therapy
Pregnancy or within one week post partum
Non-compressible punctures
Traumatic resuscitation
Refractory hypertension (systolic blood pressure 180mmHg)
Advanced liver disease
Infective endocarditis

Source: European Heart Journal, *with kind permission.*

(p=0.07). Post-procedural bleeding was confined to the repeat thrombolysis group, where it was found to be fatal in all. Repeat PE was also confined to the repeat thrombolysis group.[5] Surgical embolectomy has essentially been reserved for high-risk patients (see *Table 2*).

Open removal of the centrally obstructing embolus is carried out through a main pulmonary arteriotomy through a median sternotomy. Originally this was described without bypass (Trendelenburg procedure);[2] nowadays, both cavae are cannulated, drained and snared, allowing free systemic venous drainage (in-flow occlusion) and oxygenated arterial return into the systemic

arterial system (aorta or femoral artery). Cardiac ischaemia is avoided during open pulmonary artery exploration. The obstructing clot is removed with grasping forceps or a balloon-tipped embolectomy catheter. There is an assumption that all troublesome clots will be removed in this way. Zabbari and colleagues[6] demonstrated "a significant volume of clot" removed by retrograde flush in their report of 11 cases of surgical pulmonary embolectomy. The role of retrograde flushing is logical but not clear.

Numerous small case series of surgical embolectomy have been reported recently with survival reported between 40 and 80%, but overall in the order of 70%.[7,8] Of particular note, surgical embolectomy is an unusual procedure occurring no more than an average of eight times per year in centres reporting their experience. Stein and colleagues[9] reviewed 46 case series, concluding that risks to life with surgical pulmonary embolectomy appear to have fallen from 32% before 1985 to 20% after this time. PE with cardiac arrest had a particularly poor outcome (56% mortality) compared with high-risk patients without this complication (29%). A similar finding was reported by Alain Pavie's group in France where only 43% of patients (n=14) with cardiogenic shock due to PE surviving surgical embolectomy, in contrast to 100% survival of seven patients who did not have shock.

Pulmonary emboli suddenly obstruct pulmonary arteries as a complication of deep vein thrombosis, forming the clinical spectrum of venous thromboembolism.

Undoubtedly, survival following embolectomy will improve if undertaken on lower-risk groups; however, it may well be that little or no survival advantage will be gained by performing surgery in these groups. Similarly, we do not know the outcome of embolectomy on the late and restricting complication of CTEPH.

Pulmonary embolectomy has been reported in over 300 cases as a percutaneous procedure with catheter-based devices.[10] Here the device is introduced intravenously into the pulmonary circuit via the right-sided heart chambers where they may remove the clot by aspiration with reported success in some 80% of high-risk patients.

Reviewing two large PE registries[11,12] provides a description of the current role of surgery in the management of acute presentation of PE. Surgical embolectomy was performed in 1% of patients with massive PE and cardiogenic shock. The in-hospital mortality rate was 30%. Survival appeared to be much the same for catheter-based embolectomy.[10] This suggests mortality is linked to pulmonary embolisation rather than method of removal of PE. Vena caval filters have the advantage of capturing recurrent embolus, but are associated with long-term problems. Temporary filters are available and will be discussed as we consider CTEPH below.

So, are we any clearer over the role of surgery in the management of acute PE? It would be reasonable to conclude that surgical pulmonary embolectomy has a place in the management of acute PE and that:

- it is an unusual procedure, but there is increasing interest in the role of surgery in the management of acute PE;
- the patient shows no improvement after thrombolysis, and there is a clear role for surgical embolectomy;
- if there is a clear contraindication to thrombolysis', surgery is indicated;
- in the case of cardiac arrest and cardiac surgery is available, it can be used; and
- the role of vena caval filters is probably confined to temporary placement.

The results of this high-risk and infrequently performed procedure show a high mortality rate, which may be falling with time. It is apparent that case selection has a profound effect on mortality. A comparison of embolectomy with thrombolysis and conventional clot removal and retrograde flushing of peripheral clot would be of interest. The future role of catheter embolectomy is not clear, but will presumably take place where there is no cardiac surgery. There is no evidence about the effect of treatment of acute embolus on the development of later CTEPH.

Chronic Disease

Following acute PE, up to 3.8% of patients will develop CTEPH within two years.[13] This is defined by a mean pulmonary artery pressure of >25mmHg at rest, with the presence of typical unmatched perfusion defects in the pulmonary vasculature on imaging. However, in over 50% of patients with confirmed CTEPH, there is no evidence of previous VTE.[15] Unlike the situation with an acute embolus, the changes on CT imaging can be subtle and easily missed. It is likely that the disease is still underdiagnosed, and the possibility of pulmonary hypertension (PH) should be considered in all patients presenting with unexplained exertional breathlessness. Increased pulmonary vascular resistance (PVR) leads to right heart failure and historically prognosis without treatment was poor, with up to 50% of patients dying within two years.[14] CTEPH has recently been comprehensively reviewed.[15]

Recommendations for embolectomy are relative and should be modified to fit the risks of the case in hand, aiming for survival benefit.

The treatment of choice for most patients with symptomatic CTEPH is surgical disobliteration by pulmonary endarterectomy. This is the only treatment proved to offer significant symptomatic and prognostic benefits and should be distinguished from pulmonary embolectomy for acute PE as described above. Indeed, although a more recent intervention, and a far more technically demanding procedure, the evidence base for pulmonary endarterectomy in chronic disease is much clearer than that for acute embolectomy and the outcome is far superior, with most experienced units

achieving a 95% hospital survival rate.[16] Operability is determined by the correlation between the degree of visible disease in imaging studies and the haemodynamic dysfunction at right heart catheterisation (absolute pulmonary arterial [PA] pressure, cardiac output and the function of both, i.e. PVR). Some patients with a PVR disproportionately higher than the segmental obstruction visible by imaging derive less benefit from endarterectomy and have a higher risk of post-operative mortality because they have a proportion of secondary 'microvascular' disease contributing to PVR, but not improved by endarterectomy. Decision-making in this patient group with predominantly distal disease often depends on the experience of the surgical centre.

Many units have reported excellent early results after pulmonary endarterectomy with in-hospital mortality of only 5% once a few hundred procedures have been experienced.

The operation as performed today was developed mainly by Jamieson at the University of California, San Diego (UCSD); this centre is the world leader, having completed over 2,500 procedures. In Europe, there is also substantial experience, with three of the largest case series being in France, the UK and Germany.[17–19] However, this remarkably effective treatment is only 30 years old. Although acute embolic occlusion of the pulmonary arteries was relatively easily understood, the concept of chronic occlusion after repeated embolism took some time to become established. By the 1930s, case reports were beginning to describe the chronic form of the disease discovered at *post mortem*. The first successful planned pulmonary endarterectomy was by Dr Hufnagel in 1962. The physician caring for the patient at that time was Dr Moser, who subsequently moved to UCSD and with Dr Braunwald reported the first case of successful pulmonary endarterectomy at UCSD.[20] Cabrol and Dor reported successful operations in Europe, but by the mid-1980s fewer than 100 procedures had been performed worldwide.

The fundamental aim of the surgery is to perform a full endarterectomy (not embolectomy or thrombectomy) of both pulmonary vascular trees. The operation is performed via a median sternotomy, similar to conventional cardiac surgery, with hypothermic cardiopulmonary bypass (CPB), and right and left pulmonary arteriotomies within the pericardium. Adequate visualisation for distal dissection necessitates a reduction in bronchial arterial collateral return to the pulmonary arteries. Traditionally, this has been overcome by periods of complete deep hypothermic circulatory arrest (DHCA) for periods of 20 minutes at 200ºC, and this technique remains the gold standard.[16]

More recently, a number of alternative techniques designed to avoid complete circulatory arrest have been advocated for performance of the endarterectomy.[21] Our personal view is that dissection is technically easier with complete DHCA, but that it is not necessary in all patients and continued cerebral perfusion appears to be technically feasible in many patients. At Papworth Hospital, we have recently completed a randomised, controlled trial to compare the techniques in terms of the neurological and pulmonary outcomes (PEACOG trial).

The main element of the operation is the removal of all accessible obstructive material. The right pulmonary artery is exposed between the ascending aorta and superior vena cava (SVC) and opened with a longitudinal extended beneath the SVC laterally. The lumen of the right pulmonary artery is exposed and the endarterectomy plane raised using a scalpel and spatula. The dissection plane is within the superficial media of the vessel wall that is only 1–2mm in thickness; perforation of the artery wall within the lung parenchyma is difficult to repair and usually fatal. By the use of a nerve hook, forceps and a sucker–dissector, the plane can be extended circumferentially and then distally by careful traction as far as possible with the intention of tracing the endarterectomy into all the affected segmental and subsegmental vessels. A cast of the inner layer of the PA tree is then dissected free moving towards the periphery (see *Figure 2*). The procedure is then repeated on the left side, with access achieved through the shorter left pulmonary artery by an arteriotomy in the pulmonary trunk.

After completion of the endarterectomies, the patient is slowly re-warmed on full cardiopulmonary bypass (CPB) flow to a core temperature of 36ºC. Any concomitant cardiothoracic surgical procedures can be completed during this slow re-warming phase of the operation.

The patient is then weaned from CPB, keeping the right-sided filling pressures low, guided by invasive haemodynamic monitoring. Following surgery, patients are transferred to the intensive care unit and remain sedated and ventilated over the first night. Many patients can be extubated by the first post-operative day. Most of the general principles of post-operative cardiac surgical care apply and in addition we aim to avoid any factors that might increase PVR. Anticoagulation is re-started early following surgery and continued for life.

Longer-term survival of patients following pulmonary endarterectomy is substantially better than that expected in patients with untreated chronic thromboembolic pulmonary hypertension.

Many units have reported excellent early results after pulmonary endarterectomy in the last few years, with in-hospital mortality of only 5% once a few hundred procedures have been experienced. As with all series of surgical patients, outcome is often determined by case mix once a learning curve for the procedure has been overcome. An intra-operative disease classification has been established and outcome is better for patients with more proximal (type 1 and 2) disease than in those with more distal (type 3)

disease.[22] The two most serious complications are residual PH (usually due to a higher proportion of microvascular disease than anticipated) and reperfusion lung injury. The latter is a form of acute lung injury that is present to some extent in up to 20% of patients and is also seen in a similar proportion of lung transplant recipients. Often a combination of both problems occurs as residual PH exacerbates reperfusion damage and the resulting hypoxia and hypercarbic acidosis further increases PVR so a vicious cycle develops. When severe, these problems account for the majority of the fatalities in the post-operative period. There may be some benefit in supporting severely compromised patients in the early post-operative period with extra corporeal membrane oxygenation (ECMO) provided an adequate endarterectomy has been obtained. We have used veno-arterial ECMO in approximately 5% of our recent patients in the last few years, with four of seven patients surviving to discharge from hospital.[23]

Most reports detail substantial early post-operative haemodynamic improvement, with an immediate fall in PA pressure and a reduction in PVR to approximately one-third of the pre-operative level. The unique nature of a national, designated PH service and single centre commissioned for pulmonary endarterectomy surgery in the UK has facilitated extended patient follow-up.[18,24] Modern medical management of CTEPH has resulted in better survival than expected, with those patients undergoing endarterectomy benefiting the most.[24] In a recent review of 230 patients surviving to three-month follow-up in the UK, we demonstrated a significant increase in six-minute walk distance compared with pre- operation (276.3±17 to 375.8±14m; p<0.001). Before surgery there were no patients in New York Heart Association (NYHA) class 1, 12.4% were in NYHA class II, 62.7% were in NYHA class III and 24.9% were in NYHA class IV. At three months following endarterectomy, 30.9% were in NYHA class I, 55.9% were in NYHA class II, 12.3% were in NYHA class III and only 0.5% were in NYHA class IV (p<0.001 versus pre-operation). Conditional survival from three-month follow-up was 94% at three years, 92.5% at five years and 88.3% at 10-year follow-up.[18]

Conclusion

In summary, pulmonary endarterectomy is the treatment of choice for patients with CTEPH and mortality from surgery can be reduced to 5% in most experienced centres, which reflects improved peri-operative care and better understanding of patient selection. Patients derive significant reduction in PA pressure and PVR immediately following complete endarterectomy. This early haemodynamic improvement is sustained at three months and translates into improved exercise capacity and reduced symptoms. Longer-term survival (to five years at least) is substantially better than that expected in patients with untreated CTEPH. ■

Stephen Ralph Large is a Cardio-thoracic and Transplant Surgeon at Papworth Hospital in Cambridge, a position he has held since 1989. He has developed a particular interest in surgery for the failing heart and ran the heart transplant programme for 20 years, making Papworth the most active centre for intra-thoracic transplantation in the UK and one of the most active internationally. He currently enjoys a research partnership with Stanford California and Winnipeg Canada. Heart donation has been his career-long research interest. Interest in the failing heart has led to the development of a national programme of mechanical heart support and strategies to maximise cardiac transplant activity. Dr Large has authored 215 papers. Part of his original brief for the hospital was the establishment and provision of a programme of arrhythmia surgery. This spawned surgery for atrial fibrillation in 1992, which led to the development of the now widely accepted Papworth Cox-Maze operation.

David Phillip Jenkins is a Consultant at Papworth Hospital, a position he has held since 2001, and has led the national pulmonary endarterectomy programme in the UK since 2004. His current workload includes all aspects of adult cardiac surgery. Dr Jenkins' specialist experience includes intra-thoracic transplantation and mechanical circulatory support including ventricular assist devices and extracorporeal membrane oxygenation (ECMO). Dr Jenkins' research interests are related to pulmonary hypertension, pulmonary endarterectomy surgery and myocardial protection. He is an educational supervisor and a Royal College of Surgeons tutor, and has an interest in the training of junior surgeons. He graduated in 1989 and trained in surgery in London, trained in cardiac surgery on the west London rotation circuit and completed a period of research into myocardial protection at the Hatter Institute at the University College London (UCL), where he was awarded his MS.

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