

Review Article

Surgical Embolectomy for Acute Pulmonary Thromboembolism

Ikuo Fukuda, MD, PhD and Kazuyuki Daitoku, MD, PhD

Acute pulmonary thromboembolism is a catastrophic event, especially for hospitalized patients. The prognosis of pulmonary thromboembolism depends on the degree of pulmonary arterial occlusion. The mortality of massive pulmonary embolism is reportedly as high as 25% without cardiopulmonary arrest and 65% with cardiopulmonary arrest. In patients with unstable hemodynamics due to pulmonary thromboembolism, surgical pulmonary embolectomy is indicated for patients with a contraindication to thrombolysis, failed catheter therapy, or failed thrombolysis. Thrombolytic therapy adds an additional burden on patients who are at risk of potential hemorrhagic complications. It is also indicated if patients are already on a veno-arterial extracorporeal membrane oxygenator for circulatory collapse or cardiopulmonary arrest. The outcome for patients who require cardiopulmonary resuscitation for longer than 30 minutes is poor. Therefore, early triage for massive and sub-massive pulmonary embolism is crucial. A team approach including a cardiovascular surgeon may be effective to save critically ill patients. Prompt removal of emboli reduces the right ventricular load with quick recovery of cardiopulmonary function in the early postoperative period. A recent series reported excellent results, with in-hospital mortality of less than 10%. Surgical pulmonary embolectomy is an effective, safe, and easy procedure to save critical patients due to pulmonary thromboembolism.

Keywords: venous thromboembolism, pulmonary embolism, pulmonary embolectomy, portable cardiopulmonary bypass, ECMO

Introduction

Acute pulmonary thromboembolism (PE) was one of the major cardiopulmonary menaces to hospitalized patients before the advent of anticoagulant therapy using heparin. In 1906, Friedrich Trendelenburg in Leipzig reported the

ligation of the inferior vena cava to prevent the progression and embolization of septic thrombi in puerperal sepsis.¹⁾ He also attempted an “off-pump” pulmonary embolectomy via a left small thoracotomy in patients with a femoral neck fracture in 1908. This procedure was based on experimental study; in fact, the patient died of bleeding during the operation.²⁾ No patient survived this procedure until the first successful report from Martin Kirschner, Trendelenburg’s former trainee, in 1924.²⁾ It was a very difficult procedure with extremely high mortality; thus, it was performed only for critically ill patients, resulting in highly unreliable and uncertain outcomes. The idea of extracorporeal circulation inspired John Gibbon to develop cardiopulmonary bypass during his care of a patient with massive PE in 1931.³⁾ The initial idea was to apply extracorporeal circulation to treat massive PE, and he began research on extracorporeal circulation. In 1936, clinical application of heparin as pharmacological prophylaxis and treatment of venous thromboembolism was introduced, 30 years after the discovery of heparin in 1916.⁴⁾ With the development of the heart-lung machine and the use of heparin as an anticoagulant, Denton Cooley and his colleagues performed pulmonary embolectomy using cardiopulmonary bypass in 1961. They also reported the use of “portable” cardiopulmonary bypass as a bridge to surgical pulmonary embolectomy.⁵⁾ However, after the advent of thrombolytic therapy in the 1970s,⁶⁾ surgical pulmonary embolectomy was criticized as an obsolete therapeutic modality because patients who needed pulmonary embolectomy were too ill to transport to a specialized heart center. Thrombolytic therapy is effective for resolving clots in the pulmonary artery; however, most studies have not shown that thrombolytic therapy has a survival advantage because of the risk of critical hemorrhage.⁷⁾

Natural History of Pulmonary Embolism: Pathophysiological Considerations in Massive Pulmonary Embolism

The pulmonary circulation has a huge capillary bed because the entire systemic venous return goes into the pulmonary circulation. The pulmonary capillary bed covers nearly the entire alveoli area, with a total surface area

Thoracic and Cardiovascular Surgery, Hirosaki University Graduate School of Medicine, Hirosaki, Aomori, Japan

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Corresponding author: Ikuo Fukuda, MD, PhD. Thoracic and Cardiovascular Surgery, Hirosaki University Graduate School of Medicine, 5 Zaifu-cho, Hirosaki, Aomori 036-8562, Japan
Tel: +81-172-39-5074, Fax: +81-172-37-8340
E-mail: ikuofuku@hirosaki-u.ac.jp



of 100–140m². Because the pulmonary vasculature has a wide endothelial area, the lung has strong endogenous fibrinolytic properties.

Most pulmonary thromboemboli are generated in the venous bed of the lower extremities as deep vein thromboses. The deep venous system consists of multiple tracts embedded between muscular compartments. The venous walls are thin and highly stretchable, working as capacitance vessels and a reservoir of blood. The deep veins of the extremities have bileaflet valves to prevent regurgitation of venous blood to the feet. There are many venous sinuses in the calf muscles, especially in the soleus muscle, draining into the posterior tibial and peroneal veins. The soleal sinuses are large, short, thin-walled, and valveless. They are embedded in the soleus muscle, working as a “peripheral heart” during ambulation to eject pooled blood and resisting 80 mmHg of pressure from gravity below the heart.⁸⁾ However, the soleal sinuses may become cradles of deep vein thrombi if patients are on long-term bed rest or immobilization by a cast combined with other thrombogenic factors such as thrombophilia or intimal injury.⁹⁾ Thrombi in soleal venous sinuses extend to the proximal veins, forming a long, sausage-shaped thrombus.

From the anatomical perspective, the size of the deep veins is an important factor when considering the severity of PE. The diameters of the calf veins, the femoral vein, and the common iliac vein are 6–8, 8–10, and 10–12 mm, respectively. On the other hand, the pulmonary artery becomes smaller with distance from the right ventricle. The diameters of the main pulmonary trunk, main pulmonary arteries, and lobar arteries are approximately 25, 15, and 8 mm, respectively. A large thrombus formed in the proximal leg vein may become 8–10 mm in diameter and 30–40 cm in length. This large thrombus can easily pack proximal pulmonary arteries, inducing massive or sub-massive PE (Fig. 1).

The pathophysiological effects of massive or sub-massive PE are hypoxemia due to ventilation-perfusion mismatch and right ventricular failure due to reduced net pulmonary arterial vascular beds. The mortality of massive pulmonary embolism is very high: 25% in patients with shock and 65% in patients with cardiopulmonary arrest.¹⁰⁾ Most deaths from massive pulmonary embolism occur in the initial several days, especially within several hours after onset.¹¹⁾ Therefore, prevention of venous thromboembolism is crucial. Early detection and intervention for massive and sub-massive pulmonary embolism are also important.

Management Strategy for Massive or Sub-Massive PE

The treatment strategy for massive and sub-massive PE

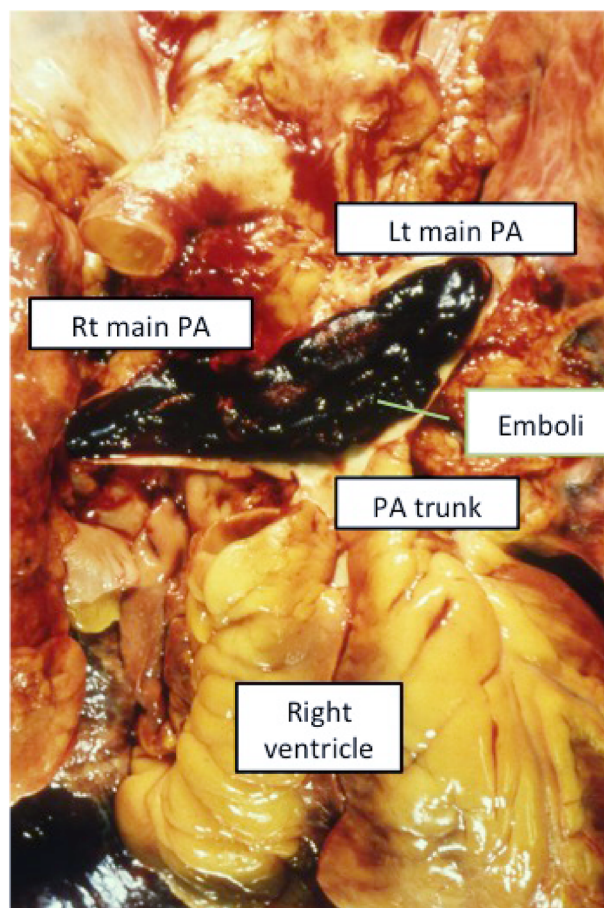


Fig. 1 Autopsy photo of the pulmonary trunk in a patient with massive pulmonary embolism. Sausage-like thrombi pack the pulmonary trunk and bilateral main pulmonary arteries.

consists of three components: i) cardiopulmonary support; ii) anticoagulation to prevent extension and recurrence of PE; and iii) reperfusion of the pulmonary artery by thrombolysis or mechanical removal of emboli. The first simple step in cardiopulmonary support is oxygen administration for perfusion-ventilation mismatch and administration of inotropes for right ventricular failure. If inotropic support fails or the patient develops cardiopulmonary arrest, portable cardiopulmonary support (veno-arterial extracorporeal membrane oxygenator: V-A ECMO) is indicated. Anticoagulant therapy is also important to inhibit the extension of the secondary thrombus in the pulmonary artery. It is also effective for inhibiting the embolization of venous thrombus, which would cause recurrent PE. Heparin should be initiated immediately when PE is suspected as long as the patient has no contraindications to anticoagulation, such as active bleeding from the gastrointestinal tract. Reperfusion therapy is a rational approach to management for occlusion of the major pulmonary arteries. Pharmacological reperfusion using tissue plasminogen activator (t-PA) is effective to improve the hemodynamics of massive or sub-massive PE. The

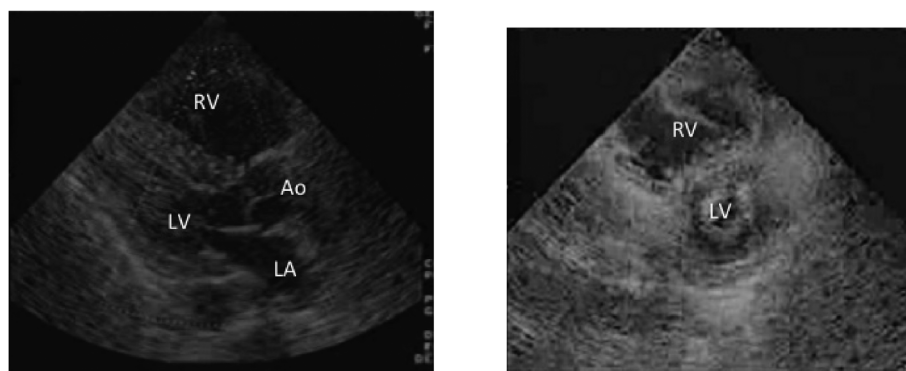


Fig. 2 Right ventricular load in massive pulmonary embolism seen on a trans-thoracic echocardiogram. Left, long-axis view of the heart in a patient with massive pulmonary embolism. Right, short-axis view of the heart in the same patient. Note the enlarged right ventricle and small left ventricle. RV: right ventricle; LV: left ventricle; Ao: ascending aorta; LA: left atrium

thrombolytic effect of t-PA is as high as 80%; however, a few randomized trials have shown that t-PA improves the prognosis of massive pulmonary embolism.¹²⁾ Hemorrhagic complications, especially in aged patients, are major adverse effects of t-PA.¹³⁾ Mechanical reperfusion consists of catheter therapy and surgical embolectomy. Catheter therapy was developed by Greenfield in 1969 using a cup-shaped catheter^{14,15)}; however, it is not commonly used because of uncertainties about the procedure. Recent catheter interventions include several modalities with or without the use of local thrombolysis. Although local thrombolysis in the pulmonary artery is efficacious, it is difficult in patients with contraindications to thrombolysis, such as patients with stroke or after major surgery. Catheter embolectomy or fragmentation is an alternative to surgical embolectomy, and excellent results for massive and sub-massive PE have been reported.¹⁶⁾ Because patients with massive PE have unstable hemodynamics, use of cardiopulmonary support, or V-A ECMO, is frequently necessary to ensure the safety of the procedure.¹⁷⁾

Indications for Surgical Pulmonary Embolectomy and Triage for Surgical Candidates

Many guidelines recommend surgical pulmonary embolectomy as an important therapeutic option for patients that have massive PE with hemodynamic instability. Because the natural history of massive PE is terrible, especially in patients with cardiopulmonary arrest, early recognition, and therapeutic intervention for this condition are important. Stein et al. performed a meta-analysis of 1,300 patients in 46 reports and found a linear relationship between mortality and the prevalence of cardiopulmonary arrest before pulmonary embolectomy in each report.¹⁸⁾ Therefore, triage of critically ill patients with massive PE before exacerbation of the hemodynamic state is essential.

The initial symptom of acute massive PE is nonspecific, such as pleuritic chest pain, dyspnea, or syncope. A clue to the presence of massive/sub-massive PE is tachycardia with or without hypotension (heart rate/systolic blood pressure > 1.0). Blood gas analysis shows hypoxemia with hypocapnia. A sensitive sign for massive/sub-massive PE is right ventricular load¹⁹⁾ (Fig. 2). Enhanced chest computed tomography (CT) using multi-detector CT is a useful tool for detecting pulmonary emboli in the pulmonary arteries with high specificity and sensitivity.²⁰⁾ It is also useful to exclude cardiovascular emergencies such as acute aortic dissection or ruptured thoracic aortic aneurysm. An echocardiogram is a useful tool to detect right ventricular load, floating right ventricular thrombi, and a straddling embolus on the patent foramen ovale. Ultrasonography is also useful to detect proximal deep vein thrombosis in the femoral vein. The advantage of echography is its portability whereas the advantage of CT is that it provides a precise three-dimensional understanding of how the pulmonary emboli occupy the pulmonary arteries. Because acute PE is a life-threatening complication for hospitalized patients, a multidisciplinary approach is important to save critically ill patients. Treatment to stabilize respiratory and hemodynamic status should be carried out simultaneously.²¹⁾

Pulmonary embolectomy is indicated for patients that have sub-massive or massive PE with: i) contraindications to thrombolysis; ii) failed thrombolysis or catheter-assisted embolectomy; or iii) shock that is likely to cause death before thrombolysis can take effect (e.g., within hours), if surgical expertise and resources are available.^{21,22)} The morphological indication for pulmonary embolectomy is massive PE in deep shock provided that large pulmonary emboli occlude proximal pulmonary arteries (main pulmonary arteries and pulmonary trunk). Pulmonary embolectomy is indicated for patients that develop mas-

sive or sub-massive PE within 2 months after craniotomy or spinal surgery and patients with intracranial hemorrhage, because thrombolysis is contraindicated in these patients, who have a high risk of re-bleeding.²³⁾ Patients with massive PE within 10 days after major surgery may be candidates for pulmonary embolectomy because of concerns about surgical site bleeding. Neely et al. reported that 46 of 115 patients who underwent pulmonary embolectomy were within 5 weeks after surgery, including 11 neurosurgical procedures.²⁴⁾ Although pulmonary embolectomy requires full heparinization, total cardiopulmonary bypass has a short duration and is safe for bleeding. Cardiopulmonary arrest due to massive PE is a risk factor for mortality with pulmonary embolectomy.¹⁸⁾ Keeling et al. reported that the in-hospital mortality of patients who received preoperative cardiopulmonary resuscitation (CPR) was significantly higher (9/28, 32.1%) than in those without CPR (16/186, 8.6%, $p < 0.01$).²⁵⁾ Takahashi et al. reported that 73% of patients who received preoperative CPR survived, whereas all patients who received CPR for longer than 30 minutes died after pulmonary embolectomy.²⁶⁾ V-A ECMO is an important life support procedure for massive PE with circulatory collapse or cardiopulmonary arrest (Table 1). Sakuma et al. reported that 73% of 193 patients undergoing V-A ECMO survived; they also reported that the survival rate of patients who received CPR longer for than 30 minutes before starting V-A ECMO was as low as 10%.²⁷⁾ Considering the devastating prognosis of massive PE patients, a survival rate of more than 70% is justified.

PE during pregnancy or the puerperal period is a complicated problem. The incidences of pregnancy-related venous thromboembolism (VTE) and PE are approxi-

mately 13 and 3 per 10,000 deliveries, respectively.²⁸⁾ However, the incidences of VTE and PE during pregnancy increase in women older than 35 years. Anticoagulant therapy using subcutaneous injection of heparin calcium or fondaparinux sodium is the treatment of choice during pregnancy in Japan, if the clinical benefit exceeds the risk of bleeding. Although the incidence of massive PE during pregnancy is low, management of massive PE during pregnancy and the postpartum period is difficult. Use of thrombolytic agents may result in critical uterine hemorrhage. Pulmonary embolectomy is one of the choices for this complicated problem. Fukuda et al. reported three patients undergoing pulmonary embolectomy during pregnancy with different approaches according to the maternal term.²⁹⁾ One patient in their series underwent a concomitant Cesarean section and pulmonary embolectomy, but pregnancy was continued in the other two patients, resulting in one successful delivery and one stillbirth. In the review of the literature, no mother died, but fetal/neonatal mortality was 25%.

Pulmonary embolectomy after failed thrombolysis is a complicated problem. Meneveau et al. compared the outcomes of patients undergoing pulmonary embolectomy and repeat thrombolysis for patients with failed thrombolysis for PE. They reported favorable outcomes in the pulmonary embolectomy group.³⁰⁾ Although pulmonary embolectomy is recommended in guidelines, surgical site bleeding is frequently intractable, causing a prolonged operation time. Therefore, as surgeons, the authors recommend prompt consultation for massive PE patients with cardiac surgeons before the use of thrombolytic agents. The outcome of pulmonary embolectomy for sub-massive PE with contraindications to thrombolytic therapy is satisfactory.^{24,25)}

Paradoxical embolism is rare, but it is a concrete indication for pulmonary embolectomy and intracardiac embolectomy. When a patient with a patent foramen ovale has massive or sub-massive PE, the right to left shunt may open due to elevated right ventricular end-diastolic pressure. This shunt will exacerbate hypoxia. Secondary emboli from the legs may pass through the shunt and may induce left-sided embolization. The thrombi may sometimes be entrapped on the patent foramen ovale. In this situation, thrombolysis may induce fragmentation of the entrapped thrombi, resulting in recurrence of arterial embolism.

Management of floating right heart emboli is a controversial issue. Some researchers regard a floating embolus as an in-transit form of pulmonary embolism. Rose et al. conducted a retrospective study of the outcomes in patients treated with heparin, surgical embolectomy, and thrombolysis. The mortality was lowest among the groups in patients who underwent thrombolysis.³¹⁾ A recent reg-

Table 1 Effect of veno-arterial extracorporeal membrane oxygenator (V-A ECMO) for massive PE

Author (year)	N	Survival rate	Comment
Maggio (2007) ³⁶⁾	21	62%	
Sakuma (2009) ²⁷⁾	193	73%	Patients with CPA: 65%, without CPA: 86% Patients with CPA-V-A ECMO ≥30 minute: survival <10%
Taniguchi (2012) ³⁷⁾	10	70%	All patients underwent pulmonary embolectomy
Hashiba (2012) ³⁸⁾	12	83%	Good neurological outcome: 58%
Takahashi (2012) ²⁶⁾	16	81%	All patients underwent pulmonary embolectomy Patients with CPA: 73% All patients who received CPR longer than 30 minutes died

CPA: cardiopulmonary arrest; CPR: cardiopulmonary resuscitation

istry for the analysis of 139 patients with floating right heart thrombi demonstrated that hypotensive patients had a significantly higher mortality than normotensive patients (42% vs. 12%, $p=0.0002$).³²⁾ Even in normotensive patients, patients with right ventricular load had a poor prognosis. Therefore, pulmonary thrombectomy combined with extraction of floating emboli is indicated in patients that have floating emboli with sub-massive or massive PE.

In patients who have undergone long-term CPR with irreversible brain damage, pulmonary embolectomy is contraindicated; CPR longer than 30 minutes is a risk factor for a poor prognosis.^{25,26)} Acute PE on chronic thromboembolic pulmonary hypertension (CTEPH) is a contraindication to pulmonary embolectomy. In this situation, longstanding hypoxia and right ventricular hypertrophy are characteristic manifestations. Pulmonary endarterectomy should be considered for this syndrome.

Surgical Procedure and Postoperative Management

Pulmonary embolectomy under cardiopulmonary bypass is an easy procedure for cardiac surgeons. After the establishment of total cardiopulmonary bypass, the pulmonary trunk is opened, and large sausage-shaped emboli are extracted from the main pulmonary arteries using forceps. If thrombi extend to the peripheral pulmonary arteries, an additional incision to the right main pulmonary artery between the ascending aorta and the superior caval vein makes it easy to remove peripheral thrombi. Aortic cross clamping is not mandatory, but is beneficial if surgeons want to remove peripheral thrombi. The authors have no concerns about peripheral thrombi, because the fibrinolytic properties of peripheral pulmonary arteries are strong enough to dissolve residual thrombi spontaneously. In the

authors' series, none of the 26 patients who underwent pulmonary embolectomy showed pulmonary hypertension in the late period. Use of a Fogarty thrombectomy catheter may injure thin and fragile pulmonary arterial walls, inducing intractable hemoptysis during reperfusion. Squeezing of the lungs via bilateral thoracotomy is not recommended, especially in patients on thrombolytic therapy. In the subacute phase of PE, gentle manipulation of the organized thrombi sticking to the endothelium of pulmonary arteries is necessary. Injury to the pulmonary arterial wall may induce pulmonary hemorrhage. A temporary or retrievable caval filter is frequently put into the inferior caval vein during or after embolectomy.

Massive wound hemorrhage in patients given preoperative thrombolysis may be managed with the infusion of fresh frozen plasma and platelet precipitate. In cases of pulmonary hemorrhage due to arterial injury, the responsible bronchus should be blocked with a balloon catheter, and heparin should be reversed after the patient is weaned from cardiopulmonary bypass. However, control of bleeding is frequently difficult in this situation, and the patient cannot be weaned from the cardiopulmonary bypass due to hypoxia. Longstanding right ventricular failure or residual pulmonary emboli may induce low output syndrome with pulmonary hypertension. V-A ECMO is the only solution for this situation. Stroke and coma are major complications after pulmonary embolectomy in patients who require CPR before pulmonary embolectomy.

Outcome of Pulmonary Embolectomy

The outcomes of pulmonary embolectomy from recent reports are shown in Table 2. The mortality varies, ranging from 3.6% to 27.2%. The volume of cases in each center was very small. Stein et al. reported that the mortality of pulmonary embolectomy for acute PE was 20% in a meta-

Table 2 Recent outcomes of pulmonary embolectomy

Author	N	Death (mortality)	Year	Term	Ref.
Leacche M	47	3 (6%)	2005	1999–2004	[39]
Zarrabi K	30	2 (6.7%)	2011	2004–2010	[40]
Fukuda I	19	1 (5.9%)	2011	1988–2009	[35]
Taniguchi S	32	6 (18.8%)	2012	1994–2006	[37]
Kilic A	2709	737 (27.2%)	2013	1999–2008	[33]
Lehnert P	33	2 (6%)	2012	1998–2010	[41]
Aymard T	28	2 (3.6%)	2013	2001–2007	[42]
Takahashi H	24	3 (12.5%)	2012	2000–2001	[26]
Worku B	20	1 (5%)	2014	1999–2011	[43]
Neely RC	105	7 (6.6%)	2015	1999–2013	[24]
Cho YH	26	4 (15%)	2016	2000–2013	[44]
Keeling WB	214	25 (11.7%)	2016	1998–2014	[25]
Edelman JJ	37	2 (5.4%)	2016	2000–2014	[45]

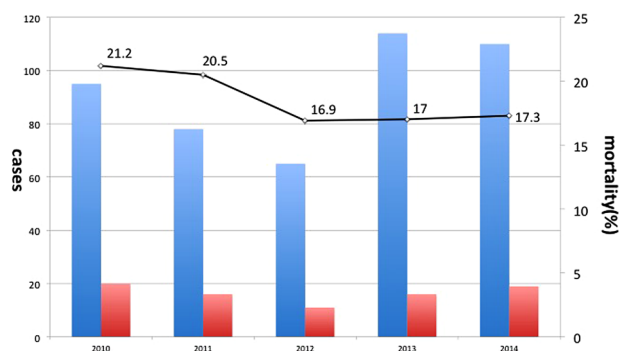


Fig. 3 Pulmonary embolectomy in Japan. A total of 462 cases of pulmonary embolectomy were performed between 2010 and 2014, with operative mortality of 17.8%.⁴⁶⁻⁵⁰⁾ Long bar, annual number of pulmonary embolectomies; short bar, annual number of deaths; solid line, annual mortality.

analysis of 1,300 cases.¹⁸⁾ A retrospective multicenter study by Kilic et al. involving community hospitals in the USA showed a mortality of 27.2% (737/2709).³³⁾ A census survey from the annual report of the Japanese Society for Thoracic Surgery showed that the mortality rate for 462 patients who underwent pulmonary embolectomy from 2010 to 2014 was 17.7% (Fig. 3). Considering the patients' severity, the high mortality of this procedure may be justified. More detailed data analyses for the risk factors of death or postoperative morbidity should be performed.

Azari et al. compared functional recovery in patients undergoing surgical embolectomy and those undergoing thrombolytic therapy for massive PE.³⁴⁾ They found significant decreases in right ventricular diameter and systolic pulmonary arterial pressure on the third day of intervention in the pulmonary embolectomy group. The mortality of pulmonary embolectomy was 3.3% (1/30). Fukuda et al. reported that the long-term outcome of pulmonary embolectomy was satisfactory, with 10-year survival of $83.5\% \pm 8.7\%$. No patients showed CTEPH in the late period.³⁵⁾

Conclusion

Surgical embolectomy is an effective procedure with a low risk of hemorrhage for patients with massive PE. Although the in-hospital mortality of pulmonary embolectomy is high, it is justified considering the life-threatening nature of the illness. Prompt triage of patients with massive PE using a team approach is important. The long-term outcome of pulmonary embolectomy is satisfactory.

Disclosure Statement

None.

Author Contributions

Study conception: IF
 Data collection: IF, KD
 Analysis: IF
 Investigation: IF
 Writing: IF
 Funding acquisition: IF
 Critical review and revision: all authors
 Final approval of the article: all authors
 Accountability for all aspects of the work: all authors

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