A More Aggressive Approach to Emergency Embolectomy for Acute Pulmonary Embolism

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OBJECTIVE: To examine operative outcomes after acute pulmonary embolectomy (APE), a recently adopted, more aggressive surgical approach.

PATIENTS AND METHODS: We retrospectively identified patients who underwent surgical APE from April 1, 2001, through March 31, 2009, and reviewed their clinical records for perioperative outcome. Operations were performed with normothermic cardiopulmonary bypass and a beating heart, absent a patent foramen ovale. For completeness, embolectomy was performed via separate incisions in the left and right pulmonary arteries (PAs) in 15 patients.

RESULTS: Of the 18 patients identified, the mean age was 60 years, and 13 patients (72%) were men. Thirteen patients (72%) had been hospitalized recently or had systemic disease. The preoperative diagnosis was established by echocardiography or computed tomography (or both). The median (range) follow-up time for all surviving patients was 16 months (2-74 months). Indications for APE included cardiogenic shock (n=12; 67%) and severe right ventricular dysfunction as shown by echocardiography (n=5; 28%). Seven patients (39%) had an embolus in transit. Seven patients (39%) experienced cardiopulmonary arrest before APE. Four early deaths (22%) occurred; all 4 of these patients had preoperative cardiopulmonary arrest, and 2 had APE via the main PA only, without branch PA incisions. Two late deaths (11%) occurred. Right ventricular function improved in all survivors.

CONCLUSION: The results of emergent APE are encouraging, particularly among patients without cardiopulmonary arrest. It should not be reserved for patients in extremis; rather, it should be considered for patients with right ventricular dysfunction that is an early sign of impending hemodynamic collapse.

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ACCP = American College of Chest Physicians; APE = acute pulmonary embolectomy; CPR = cardiopulmonary resuscitation; ECMO = extracorporeal membrane oxygenation; IVC = inferior vena cava; PE = pulmonary embolism; PEA = pulseless electrical activity; PFO = patent foramen ovale; PTE = pulmonary thromboendarterectomy; RV = right ventricular

Acute massive pulmonary embolism (PE) is associated with considerable mortality and morbidity, despite advances in diagnosis and therapy.¹ Aggressive anticoagulation is the mainstay of therapy. However, in the presence of hemodynamic compromise, pharmacologic lytic therapy² or catheter-based rheolytic therapy³ may be considered. Surgical embolectomy became the treatment of last resort at most institutions after early reports showed poor outcomes.^{4,5} However, in many reported cases, surgery was considered only after hemodynamic collapse, and a high percentage of deaths occurred among patients with preoperative cardiopulmonary arrest. More recent reports suggest satisfactory outcomes when echocardiographic

evidence of right ventricular (RV) dysfunction prompts surgical intervention before hemodynamic collapse occurs.^{6,7} On the basis of these reports, we have recently adopted a more aggressive approach to acute pulmonary embolectomy (APE) at our institution. Accordingly, we examine our current operative results of APE.

PATIENTS AND METHODS

All patients in this study gave authorization to be involved in clinical research. The Mayo Clinic Institutional Review Board approved this retrospective study, waiving the requirement for study-specific consent.

Medical records from April 1, 2001, through March 31, 2009, were searched to identify patients with acute PE who underwent emergency APE at Mayo Clinic (Rochester, MN). Data abstracted from the patient records included medical history, clinical notes, surgical notes, and echocardiographic and radiologic findings. Late follow-up information was obtained by reviewing clinical records of all surviving patients.

All procedures were performed via median sternotomy with bicaval cannulation and normothermic cardiopulmonary bypass. The right atrium was opened if an embolus was in transit, and aortic cross-clamping was performed only if a patent foramen ovale (PFO) was present. A longitudinal incision in the main pulmonary artery was made in all patients; however, more recently, we extended this arteriotomy onto the left pulmonary artery and explored the right pulmonary artery directly between the superior vena cava and aorta in the same manner as we perform pulmonary thromboendarterectomy (PTE).⁸ The pulmonary arteries were gently explored using stone forceps, and both pleural spaces were routinely opened and lungs

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TABLE 1. Patient Characteristics (N=18)

Age (y), mean (range)	60 (28-78)
Male	13 (72)
Preoperative hypotension	12 (67)
Preoperative inotrope	9 (50)
Preoperative intubation	9 (50)
Preoperative cardiopulmonary resuscitation	4 (22)
Recent hospitalization or systemic disease	13 (72)
Cancer	4 (22)
Neurosurgery	3 (17)
Trauma	2 (11)
Cesarean delivery	1 (6)
Gastrointestinal tract bleeding	1 (6)
Cholecystectomy	1 (6)
Nephrectomy	1 (6)
Preoperative deep venous thrombosis	9 (50)
Method of preoperative diagnosis	
Computed tomography and echocardiography	12 (67)
Echocardiography only	5 (28)
Clinical findings	1 (6)

Data are provided as number (percentage) of patients, unless otherwise indicated.

gently massaged and suctioned. An inferior vena cava (IVC) filter was placed before or within 24 hours after the procedure.

RESULTS

Eighteen patients met the inclusion criteria for the study. Patient characteristics are presented in Table 1. The diagnosis of massive PE was established by echocardiography or computed tomography (or both) (Figure 1). The principal indications for APE were cardiogenic shock (n=12; 67%), severe RV dysfunction as shown by echocardiography (n=5; 28%), and large PFO (n=1; 6%) (Table 2). Seven patients (39%) had an embolus in transit, including one in transit across a PFO (Figure 2). Fifteen patients (83%) underwent extended arteriotomy. Seven patients (39%) experienced cardiopulmonary arrest (pulseless electrical activity [PEA]) before APE. In 3 patients, PEA occurred in the operating room (all survived). Right ventricular function was immediately improved in all survivors (Table 3). The median hospital stay was 9 days (range, 5-38 days).

EARLY DEATHS

Four early deaths (22%) were recorded; these patients all had experienced PEA preoperatively. One patient was a 43-year-old woman who had a brief period of cardiopulmonary arrest during an orthopedic procedure. Cardiac surgeons were consulted. Intraoperative transesophageal echocardiography showed a right atrial thrombus and a markedly enlarged RV. After a presumed diagnosis of APE, the chest was opened under ongoing cardiopulmo-

FIGURE 1. Pulmonary embolus. Top and middle, Computed tomograms. Bottom, Surgical specimen.

nary resuscitation (CPR). Emergent cardiopulmonary bypass was initiated, and the pulmonary arteries were explored via the main pulmonary artery, with scant thrombus removed. The patient could not be weaned from cardiopulmonary bypass, and an RV assist device was placed. The patient died 2 days later of multisystem organ failure and persistently high pulmonary pressures, suggesting incomplete embolectomy.

The second patient was a 62-year-old man who had undergone a right hemicolectomy a week prior for a benign

TABLE 2. Indications for Acute Pulmonary Embolectomy (N=18)

Indication	No. (%) of patients
Cardiogenic shock	12 (67)
Cardiopulmonary arrest	
At admission	4 (22)
In operating room	3 (17)
Contraindication to thrombolytic agents	
Recent surgical intervention	10 (56)
Recent major trauma	2 (11)
Major bleeding	1 (6)
Large right atrial–right ventricular thrombus	7 (39)
Right ventricular hemodynamic dysfunction	5 (28)
Large patent foramen ovale	1 (6)

adenoma. He was diagnosed as having a PE, and initial echocardiography showed mild-to-moderate RV dysfunction. After admission to another hospital, his condition progressively deteriorated to PEA, and he was transferred to our clinic on inotropic support 24 hours after the embolism was diagnosed. Thrombolytic therapy was considered, but there was concern for gastrointestinal bleeding. He underwent emergent APE but could not be weaned from cardiopulmonary bypass and returned to the intensive care unit on extracorporeal membrane oxygenation (ECMO) support. On postoperative day 5, he was weaned from ECMO but was neurologically unresponsive. Computed tomography of the head showed considerable brain injury. In accordance with the family's wishes, support was withdrawn.

The third patient was a 27-year-old man who presented to the emergency department with sudden-onset diaphoresis and tachypnea. Doppler ultrasonography showed a probable deep venous thrombosis. Acute PEA developed, at which time CPR was initiated. He was transferred to the operating room for an APE after 40 minutes of ongoing CPR. Bilateral, massive clots were removed via an incision in the main pulmonary artery only, and ECMO support was initiated. On postoperative day 6, he was weaned from ECMO, but his neurologic function was very poor. Computed tomography of the head showed massive global anoxia, and support was withdrawn.

The fourth patient was a 28-year-old woman who had PEA develop 2 hours after an uncomplicated cesarean delivery. She was transferred to our clinic with a presumed PE after successful CPR. After admission, she again experienced PEA and was brought to the operating room with ongoing CPR. She underwent bilateral APE but had irreversible hypoxic brain injury. Support was withdrawn at the request of the family, 38 days postoperatively.

The overall 30-day survival rate was 83.3% (95% confidence interval, 67.8%-100.0%), and the 60-day survival rate was 77.8% (95% confidence interval, 60.8%-99.6%).

FIGURE 2. Pulmonary embolus in transit. Top, The embolus was trapped in the patent foramen ovale. Bottom, Surgical specimen.

LATE DEATHS

Two late deaths (11%) occurred. One patient died of prostate cancer 3 years after APE. The second patient was a 74-year-old man with sarcoma of the bladder who underwent APE via the main pulmonary artery only. Postoperatively, he required prolonged ventilatory support and tracheostomy. He was dismissed after a prolonged hospital course but died 4 months after the APE operation at another facility.

LATE FOLLOW-UP

All dismissed patients had an IVC filter placed before the procedure (n=2) or within 24 hours after the procedure (n=14), and patients were asked to continue oral anticoagulant medications for 6 months, with a goal international normalized ratio of 2 to 3. Follow-up was available for all surviving patients (n=14) for a median of 16 months

TABLE 3. Echocardiographic Findings (n=14)

Parameter	Preoperative value	Postoperative value
D-shaped left ventricle	10 (71)	0 (0)
Severe right ventricular dysfunction	13 (93)	3 (21)
Ejection fraction (%)	62	60
Right ventricular systolic pressure (mm Hg)	58	34
Moderate tricuspid regurgitation	6 (43)	1 (7)

Categorical data are provided as number (percentage) of patients.

(range, 2-74 months) after the operation. None of the survivors showed development of pulmonary hypertension requiring PTE.

DISCUSSION

Acute PE remains a remarkably common clinical problem, with an average annual incidence of venous thromboembolism in the general population of the United States estimated at 1 per 1000 (approximately 250,000 incident cases).⁹⁻¹¹ Although most patients recover with anticoagulation therapy alone,⁵ a subset of patients with massive APE ultimately experience hemodynamic collapse and die.^{12,13} The ideal therapy for patients with documented PE is medical management with heparin derivatives and oral anticoagulants.⁵ However, in the prethrombolytic era, surgical embolectomy was the only option for patients in shock. Yet high operative mortality rates discouraged its application, and surgical intervention fell into disfavor. In the presence of hemodynamic compromise, thrombolytic therapy is now strongly recommended (grade 1 American College of Chest Physicians [ACCP] recommendation), unless major contraindications for bleeding are present.⁵ Recent guidelines for antithrombotic therapy for patients with thromboembolic disease largely ignore the surgical option and very weakly recommend (grade 2C) pulmonary embolectomy during the initial treatment of PE.⁵ This is particularly ironic, given that this condition inspired the development of the heart-lung machine.

It has been our view that the role of surgical treatment of acute PE should be re-evaluated, and our results reported here support its more frequent use. More recent reports of surgical APE show an improvement in outcome, with mortality rates decreasing from over 30% before 1985 to 20% from 1985 through 2005.^{4,6,7} Of more importance, however, is the recognition that the bulk of operative deaths occur among patients who had preoperative PEA.^{14,15} This may partly explain the worse operative results in early series, as APE was reserved for patients in extremis. This also is consistent with our experience—all of our early deaths occurred in patients who presented with PEA and ongoing CPR. Furthermore, 3 of the 4 early deaths were due to cerebral ischemia, which likely occurred during the PEA before APE. In addition, greater attention has been paid recently to performing a complete embolectomy of both sides,^{6,16} which we also think is important for a successful, long-term outcome.

The place of surgery with regard to thrombolytic agents is unclear. There is a paucity of evidence supporting use of thrombolytic agents for acute PE. Only 11 randomized controlled trials have compared thrombolytic therapy to conventional anticoagulation in such patients,² and fewer than 800 patients are represented. Further, only 1 of the

11 studies was sufficiently powered to detect death as an end point. At best, meta-analysis¹⁷ and systematic review¹⁸ provide only a suggested benefit of thrombolytic agents over heparin for those with the highest risk of death. The MAPPET-3 study (from the Management Strategy and Prognosis of Pulmonary Embolism Registry), the largest and most recent randomized trial of the use of thrombolytic agents vs heparin alone, enrolled 256 patients with normal blood pressure but evidence of RV dysfunction. Although it showed that thrombolysis reduced the need for “escalation” of therapy, the study was criticized because of the subjective ability to use “rescue thrombolysis.”¹⁹

In its evidence-based clinical practice guidelines on antithrombotic therapy for venous thromboembolic disease, the ACCP supports thrombolytic administration to hemodynamically unstable patients with acute PE (grade 1B; strong recommendation, moderate-quality evidence).⁵ Patients with acute PE who are hemodynamically stable but have evidence of RV failure or strain are considered to have “sub-massive” PE. Such a scenario accounts for 40% to 50% of patients with acute PE.^{20,21} The data supporting the use of thrombolytic agents in such patients are less robust, and the ACCP assigns the grade 2B (weak recommendation, moderate-quality evidence) to this indication. The use of thrombolytic agents for PE-associated hypoxemia has even less supporting evidence, although it would be considered by many clinicians.²² The ACCP recommends against using thrombolytic therapy “for the majority of patients with PE” (grade 1B).⁵

Intracranial hemorrhage is the most feared complication, although it has been reported in less than 1% of patients in clinical trials and in about 3% of patients in the large ICOPER (International Cooperative Pulmonary Embolism Registry) database.^{10,23} When it occurs in association with thrombolytic use, however, intracranial hemorrhage is associated with a grim prognosis. Gastrointestinal and retroperitoneal hemorrhage, as well as bleeding from surgical incisions and sites of recent invasive procedures, can occur; in the ICOPER, 21.9% of patients who received thrombolytic therapy had a major bleeding complication (compared with 8.8% in the heparin-treated group). Pulmonary artery catheter-directed thrombolysis has not been shown to be safer or more effective than intravenous thrombolytic therapy.

Another therapeutic option for the treatment of acute PE is mechanical, nonsurgical, nonpharmacologic thrombus removal, which offers the potential of effective thrombus clearing without major bleeding. In experienced hands, such techniques may be useful,³ although it is difficult for any given center to obtain such expertise. Furthermore, there is concern that mechanical devices may dislodge the thrombus more distally into the pulmonary vasculature, making subsequent surgical approaches increasingly difficult.

Few studies have compared thrombolysis with surgical therapy. In a series of 488 patients with acute massive embolus, 8.2% did not respond to thrombolytic therapy.²⁴ Rescue surgical embolectomy resulted in a better in-hospital course compared with repeated thrombolytic treatment in patients with massive PE that did not respond to the initial thrombolysis attempt.²⁴ In a smaller study of 23 patients, follow-up computed tomographic images showed more RV and left ventricular regression in patients with APE than those receiving thrombolytic therapy alone.²⁵ Postprocedure residual RV dysfunction and clots in the pulmonary artery may have devastating effects in the future. Patients with less ideal treatment might be future candidates for chronic thromboembolic events or PTE.^{26,27} Even if surgical embolectomy is not considered initially, a clinically significant lack of response to thrombolytic agents should not be ignored. A second chance with surgical embolectomy should be given; otherwise, these patients become future candidates for PTE.

Although it is axiomatic that a more aggressive surgical approach will improve results (simply because less ill patients will also undergo surgery), waiting until PEA has occurred is too late for many patients. Early diagnosis with improved imaging techniques permits earlier intervention. As the patient outcomes are not solely a function of the size of the clot but also of the functional capability of the cardiovascular system, echocardiographic evidence of RV dysfunction should be considered in the decision-making process. Echocardiography is also helpful in identifying emboli in transit and PFO. Recently, several reports advocated prompt surgery for patients with moderate-to-severe RV dysfunction.^{6,7} Right-to-left ventricle dimensions (ratio, >0.9 on the 4-chamber view) were an independent predictor for adverse events in patients with APE.²¹

All patients had IVC filters placed before hospital dismissal because a previous report indicated that 8% of patients have recurrent PE within 3 months after presentation of massive PE.²⁴ In addition, although thrombolysis does not reduce mortality or recurrent PE within 90 days, IVC filters are associated with a reduction in 90-day mortality rates.¹ Most patients undergoing APE have an ongoing risk of deep venous thrombosis. We think that IVC filters not only have early protective effects⁶ but also are useful adjuncts to anticoagulant therapy and protect patients from future chronic emboli and a more complex surgical procedure, namely PTE.

This is a retrospective review and, as such, is influenced by typical biases. The small sample size limits the generalizability of our findings; however, our results of emergent APE were encouraging, particularly among those who had not yet experienced cardiopulmonary arrest. APE should not be reserved for patients in extremis; rather, it should be considered for patients with RV dysfunction that is an early sign of impending hemodynamic collapse. Aggressive and

accurate surgical intervention and precautions such as IVC filter placement improved early results of acute PE. The impact of such an intervention on the prevention of chronic pulmonary thromboembolic hypertension is unknown.

CONCLUSION

Although most patients with acute PE respond to medical therapy, many die of persistent pulmonary vascular obstruction and right-sided heart failure. The current results of surgical embolectomy, particularly when performed with attention to complete embolectomy via separate incisions in the right and left pulmonary arteries, are encouraging. Because the mortality rate remains high among patients who undergo surgery after PEA, better stratification of patients at risk of catastrophic decompensation, whether by echocardiographic or other criteria, could improve outcomes further by encouraging earlier operative intervention. Currently, surgical embolectomy should be considered for patients with hemodynamic compromise in whom anticoagulation is contraindicated, those with persistent shock, and those with an embolus in transit.

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