Original Article
Surgical embolectomy for acute massive pulmonary embolism

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Abstract: Objective: Acute massive pulmonary embolism (PE) is associated with significant mortality rate despite diagnostic and therapeutic advances. The aim of this study was to analyze our clinical outcomes of patients with acute massive PE who underwent emergency surgical pulmonary embolectomy. Methods: This retrospective study included 13 consecutive patients undergoing emergency surgical pulmonary embolectomy for acute massive PE at our institution from March 2000 to November 2013. The medical records of all patients were reviewed for demograhic and preoperative data and postoperative outcomes. All patients presented with cardiogenic shock with severe right ventricular dysfunction confirmed by echocardiography, where 4 (30.8%) of the patients experienced cardiac arrest requiring cardiopulmonary resuscitation before surgery. Results: The mean age of patients was 61.8 ± 14 years (range, 38 to 82 years) with 8 (61.5%) males. The most common risk factors for PE was the history of prior deep venous thrombosis (n = 9, 69.2%). There were 3 (23.1%) in-hospital deaths including operative mortality of 7.7% (n = 1). Ten (76.9%) patients survived and were discharged from the hospital. The mean follow-up was 25 months; follow-up was 100% complete in surviving patients. There was one case (7.7%) of late death 12 months after surgery due to renal carcinoma. Postoperative echocardiographic pressure measurements demonstrated a significant reduction (P < 0.001). At final follow-up, all patients were in New York Heart Association class I and no readmission for a recurrent of PE was observed. Conclusion: Surgical pulmonary embolectomy is a reasonable option and could be performed with acceptable results, if it is performed early in patients with acute massive PE who have not reached the profound cardiogenic shock or cardiac arrest.

Keywords: Acute massive pulmonary embolism, surgical embolectomy, thrombus, emergency operation, cardiopulmonary bypass

Introduction

Acute massive pulmonary embolism (PE) is associated with high mortality rate despite diagnostic and therapeutic advances. Indeed, acute PE is the third most common cause of cardiovascular death after acute myocardial infarction and stroke among hospitalized patients in Western countries [1, 2]. Data of 2454 consecutive patients with acute PE from the world's largest International Cooperative Pulmonary Embolism Registry (ICOPER) study from 52 large institutions in 7 countries show an overall crude mortality rate of 17.4% within 90 days [3]. However, mortality rates vary greatly based on severity of PE.

Acute massive PE is characterized by thrombus occlusion of more than 50% of the pulmonary artery cross-sectional area or occlusion of two or more lobar arteries or clinically hemodynamic compromise or severe right ventricular (RV) dysfunction detected by echocardiography [4, 5]. Acute massive PE has an estimated incidence between 4.5% and 10% of all cases of PE [1-3]. The patients suffering from acute massive PE have usually hemodynamic instability and are inclined to sudden cardiac arrest.

Table 1. Preoperative characteristics of patients

Variables	Patients (n = 13)
Age (years)	
Mean ± SD	61.8 ± 14
Range	38-82
Gender (Male/Female)	8/5
Cardiogenic shock (n,%)	13 (100)
Cardiac arrest (n,%)	4 (30.8)
Mean LVEF (%)	48% ± 7%
Mean SPAP (mmHg)	61.2 ± 4.6
Dispnea (n,%)	13 (100)
Syncope (n,%)	8 (61.5)
Chest pain (n,%)	5 (38.5)
Inotropics need (n,%)	13 (100)
Risk Factors for PE (n,%)	
Prior DVT	9 (69.2)
Malignancy	3 (23.1)
Recent surgery	3 (23.1)
Obesity	8 (61.5)
Previous CVE	2 (15.4)
Oral contraceptive use	1 (7.7)
Smoking	9 (69.2)
Unknown	1 (7.7)
Diagnostic tools (n,%)	
Echocardiograhy	13 (100)
Computed tomography	9 (69.2)

CVE = cerebrovascular event; DVT = deep venous thrombosis; EF = left ventricular ejection fraction; PE = pulmonary embolism; SD = Standard deviation; SPAP = systolic pulmonary artery pressure.

Accordingly, these patients require rapid diagnosis, emergent and suitable therapeutic approaches.

The main goal of the treatment for massive PE is elimination of the embolic material and prevention of recurrent PE. The optimal therapeutic strategies for patients with acute PE still remain controversial, because there are no randomized controlled trials supporting an ideal treatment modality. In these complicated patients, there are various treatment options including anticoagulation with heparin, thrombolysis, catheter-directed thromboembolectomy, and surgical embolectomy [4, 5].

Anticoagulation with heparin is the mainstay of therapy in all patients of PE. However, patients with massive PE resulting in hemodynamic compromise, with or without RV dysfunction, may benefit from more aggressive therapy than from standard anticoagulation only. Thrombolytic therapy and catheter thromboembolectomy can be considered in restoring hemodynamic stability in these patients [4-6]. However, these procedures have recently shown various complications including a high rate of intracranial hemorrhage, recurrent emboli, failure to completely retrieve all of the thrombus materials, and increased risk to develop chronic pulmonary hypertension [3-7].

Surgical embolectomy has traditionally been reserved as the last therapeutic resort for patients with massive PE who present with cardiogenic shock because of early poor outcomes with high mortality rates. It is also reserved in patients whose thrombolysis is absolutely contraindicated or has failed [4, 5, 8-10]. However, recent studies have shown favorable results over time and surgery has now been liberalized in hemodynamically stable patients with evidence of moderate to severe RV dysfunction on echocardiography [8, 11-13].

In this study, we aimed to evaluate our experience of emergency surgical pulmonary embolectomy as an effective and aggressive therapeutic approach to patients with acute massive PE at our institution.

Materials and methods

Patients

This retrospective study included 13 consecutive patients undergoing emergency surgical pulmonary embolectomy for acute massive PE at our institution from March 2000 to November 2013. Institutional Review Board approved the study protocol, and informed consent was obtained from each patient undergoing the surgical procedure described herein. Hospital records of all patients were reviewed for demograhic data, predisposing factors, inital clinical presentation, time interval between hospital admission of the patients and operating room, diagnostic studies, preoperative hemodynamic status, surgical technique, thrombus location, and postoperative outcomes.

The inclusion criteria for surgical pulmonary embolectomy in the present study were throm-
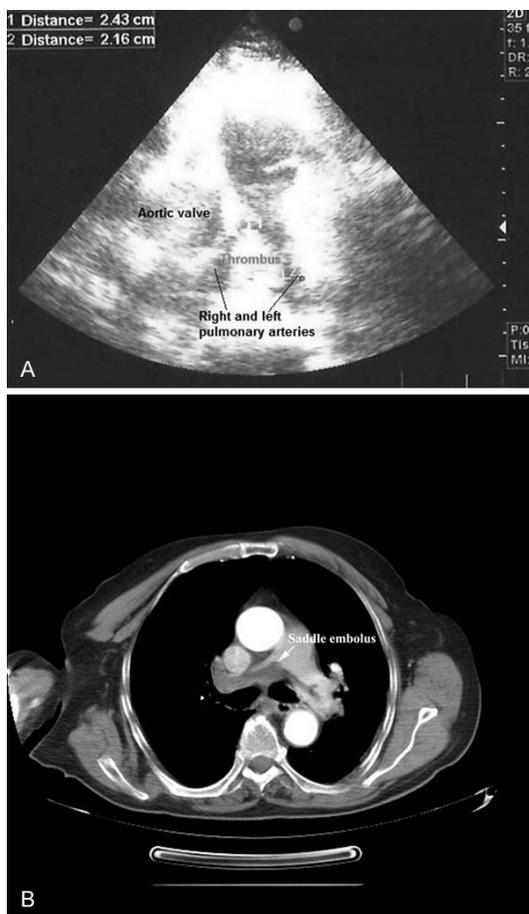
Figure 1. Diagnostic multimodal imaging of the massive pulmonary embolism. A. The short-axis echocardiographic display of the thrombus on the main pulmonary artery. B. Chest computed tomographic scan (axial section) showing saddle pulmonary embolus extending into both main pulmonary arteries.

boembolism of the main pulmonary artery trunk or pulmonary artery branches, severe hemodynamic instability (refractory cardiogenic shock), cardiac arrest requiring cardiopulmonary resuscitation (CPR), respiratory compromise (pressure in the pulmonary artery above 50 mmHg, poor oxygen saturation), contraindication for thrombolysis (recent surgery, recent cerebral vascular accident), concomitant atrial septal defect or mitral valve surgery, or thrombus-in-transit in the right atrium. Patients with acute-on-chronic PE undergoing pulmonary thromboendarterectomy, were excluded from this study.

All patients presented to our emergency department with hemodynamic instability, 4 (30.8%) of whom had cardiac arrest and required CPR

before surgery. Initial presenting other features included acute onset of shortness of breath (n = 13, 100%), chest pain (n = 5, 38.5%), syncope (n = 8, 61.5%), and poor oxygen saturation (n = 9, 69.2%). Eight (61.5%) patients had atrial fibrillation, and only 2 patients were receiving prophylaxis for venous thrombosis. Mean ejection fraction was 48%±7% (range: from 30% to 65%) based on echocardiographic assessment. Preoperative demographic data, clinical characteristics, and risk factors are shown in **Table 1**.

The most common predisposing factors for PE were the history of prior deep venous thrombosis (n = 9, 69.2%), followed by malignancy (n = 3, 23.1%) and recent surgery (n = 3, 23.1%). No risk factor was identified in one patient (see **Table 1**). The diagnosis of acute massive PE was based on acute initial clinical presentation of the patients (hemodynamically unstable) and the transthoracic echocardiography (TTE) performed preoperatively in all patients, which showed a thrombus on the main pulmonary artery (**Figure 1A**), intracardiac thrombus material, or RV dilatation and severe RV dysfunction. There was also evidence of significantly elevated pulmonary artery pressures. Intraoperative transesophageal echocardiography (TEE) was used in nine patients in our series. Only 9 (69.2%) patients had undergone the computerized tomography (CT) showing a thrombus either on the pulmonary trunk as saddle emboli (**Figure 1B**) or on the right or left pulmonary arteries. Bedside ventilation-perfusion scanning was not performed in any patient. No patient was taken to the operating room on clinical suspicion alone.

Acute massive PE was defined as thrombus occlusion of more than 50% of the pulmonary artery cross-sectional area or oclusion of two or more lobar arteries, clinically hemodynamic compromise including cardiogenic shock (systolic blood pressure < 90 mmHg or a pressure drop of ≥ 40 mmHg for > 15 minutes) or cardiac arrest, or severe RV dysfunction on echocardiography. These patients are characterized by hypotension, tissue hypoperfusion, and hypoxemia [4, 5]. RV dysfunction was defined by an RV end-diastolic diameter of greater than 30 mm or an RV/left ventricular end-diastolic diameter ratio of greater than 1 in the apical 4-chamber view, paradoxical septal systolic

Figure 2. Intraoperative appearance. A. A separate longitidunal incision of the right pulmonary artery between the aorta and superior vena cava for further exposure. B. The extraction of embolus gently as en bloc from the main pulmonary artery. C. The materials of thrombus removed from the main pulmonary artery and its branches in one of our patients.

removed. A longitudinal incision was then made into the main pulmonary artery trunk distal to the pulmonary valve and extended as needed toward left pulmonary artery branches. An additional arteriotomy was also performed on the right pulmonary artery between the aorta and superior vena cava if necessary for further exposure, or both of these techniques were used (**Figure 2A**). The arteriotomy was retracted with a vein retractor. The thrombotic material was gently extracted under direct vision by means of forceps en bloc if possible (**Figure 2B**, **2C**).

All branches were carefully inspected. Short episodes of reduced CPB flow and suction usage were occasionally needed for adequate clot visualization. The pulmonary arterial tree was irrigated vigorously by bolus saline flush and aspirated. External lung compression was not performed to avoid damage to already the infarcted loose lung tissue in the distal pulmonary branches. Also, Fogarty catheter clot extraction was avoided to reduce the possibility of injury to the pulmonary artery branches. At the end of the operation, the repair of concomitant lesions was performed. The pulmonary arteriotomy and the right atriotomy were then closed with two layers of continuous 4-0 polypropylene suture, and the patients were weaned from CPB after aortic declamping (if used).

Postoperative anticoagulant regimen

The patients received anticoagulant therapy using intravenous unfractionated heparin 6 hours after surgery when the risk of surgical site bleeding disappeared (activated partial thromboplastin ratio of 2.0 to 2.5). Anticoagulation with heparin was continued until oral warfarin (coumadin) reached therapeutic range (target international normalized ratio of

motion, RV free wall hypokinesia, and pulmonary hypertension (right ventricular/right atrial gradient of > 30 mmHg) [14].

Surgical technique

Surgery was performed through median sternotomy with aorto-bicaval cannulation and normothermic or moderate hypotermic cardiopulmonary bypass (CPB). The choice between cross-clamp and beating heart was preferred according to possible concomitant procedures. Nine patients underwent pulmonary embolectomy with aortic cross-clamping, and 4 patients underwent surgery on beating heart.

Firstly, a right atriotomy was performed in all patients. The right atrium and RV were explored routinely; thrombus-in-transit was carefully

Table 2. Operative characteristics and postoperative outcomes

Variables	Patients (n = 13)
Mean CPB time (minutes)	53.4 ± 27
Median MV need time (days)	3 (range: 1-29)
Localisation of removed thrombus (n,%)	
Main PA and bilateral PA	8 (61.5)
Right PA only	3 (23.1)
Left PA only	2 (15.4)
Right atrium	5 (38.5)
Right ventricle	2 (15.4)
Complications (n,%)	
Renal failure	1 (7.7)
Cerebrovascular event	1 (7.7)
Massive lung bleeding	1 (7.7)
SVT	4 (30.8)
Prolonged ventilation	3 (23.1)
Wound infection	0
Reexploration	0
In-hospital mortality (n,%)	3 (23.1)
Beating heart surgery (n,%)	4 (30.8)

MV = mechanical ventilation; PA = pulmonary artery, SVT = supraventricular tachyarrhythmias.

2.0 to 3.0). Coumadin was usually started on the second day and continued for at least 9 months. All patients were referred to Hematology Department for possible coagulopathies.

Statistical analysis

Statistical analyses were performed using the SPSS software package (SPSS for Windows, version 19; SPSS Inc, Chicago, IL, USA). The results of descriptive statistical analysis are presented as the mean ± the standard deviation of the mean with minimum and maximum values or number (percent) when necessary. According to the distribution, the comparison between the preoperative and postoperative data was performed using Student's t-test or the Mann-Whitney U test. Values of p less than 0.05 were considered statistically significant.

Results

Among the 13 patients undergoing emergency operation, eight (61.5%) were male and 5 (38.5%) were female with a mean age of 61.8 ± 14 years, ranging from 38 to 82 years. The mean time interval between hospital admission of the patients and operating room was 2.1 hours (range: from 30 minutes to 4 hours). All patients arrived in the operating room on inotropic support, and four (30.8%) arrived with ventilatory support. Thrombolytic therapy was not initiated in any patients before surgical pulmonary embolectomy. No patients were treated with extracorporeal membrane oxygenation (ECMO) preoperatively because it was not yet available at our hospital at the presentation time of these patients.

Nine patients (69.2%) had a history of previous deep venous thrombosis, and three patients (23.1%) had undergone surgical procedures including endovenous laser ablation, gynecologic surgery, and orthopedic surgery between 3 and 21 days prior (**Table 1**). Three (23.1%) other patients had been diagnosed with malignancy including renal carcinoma in 2 patients and ovarian cancer in 1 patient, all of which had recently received chemotherapy. One patient had also no identifiable predisposing factor for PE. One (7.7%) other patient had oral contraceptive use, and two (15.4%) patients suffered from cerebrovascular event in the preceding 3 months. Four patients (30.8%) had experienced hemodynamic collapse (cardiac arrest) that required CPR before surgery. After endotracheal intubation and resuscitation, TTE showed severe RV dilatation and massive PE. In preparation for surgery, two patients (15.4%) were taken directly to the operating room due to repeat cardiac arrest with ongoing CPR. In these patients, CPR was continued with internal cardiac massage after sternotomy and emergent CPB was initiated.

In all patients, the right atrium was opened and checked for the presence of thrombus. The thrombus-in-transit was gently removed from the right atrium in 5 patients and the RV in 2. Two patients had associated procedures. Concomitant mitral valve replacement was performed for severe calcific mitral stenosis in one patient. In another patient, atrial septal defect repair associated with bilateral femoral embolectomy was also performed in addition to pulmonary embolectomy. Patients had the following distribution of emboli with respect to the pulmonary arteries: bilateral pulmonary arteries and main trunk in 8 (61.5%) patients, only right pulmonary artery in 3 (23.1%) patients, and only left pulmonary artery in 2 (15.4%) patients (**Table 2**).

The patients had a cross-clamp of mean 34.1 ± 13.7 minutes (range: from 23 to 67 minutes), with a mean CPB time of 53.4 ± 27 minutes (range: from 41 to 78 minutes). The patients needed mechanical ventilation for a median time of 3 days (ranging from 1 day to 29 days). Mean length of postoperative hospital stay for those surviving patients was 11 days (range 8-15 days). Major complications included renal failure (n = 1, 7.7%), cerebrovascular event (n = 1, 7.7%), massive lung bleeding (n = 1, 7.7%), prolonged ventilation (n = 3, 23.1%), and supra-ventricular tachyarrhythmias (n = 4, 30,8%). There was no sternal infection or reoperation due to mediastinal bleeding (**Table 2**).

Ten (76.9%) patients survived and were discharged from hospital. Only one (25%) of the 4 patients with cardiac arrest before operation survived. Operative mortality was 7.7%. The overall in-hospital mortality rate in our study was 23.1% (3/13). Two of these patients entered the operating room with ongoing CPR and the other experienced multiple cardiac arrests responding to CPR preoperatively. The first was a 72-year-old woman with unknown etiology who died in the operation room with massive right lung bleeding after pulmonary embolectomy. This patient had been urgently brought to the operating room with ongoing CPR. During surgery, multiple bilateral clot materials were found in her peripheral pulmonary arteries. She underwent right middle lobectomy. Intraoperatively, intra-aortic balloon pump was inserted, but she could not be weaned from CPB. The second patient, 38-year-old man who had undergone endovenous laser ablation, was in hemodynamic instability on arrival. He had a massive right atrial clot extending into the RV and pulmonary trunk by echocardiographic study. During this diagnostic examination, he had cardiac arrest and underwent to surgery with ongoing CPR. Although he recovered hemodynamically after pulmonary embolectomy, he was unconscious. He died from multiorgan failure on postoperative day 7 [15]. The third patient was an 82-year-old man who presented with worsening hypoxia and hypotension leading to cardiac arrest and required CPR 4 times before being taken to surgical embolectomy. In postoperative period, he required prolonged ventilatory support and tracheostomy. He had renal failure requiring hemodialysis. He died from multiorgan failure on postoperative day 29.

Follow-up

At postoperative follow-up, TTE was performed at 1 month and 6 months and then yearly thereafter. Follow-up was carried out by visits to the our Outpatient Department. The patients' systolic pulmonary artery pressure (SPAP) was measured by echocardiography. Preoperative mean SPAP was 61.2 ± 4.6 mmHg (range: 54-76 mmHg). Postoperative mean SPAP decreased to 29 ± 2.1 mmHg (range: 25-38 mmHg) at 1 month and 27.4 ± 5.7 mmHg (range: 24-36 mmHg) at 6 months. Postoperative echocardiographic pressure measurements demonstrated a significant reduction (P < 0.001). RV function was immediately improved in all survivors. The follow-up periods of the 10 survivors ranged from 6 months to 170 months (mean, 25 months), with one case (7.7%) of late death 12 months after surgery due to renal carcinoma. All patients were anti-coagulated with warfarin postoperatively for at least 9 months, and an inferior vena cava (IVC) filter was placed in 2 patients at postopearive 2nd and 4th months, respectively, due to a repeat deep venous thrombosis in the lower extremity. During follow-up study, two patients suffered from symptoms of coronary artery disease and both underwent percutaneous coronary intervention. As of May 2014, at final follow-up, all patients were in New York Heart Association class I (indicative of only slight limitation of activity). No readmission for a recurrent of PE was observed. There were no complications as a result of postoperative placement of two permanent IVC filters.

Discussion

Acute massive PE is a serious and potential life-threatening condition with clinical manifestations of hemodynamic instability, acute RV failure, and cardiogenic shock and/or cardiac arrest [4, 6, 16]. Acute PE can be classified into massive (high-risk), sub-massive (intermediate-risk) and non-massive (low-risk) PE, based on the degree of hemodynamic compromise [4, 13]. Risk stratification is currently directed toward the evaluation of the risk of early PE-related death. In massive PE, the overall mortality rate remains at approximately 30%

[7]. The 3-month mortality for patients with acute massive PE was 52.4% in the ICOPER study [1, 2]. If CPR is required, mortality rates increase dramatically. Patients with massive PE, who present with cardiac arrest and require CPR, have a mortality of up to 70% within the first hour of presentation [1, 12, 16].

Patients with massive PE, hemodynamic instability, and RV dysfunction have a poor prognosis; therefore, they require early diagnosis, prompt risk stratification, and aggressive therapeutic strategies to reduce the high mortality rate [17]. There are three components for patients' risk stratification including clinical assessment, determination of cardiac biomarkers levels such as troponin, and evaluation of RV function and/or size by echocardiography and/or CT imaging [18].

There are many well-recognized risk factors for PE. These include the presence of deep venous thrombosis, previous surgical procedures (major general/orthopedic surgery), trauma (major fracture), hypercoagulable disorders (factor V Leiden and prothrombin mutations), malignancy (chemotherapy), and long-standing immobilization [4, 8. 10]. However, there are also many other common predisposing conditions including advanced age, obesity, smoking, stroke, congestive heart failure, respiratory failure, sepsis, inflammatory bowel disease, pregnancy, hormone replacement therapy, and use of oral contraceptive agents [16]. Commonly, more than one risk factor is available. For all that, no predisposing factors are identified in approximately 20% of patients [3]. The most important risk factors for the development of PE in our case series were the history of prior deep venous thrombosis (69.2%), followed by malignancy (23.1%) and recent surgery (23.1%). These findings were similar to another major series where it comprised 36% of the cases [8]. Massive PE has a serious nature [10]. Dyspnea and syncope, with or without cardiac arrest, are expectedly the most commonly presenting features. Thirty-one percent of patients in our series suffered from a cardiac arrest requiring CPR as their initial clinical presentation.

Early diagnosis of acute massive PE permits an appropriate and emergent treatment strategy. Definitive diagnosis is made on the basis of imaging studies including echocardiography, CT, contrast pulmonary angiography, and ventilation-perfusion scanning. Successful patient outcomes are dependent on the size of the clot and the functional capability of the cardiovascular system. Therefore, two-dimensional echocardiographic evidence of RV dysfunction, which has been shown to be an independent predictor of adverse outcome, should be considered in the decision-making process [6]. Perioperative echocardiography provides important diagnostic and prognostic information to coordinate the management of patients with massive PE. It is also helpful in identifying emboli-in-transit, atrial septal defect, and other valve pathologies [8, 19]. These contemporary diagnostic modalities allow for improved risk stratification and patient selection for surgical pulmonary embolectomy as part of a multimodality approach to acute massive PE [4, 12, 19-21]. TEE is advantageous in evaluating extrapulmonary thrombi in localization such as the right atrium, RV and IVC [22]. Also, TEE in the operating room for evaluating residual clots after surgical embolectomy has an important role. The chest CT imaging is the preferred tool for rapid and noninvasive detection of large central clot and helps to identify patients with centrally localized emboli, which are surgically accessible [8, 19, 21]. In our series, echocardiography was used in determination of the RV dysfunction as a consequence of massive PE in all patients. The precise diagnosis of PE in this study was obtained preoperatively in nine (69.2%) patients by both echocardiography and CT imaging. On the other hand, four patients did not receive preoperative CT analysis because their conditions were unstable, but all of them underwent intraoperative TEE evaluation.

The ideal treatment strategies for patients with acute massive PE with cardiogenic shock and/or cardiac arrest have been a controversial issue because the randomized controlled studies do not exist to make evidence-based management guidelines. There are various available therapeutic options and strategies for improving outcomes in patients with PE including hemodynamic and respiratory support, standard anticoagulation, intravenous thrombolytics, catheter-directed intrapulmonary thrombolytic infusion, percutaneous catheter aspiration embolectomy and clot fragmentation,

rheolytic thrombectomy, surgical pulmonary embolectomy, ECMO, IVC filter insertion, triage to an intensive care unit bed, and postoperative long-term anticoagulation and secondary prophylaxis [4, 5, 17, 23, 24].

Patient's survival depends on rapid restoration of the pulmonary blood flow obstructed by thrombus and reduction of the RV afterload. The treatment of massive PE requires a multidisciplinary approach [8, 12, 14, 17, 19, 25-27]. This approach to diagnostics and optimal timing of surgery with efficient perioperative management plays an important role in treating acute massive PE. Aggressive anticoagulation using heparin is the mainstay of therapy of PE, but it is insufficient in severe patients of massive or submassive occlusion of pulmonary vasculature. According to the guidelines from the European Society of Cardiology, treatment of massive (high-risk) PE is thrombolysis or surgical embolectomy [4].

Systemic thrombolysis is associated with major bleeding risks in about 13% of the patients, and intracranial or fatal hemorrhage in up to 3% of those [3, 4, 8, 12, 28]. Furthermore, fifty percent of the patients with massive PE because of surgery within the previous three weeks, trauma, previous hemorrhagic stroke or any ischemic cerebral event within six months, the presence of oral anticoagulants, advanced hepatic disease, active peptic ulcers, pregnancy, and CPR cannot receive this therapeutic modality due to contraindications [2, 16, 17, 20, 23]. This treatment option has also an increased risk of recurrent PE or distal embolization and fails to completely resolve the intraluminal thrombus, with the potential risk of late chronic thromboembolic pulmonary hypertension [7, 16, 17, 29]. According to an observational study from the ICOPER, the rates of mortality and recurrent PE in 90 days do not decrease in patients with massive PE receiving thrombolysis [1]. Moreover, the long-term outcomes for 249 patients treated with thrombolytics for acute high-risk and intermediate-risk PE has been investigated by Meneveau et al. [30] during a mean follow-up of 5 years. They demonstrated a recurrent PE of 12% and a higher mortality of up to 25% in patients with pulmonary hypertension secondary to partial resolution of the PE. In contrast to these studies, a meta-analysis of 748 patients in eleven

randomized thrombolysis trials by Wan et al. [31] demonstrated a significant reduction in recurrent PE or death with thrombolysis compared with heparin alone (9.4% versus 19%), but the major bleeding rate doubled among thrombolysis-treated subjects.

Currently, there are no randomized trials that compare thrombolysis with surgical embolectomy in patients with acute massive PE [6, 28]. However, in a retrospective nonrandomized comparison of thrombolysis and surgical embolectomy in 37 patients, where 13 of the patients underwent surgery and 24 received thrombolysis, with cardiogenic shock secondary to massive PE, Gulba et al. [7] showed that patients treated with thrombolytics had an increased mortality rate (33% versus 23%), more hemorrhagic events (25% versus 15%), and a higher rate of recurrent PE (21% versus 7.7%). The survival rate of the patients was 77% in the surgery group compared with 67% in the thrombolysis group. Thrombolytic therapy should be given carefully to patients who are potential candidates for surgical embolectomy [20]. After unsuccessful thrombolytic therapy, surgical approach can be particularly risky. Meneveau et al. [32] compared the outcomes of repeated thrombolytic therapy (26/40) and surgical embolectomy (rescue therapy) (14/40) in a series of 40 patients in whom initial thrombolytic therapy failed. They reported significantly reduced mortality (38% versus 7%) and recurrence of PE (35% versus 5%) in the surgical group. Patients with massive PE refractory to thrombolysis have risk of bleeding. Management of bleeding is very important in this complicated condition [2]. However, rescue surgical embolectomy is legitimatized because there is no efficient alternating approach to save these critically ill patients [27].

Catheter-based embolectomy is a minimally invasive technique with successful initial treatment for massive PE and is efficacious in removal of clots and recovery of RV function. It includes aspiration thrombectomy, fragmentation, and rheolytic thrombectomy [3, 6, 24]. The long-term implications of this therapeutic modality have yet not been fully studied. However, it has increased risk with hemorrhage, injury and perforation of pulmonary arteries and RV, PE recurrence, pulmonary hypertension, arrhythmias from catheter pas-

sage through the right heart, severe hemolysis, and acute pancreatitis [11, 16, 17]. Besides, this advanced technique is not always readily available [16]. In our series, no patients underwent catheter-based clot removal due to the limited availability of the technique in our center during this study period. New catheter-directed techniques are evolving and they seem promising for the management of patients with massive PE in the future, where local thrombolysis can be administered or suction embolectomy can be performed [23, 24]. However, these techniques are not without complications. They can lead to vascular and ventricular injuries and arrhythmias. Commercially available catheters have been shown to fragment the embolus rather than its complete extraction. Clot fragmentation can also potentially cause showering of emboli into the distal peripheral pulmonary vasculature, ultimately resulting in chronic thromboembolic pulmonary hypertension and decreased long-term survival because of incomplete embolectomy [3, 7, 8, 16, 17, 20, 24, 33].

To date, there are no randomized studies to compare the outcomes between catheter-based embolectomy and surgical pulmonary embolectomy. In a meta-analysis of 594 patients from 35 studies (6 prospective, 29 retrospective) with acute massive PE treated with modern catheter-directed therapy, Kuo et al. [24] found that the pooled clinical success rate was 86.5%, with success defined as the stabilization of hemodynamics, resolution of hypoxia, and survival to hospital discharge. Pooled risks of minor and major procedural complications were 7.9% and 2.4%, respectively. A recent study of 39 patients by Ina and co-workers [23] assessed the efficacy and safety of local thrombolysis with a pulse-infusion-thrombolysis catheter in the management of acute massive PE. They demonstrated that procedural success was achieved in all patients (100%) and that clinical success was archieved in 36 of 39 patients (92.3%).

Current indications for surgical pulmonary embolectomy include patients with massive central PE and contraindications to thrombolytics or those who are hemodynamically unstable or who had RV dysfunction after receiving thrombolytic therapy (Class IIa; Level of Evidence C) [5]. In addition, patients with free-floating thrombus within the right atrium or RV

and patients in whom a patent foramen ovale poses an imminent risk for paradoxical embolization also require surgical embolectomy [4, 5]. Although surgical intervention is performed in these severely compromised patients, there are recent encouraging results with low mortality after early surgery [6, 28]. Some centers have nowadays taken a more aggressive approach and extended the indications to also include hemodynamically stable patients with massive central clot burden and signs of RV dysfunction on echocardiogram (intermediate-risk PE) [8, 11-13, 17, 21, 33].

Although surgical embolectomy is an invasive intervention, prompt removal of thrombus localized centrally in the main pulmonary artery reduces RV afterload and assists rapid imrovement of RV function if emergency surgery is performed [28]. Emergency surgical embolectomy can be performed as life-saving in critically ill patients with acute massive PE. Early surgery associated with acceptable morbidity and mortality particularly in carefully selected patients can also prevent them from potential future complications such as recurrence of PE and chronic thromboembolic pulmonary hypertension [29]. The most important determinants of early mortality after surgical embolectomy include mainly preoperative cardiac arrest requiring CPR, RV dysfunction, thrombus material extending peripherally into and beyond the subsegmental pulmonary arteries, interstitial pulmonary edema, and massive parenchymal and intrabronchial bleeding [3, 16, 19, 34].

Previous series have a high surgical mortality rate for patients with high-risk PE and circulatory collapse. Depending on the patient's preoperative hemodynamic status, the overall mortality rate after surgical embolectomy varies from 32% to 64% [9]. However, more recent studies have reported promising results, with mortality rate ranging from 3.6% to 27.2% [14, 34]. These better outcomes are attributed to extended indication for surgery including hemodynamically more stable patients with submassive PE with RV dysfunction, careful risk stratification such as appropriate patient selection and rapid recognition of RV dysfunction by contemporary diagnostic modalities, early surgical intervention before the development of cardiac arrest requiring CPR, and improved surgical techniques to prevent residual clot material

and, thus, chronic tromboembolic pulmonary hypertension [6, 8, 14, 17, 29, 34].

In a systematic review of the outcomes of surgical embolectomy in 1300 patients obtained from 46 case series from 1961 to 2006, Stein et al. [9] demonstrated that the overall mortality was 30%. However, they also reported that the average mortality was 32% for patients operated on before 1985, while it was improved to 20% for patients operated on from 1985 to 2005. Preoperative cardiogenic shock is an important prognostic factor for early survival after acute massive PE. In patients with preoperative cardiac arrest, the operative mortality rate was 59%, compared with 29% in patients who did not have cardiac arrest before surgery [9]. Dauphine and Omari [16] reported similar results with an overall mortality rate of 57% for patients who required CPR, compared with 12% for those who did not. This improvement shows the importance of rapid triage and early surgery for hemodynamically compromised patients because of acute massive PE.

Recently, many experienced centers have reported excellent results for surgical embolectomy [8, 17, 19, 27]. In a study reported by Dauphine and Omari [16], surgical mortality had a relatively high rate of 27.3% in 11 patients. Stein and Matta [35] analyzed the in-hospital all-cause case fatality rate of surgical embolectomy from the Nationwide Inpatient Sample from 1999 to 2008. They found that the case fatality rate in unstable patients who underwent surgery remained at 39%-40% from 1999-2003 to 2004-2008, and in hemodynamically stable patients before undergoing surgery it decreased only from 27% to 23%, respectively. Also, more recently, an analysis of 2,709 patients from the weighted Nationwide Inpatient Sample showed a high inpatient mortality rate of 27.2% [34]. In a recent meta-analysis, the cumulative operative mortality for surgical embolectomy from 2000 to 2008 was demonstrated to have significantly improved from 30%-35% before 1999 to 19.1% thereafter, where 3 of the 11 papers included patients with stable haemodynamics [17]. In a study of 21 patients by Vohra et al. [26], mortality was 19% and the long-term outcomes were good, with acceptable actuarial survival of 76.9% at 5 years and 51.2% at 8 years.

The use of percutaneous cardiopulmonary support (PCPS) for hemodynamic stabilization as a bridge to pulmonary embolectomy is an important therapeutic option for acute massive PE [25, 27, 33, 36]. More recently, in an analysis of 32 patients from a multicentre registry in Japan, Taniguchi et al [25] reported that the operative mortality of surgical embolectomy was 18.8% despite the fact that most of the patients were critically ill, including 3 patients with preoperative cardiac arrest and 10 patients with preoperative PCPS. In a recent series of 24 consecutive patients, Takahashi et al [33] also found that the in-hospital mortality rate was 12.5% and the 5-year cumulative survival rate was 87.5%. On the other hand, survival after surgical pulmonary embolectomy was 100% if preoperative cardiac arrest could be avoided.

Carvalho et al. [6] reported a 30-day mortality of 85% in seven patients undergoing salvage surgical pulmonary embolectomy. These patients had a cardiogenic shock receiving CPR or a recent history of cardiac arrest. However, hemodynamically stable patients undergoing emergency surgery have an operative mortality of 11%. Aklog et al. [12] reported mortality of 10.3% in 29 consecutive patients with massive proximal PE, RV dysfunction, but preserved hemodynamics and an impressive 30-day survival rate of 89%. Kadner et al. [19] reported a 30-day mortality of 8% following salvage pulmonary embolectomy in 25 critically ill massive PE patients. In their experience, 32% of patients had significant hemodynamic compromise including preoperative arrest. Leacche et al. [8] reported on 47 patients who underwent surgical embolectomy with an operative mortality rate of 6% and 3-year survival of 83%. However, in 6 (11%) of their patients who required CPR before surgery, operative death was substantially higher (33%). Fukuda et al. [27] reported lower hospital mortality of 5.3% and 10-year survival of 83.5% in 19 patients, who underwent emergency pulmonary embolectomy, including 2 patients with preoperative PCPS. More recently, Aymard et al. [14] reported that the early mortality rate was 3.6% in patients with massive PE undergoing surgical embolectomy, whereas early mortality was 27% in those patients treated initially with thrombolysis and subsequently requiring surgery.

The primary evidence of present study is that surgical pulmonary embolectomy can be performed with an acceptable morbidity and mor-

tality in patients with acute massive PE. We had an overall in-hospital mortality rate of 23.1% (3 patients), with operative mortality of 7.7%, which was lower than the results of earlier study [9, 16] but relatively higher than that of recent studies. In our series, one patient could not be weaned from the CPB and the remaining two died of multiorgan failure in the intensive care unit. This discrepancy of mortality may have been because two of our patients entered the operating room with ongoing CPR and the other experienced multiple cardiac arrests responding to CPR preoperatively. The mortality rate was 75% (3/4) in patients with cardiac arrest requiring CPR before operation. However, when preoperative cardiac arrest was avoided, our in-hospital mortality rate could be reduced to 0%.

Surgical embolectomy is generally performed for large central PE through the main pulmonary artery trunk incision or the separate right pulmonary artery incision by using appropriate forceps, rigorous irrigation and suction. However, removing the thrombus located more peripherally is difficult, and incomplete removal of clot material from the distal pulmonary vasculature can cause persistent pulmonary hypertension leading to RV dysfunction [19]. Distal thrombotic material is traditionally extracted using a Fogarty balloon catheter without visual assistance or by manual lung compression. Both blind methods cannot be well controlled and can cause mechanical injuries to the pulmonary arterial wall, especially in the segmental branches, and provoke parenchymal and endobronchial bleeding [12, 19, 33]. From all reasons above, in our series we did not extract distal thrombi in the branches of the pulmonary artery by means of Fogarty catheter extraction or manual compression of the lungs to avoid blind instrumentation. Our approach to clot extraction was limited to directly visible thrombus. Thus, we could accomplished the removal of thrombotic material by forceps from the level of the segmental pulmonary arteries. In this complicated situation with more peripherally localized clot material, as additional maneuver, cooling on CPB of the patient could also be considered to reduce CPB flow for improved visualization. Furthermore, optimal visualization of the distal pulmonary arterial tree for complete embolectomy can be extended with use of an arterioscope or deep hypothermic circulatory arrest [19, 37].

Amirghofran et al. [20] have used stone forceps including different sizes and tip angulations instead of ring forceps for thrombotic removal in medium-sized pulmonary artery branches. They reported that these instruments are very useful for gentle extraction of trapped particles of clot.

Retrograde pulmonary perfusion via direct cannulation of the pulmonary veins from the left atrium as an adjunct to surgical pulmonary embolectomy has been recommended to remove residual thrombotic material lodged in the distal pulmonary arterial branches and prevent air embolism within the pulmonary artery [29, 38]. In a retrospective study, Spagnolo et al. [38] analyzed a series of 21 consecutive critically ill patients undergoing retrograde pulmonary perfusion while performing standard pulmonary embolectomy. They reported that no patient died or experienced major postoperative complications. More recently, Zarrabi et al. [29] also reported the long-term outcome of 30 patients undergoing surgical embolectomy complemented by retrograde embolectomy technique and demonstrated the safety and favourable long-term outcome of this technique. They presented that the pulmonary arterial pressure drop immediately following operation and the trend toward normalization continues long after surgery. We did not need to use this tecnique in any of our patients.

Recurrence of PE can occur early after surgical embolectomy and is one of the most important causes of early postoperative mortality. Its recurrence rate can be as high as 5% [25]. Therefore, IVC filter insertion can be performed during or immediately after surgical intervention to prevent recurrent PE. However, the role of IVC filters usage following surgery is a debatable subject. Furthermore, IVC filters could prohibit the recurrence of PE, but they are known to increase deep vein thrombosis [19]. Eight-year follow-up of a randomized controlled trial in patients with permanent IVC filters demonstrated that these filters reduce the risk of PE but increase the risk of deep vein thrombosis [39]. Some studies proposed routine placement of IVC filters [1, 8, 10, 26, 40]. In ICOPER study, Kucher et al. [1]. reported that IVC filter placement in patients with massive PE has reduced recurrent PE and 90-day mortality. These findings in their study should be cau-

tiously commentated because an IVC filter has been placed only in 10% of the 108 patients with massive PE and surgery was performed only in 3 patients. Recently, 93% of patients treated surgically by Greelish et al. [21] had intraoperatively placed IVC filters. In a more recent study reported by Taniguchi et al [25], perioperative IVC filter was inserted only in 57.7% of the surviving patients. Leacche et al. [8] have also reported IVC filter usage of 81% in patients undergoing surgical embolectomy. Besides these, Sadaba et al. [40] reported that usage of the IVC filters approximates 100%. Guidelines of the European Society of Cardiology [4] recommend that IVC filters may be used when there are absolute contraindications to anticoagulation and a high risk of venous thromboembolism recurrence (Class IIb, Level of Evidence B). Kadner et al. [19] do not routinely place IVC filters after surgical embolectomy and have also demonstrated no evidence of long-term recurrences of PE in absence of these filters. In our series, IVC filters were not used intraoperatively in any of our patients. However, as an anticoagulant, warfarin was prescribed postoperatively to all patients for at least 9 months, and an IVC filter was placed in 2 patients at postopearative 2nd and 4th months, respectively, due to a repeat deep venous thrombosis in the lower extremity.

In our series, surgical embolectomy saved all patients without preoperative cardiac arrest. The follow-up periods of the 10 (76.9%) survivors ranged from 6 months to 170 months (mean, 25 months), with one case (7.7%) of late death 12 months after surgery due to renal carcinoma. Postoperative echocardiographic pressure measurements demonstrated significant reduction, compared with preoperative ones (P < 0.001). RV function was immediately improved in all survivors. At final follow-up, all surviving patients were in New York Heart Association class I and have a good quality of life. No readmission for a recurrent of PE was observed, and also no patient subsequently went on to develop chronic thromboembolic pulmonary hypertension due to incomplete embolus removal. There were no complications as a result of postoperative placement of two permanent IVC filter.

Limitations of the study

The present study has several limitations. Firstly, it was a small sample size limiting the generalizability. However, in our series emergency surgical embolectomy has encouraging results especially in patients who had yet not experienced cardiac arrest requiring CPR. Secondly, this was a retrospective nonrandomized study and as such, it was influenced by bias. It was conducted without a control or another study group including medically treated with heparin alone, catheter-based treatment patients, or thrombolysed patients. Comparison of the results of these groups in a randomized trial would be optimal. Finally, further studies are needed to define the subgroups in patients that are most likely to benefit from more aggressive treatment.

Conclusions

A multidisciplinary approach with rapid diagnosis by CT and echocardiography, careful patient selection, early surgery, and advanced surgical techniques can make a significant contribution to the outcomes of surgical pulmonary embolectomy in the high-risk patients with acute massive PE and hemodynamic instability. A successful outcome after surgical embolectomy necessitates emergency surgery before cardiac arrest develops. Furthermore, liberalization of surgical indication should be considered even to hemodynamically stable patients with RV dysfunction.

Disclosure of conflict of interest

None.

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