

# Clinical Outcome of Acute Pulmonary Embolectomy Taken as to be the First Line Treatment for Massive and Submassive Pulmonary Embolism: Experience from One Single Center in China

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## Research article

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# Abstract

**Background:** Acute pulmonary embolism (PE) is one of the most critical cardiovascular disease. The treatment for PE depends on the severity of disease including anticoagulation, systemic thrombolysis, surgical embolectomy, and catheter embolectomy. The indication of surgical pulmonary embolectomy is still controversy. Although there have been more favourable reports of the of surgical embolectomy (SE) over past decades, SE has still been used as a resort or rescue treatment for acute massive PE with significant hemodynamically unstable or present with cardiogenic shock or patients whose thrombolysis failed—therefore the high mortality of pulmonary surgical embolectomy was still reported. SE has not yet been accepted broadly as initial therapy in the algorithm for massive and submassive PE.

**Objective :** The purpose of this study is to evaluate the early and midterm outcome of surgical pulmonary embolectomy which was taken as the first line therapy for acute central major pulmonary embolism in one single center in China

**Methods:** A retrospective review of patients who underwent surgical pulmonary embolectomy for acute pulmonary embolectomy was conducted from July of 2005 to Sept of 2019 at a single heart center in China. Patients with chronic thrombus or thrombendarterectomy were excluded. The risk factors for morbidity and mortality of the surgical pulmonary embolectomy were reviewed, The institutional echocardiographic database was searched for follow-up studies to compare markers of right ventricular function.

**Results:** A total of 41 patients were included for the study, 17 cases (41.5%) had submassive PE and 24 (58.5%) had massive pulmonary embolism required preoperative positive inotropic treatment. Mean cardiopulmonary bypass time was  $103.2 \pm 48.9$  minutes, and 10 patients (24.4.%) underwent procedures without aortic cross-clamping. Ventilatory support time was  $80.6 \pm 21.3$  hours. ICU stay was  $4.51 \pm 3.23$  days. Hospital stay was  $12.8 \pm 6.4$  days. There was operative mortality 3 (7.32%) for massive pulmonary embolism and no death case of submassive pulmonary embolism. For massive PE patients, if the first choice treatment was surgical embolectomy, the mortality was low, only 2.56%, even though there were 2 cases suffered from cardiac arrest preoperatively. However, if 2 cases who received systemic thrombolysis firstly were included in the data, the mortality rate of SE increased to 12.5%. All cases had echocardiography results available for follow-up at discharge, and 30 cases at three months, only 10 cases at one years after surgical embolectomy. There were no death event related with recurrent PE in the follow-up, but 3 patients died of cerebral intracranial bleeding, gastric cancer and gastric cancer at 1 year, 3 years and 8 years after surgical embolectomy respectively.

**Conclusions:** In this small retrospective single center experience, SE presented with low mortality rate when it was rendered as the first line treatment in selected patients for massive and submassive acute pulmonary embolism. SE should play the the same role as ST in the treatment algorithm for acute PE. Echocardiographic showed right ventricular function was improved in the early and midterm follow-up term

# Introduction

Acute pulmonary embolism (PE) is one of the most critical cardiovascular disease. According to the severity of disease, PE has been stratified into high-risk (massive), inter-mediate risk (submassive), and low-risk<sup>(1)</sup>. The treatment for PE depends on the stratification, ranging from anticoagulation to systemic thrombolysis (ST), surgical embolectomy (SE), and catheter embolectomy<sup>(2)</sup>. Surgical pulmonary embolectomy had traditionally been used as a final or rescue treatment for acute massive PE with significant hemodynamically unstable or present with cardiogenic shock or patients whose thrombolysis failed (therefore the high mortality rate more than 30% of pulmonary surgical embolectomy was reported<sup>(3,4)</sup>). However, with rapid advanced diagnosis, improvement of the surgical techniques and experience of surgeon, more favourable results in surgical embolectomy for acute PE had been reported<sup>(5-8)</sup>. Increasing excellence reports of SE for acute massive PE extended the indication of pulmonary embolectomy for acute PE. SE has been positively considered as contemporary algorithm for PE elective treatment rather than a final rescue tool (but it is still controversy report of the mortality rate for SE, which varied from 2.3%<sup>(9)</sup> to 27.2%<sup>(10)</sup>). So further research is needed to estimate the certain role of SE in the algorithm for PE. Most of studies were reported by authors from the USA and European countries, only few from developing country<sup>(11)</sup>. The aim of the study is to assess clinical outcome of surgical embolectomy for acute PE patients in one single heart center in China.

## Patients And Methods

This was a single-center, retrospective uncontrolled study in China. The study protocol was approved by Medical Ethics Committee of Union Hospital of Fujian Medical University. 41 consecutive patients with acute PE who underwent surgical pulmonary thrombolectomy were included from July 2005 to August 2019 in our department. 24 patients received emergent surgery, whereas sub-emergent operation were performed in 17 patients. There are 21 male patients, 20 female patients. Mean age was 56±11 years old (range, from 28 to 75 years old).

Acute pulmonary embolism was defined as the acute onset of illness with duration of less than 2 weeks. Patients with acute-on-chronic PE undergoing pulmonary thromboendarterectomy were excluded from this study.

Massive PE was defined as thrombus occlusion more than 50% of pulmonary vasculature or occlusion of two or more lobar arteries or clinically hemodynamic compromise such as cardiogenic shock, systolic blood pressure lower than 90 mmHg or a pressure drop of more than 40 mmHg for more than 15 minutes, or cardiac arrest. Submassive PE was characterized by a hemodynamically stable condition with moderate and severe right ventricle dysfunction (RVD) and with one more of the following criteria present: clinical signs of organ hypoperfusion or hypoxia and syncope, or abnormal biomarkers suggestive of myocardial injury (troponin) or myocardial distension (brain natriuretic peptide <BNP> or N-terminal pro-BNP) or elevation level of lactate<sup>(8)</sup>. Right ventricle dysfunction (RVD) on echocardiography was defined as the presence of an RV end-diastolic diameter  $\geq 30$  mm or an RV/left ventricle end-diastolic

diameter ratio of greater than 1 in the apical 4-chamber view, paradoxical septal systolic motion, RV free wall hypokinesia, and pulmonary hypertension (right ventricular/right atrial gradient of more than 30mmHg)<sup>(16)</sup>

The most common presenting symptom was dyspnea (n=41 100%), chest pain (n=13 31.71%), syncope (n=10 24.39%), cardiac arrest (n=3 7.31%) hemoptysis (n=4 9.75%) hemodynamic instability (n=14 34.14%). All patient was examined by echocardiograph, right ventricle dysfunction (RVD) was presented in (n=34 82.93%).

Pulmonary arterial computed tomography angiography (PACTA) were performed in all patient but 2 patients who were diagnosed without PACTA because the patients experienced heart arrest need continued CPR till to operation. 39 cases patients were diagnosed with PACTA. There were 4 cases whose thrombosis clot were in right atrium, 2 cases of clots in right ventricle chamber. There were 18 cases of thrombosis clots in main trunk of Pulmonary arterial, and /or 16 cases of thrombus clot in right and /or left branch of pulmonary artery branches.

## **Surgical technique**

The surgery was performed through median sternotomy. After cardiopulmonary bypass, firstly, a right atriotomy was performed and the right atrium and right ventricle were explored routinely, thrombus was removed if there existed. A longitudinal incision then was made on the main pulmonary artery trunk, extending the incision into the left pulmonary artery and addition incision was performed in the right pulmonary artery between the aorta and superior vena cava for further exposure. The thrombus removal was performed by means of forceps en bloc if possible. In order to extract thrombotic materials inside segmental and sub segmental pulmonary branches gallbladder forceps is option tool. All branches were carefully inspected. The pulmonary artery tree was irrigated vigorously by bolus saline flush and aspirated till flesh red blood flew out from distal pulmonary arterial branch. Performing extraction should be done very gently and carefully to avoid damage to the distal smaller pulmonary branches and lung tissue already infarcted. The incision of right atrium and pulmonary artery were closed with 4-polypropylene suture. It is important on beating heart to perform to prevent right ventricle already overloaded from ischemic-reperfusion injure. After surgery, thrombus filter was implanted in the inferior vena cava in patients with deep venous thrombosis (DVT) in the legs.

## **Post-intervention treatment**

The patients received anticoagulation by using low molecular weight heparin 6-10 hours after operation when the risk of surgical site bleeding disappeared. Additional some patients received low dose of streptokinase or recombinant tissue plasminogen activator therapy for 3 days when the activated partial thromboplastin time (aPTT) was less than 80ms. Anticoagulation with heparin was continued until oral warfarin reached therapeutic range (target international normalized ratio of 2.0 to 3.0). Warfarin was continued for at least one year. All patients were referred to our department for follow-up.

## Statistical analysis

Statistical analyses were performed by SPSS software package [SPSS for windows, version 19]. The data of descriptive statistical analysis are presented as the mean±the standard deviation of the mean or media with interquartile range. The comparison between the groups data was performed using Student' t-test or the Manna –Whitney U test. Values of P 0.05 were considered to indicate statistical significance.

## Results

There were 24 (58.5%) cases of massive PE, 17 cases (41.5%) of submassive PE. All patients were diagnosed with echocardiography which indicated not only thrombin clot location in the heart but also assecesed right ventricle function. There were 34 cases (n=34 82.9%) of patient presented with RVD. Size of right ventricle was 32.8mm±9.34mm and pulmonary arterial pressure was 73.3±25.9mmHg. Tricuspid valve regurgitation was 3.6±1.3 Grade.

In the study, 2 patients accepted systemic thrombolysis as first choice of treatment but failed to work, the other 39 patients accepted SE as first line therapy. There were 15 cases who were contraindications of thrombolysis, of whom were 3 cases of recent surgery, 4 case old ages (more than 70 years old ), 4 cases of right atrium thrombi-clot, 1 case of pregnant, 1 cases of brain tumor, 1 cases of atrial tumor, 1 case of with mitral valve replacement. 24 cases were recommended SE to be first line treatment rather than thrombolysis, of whom 20 cases were massive PE, 4 were submassive PE.

The concomitant operation was right atrial tumor resectomy 1 case, mitral valve replacement 1 case. The CPB time was 103.2±48.9mins. The aortic clamp time was 68.5±29.8mins (10cases only). Ventilatory support time was 80.6±21.3hours. ICU stay was 4.51±3.23 days. Hospital stay was 12.8±6.4days.

Before surgery, there were three patients suffering from cardiac arrest, of whom 2 received long time cardiopulmonary resuscitation (CPR), one was 40mins continued CPR, another last 123 mins continued CPR till to surgery, these 2 patients recovered very well without any brain damage. The other one who recovered from short time CPR, accepted systemic thromblysis as first choice of therapy but failed to and resorted to surgical treatment.

There was no death patients with submassive PE. There were 3 death cases who were massive PE. One patient, who accepted systemic thrombolysis for the first treatment before operation, died of uncontrolled massive lung hemorrhage during operation. Another one patient died of severe hypoxemia resulted from severe ARDS, which leading multiple organ dysfunction even supported with ECMO postoperatively. The other one patient died of severe bleeding in surgical site leading to multiple organ dysfunction even were supported with ECMO postoperatively. The operative mortality rate was 7.32% [3/41] overall totally. However, there were 2 patients who reviewed thrombolysis as to be first line treatment, if these 2 case were excluded from the datus, the mortality rate was only 2.56% (1/39).

All patients received inotropic treatment and needed prolong ventilation supports which last more than 24 hours. The postoperative complication is showed in table 2. There were 16 cases patients who were implanted thrombus filters in inferior vena cava (IVC) postoperatively for DVT patients.

For all survival patients, postoperative echocardiograph was performed at 2 weeks, 3 months and 1 year survival postoperatively respectively. The datus is showed in Table 3.

Follow-up was conducted in all survival patients (n=38) for average duration 5.8 years(range from 0.5 years to 14 years ). There was one patient, who had cerebral metastasis cancer, did not wake up and was diagnosed as brain death 2 months after surgical pulmonary emblectomy. One patient died because of cerebral incranal bleeding at 1 year after SE. One cases died from gastric cancer at 3 years after SE. One patient died from brain cancer at 8 year after SE. There were no case related with re-occurrent PE.

Table 1 Preoperative Baseline characteristics of patients

Variables	patient (n=41)
Age (years)	
Mean±SD	56±11
Range	28—75
Gender (Male /Female)	20/21
Cardiac arrest (n, %)	3 ( 7.31% )
Inotropics need (n, %)	14 ( 34.14% )
Mean LVEF (%)	50.1%±13.6%
Mean SPAP (mmHg)	73.3±25.9
RV (mm)	32.8±9.34mm
Symptoms	
Dispnea (n, %)	41 ( 100% )
Syncope (n, %)	10(24.4%)
Chest pain (n, %)	13(31.7% )
Hemoptysis (n, %)	4(9.75%)
Risk Factor for PE (n, %)	
Prior DVT	16 (39.2%)
Malignancy tumor	2(4.87%)
Recent Surgery	8 ( 19.5% )
Smoking	7(17.15%)
Pregnant	1(2.43%)
Unknown	5(12.2%)
Diagnostic tools (n,%)	
Echocardiography	41 (100%)
CTA of PA	39(95.1%)
D-Dimer >5 U <sub>g</sub> /L	41(100%)

SD=standard deviation ; LVEF=left ventricle ejection fraction ;SPAP=systolic pulmonary artery pressure ;CVE=cerebrovascular event ;DVT=deep venous thrombosis; CTA=computed tomography angiography; PA=pulmonary artery ;

Table 2. characteristics and postoperative outcome

Variables	patients (n=41)
Mean CPB time (minutes)	103.2±48.9 (100%)
Aortic clamp time (minutes)	68.5±29.8(n=12 29.26%)
Ventilatory Assist time (hours)	80.6±21.3
ICU Stay (day)	4.51 ±3.23
Complication (n,%)	
Massive lung hemorrhage	3 (7.32%)
Lung infection	14(34.1%)
ARDS	4 (9.76%)
Cerebrovascular event	2 (4.87%)
Renal failure	2 (4.87%)
Surgical site bleeding	1(2.44%)
Multiple organ failure	2 (4.87%)
ECMO support	2(4.78%)
Inspidus	1 (2.44%)
Hydrothoracic	6 (14.36%)
Mortality rate totally	3 (7.32% 3/41)
ST Excluded mortality rate	1 (2.56% 1/39)
Mortality rate for Massive PE	3 (12.5% 3/24)
Mortality rate for submassive PE	0

CBP=cardiopulmonary bypass; ARDS=adult respiratory distress syndrome; ECMO=extracorporeal oxygenated membrane; PE=pulmonary embolism; ST=systemic thrombolysis; ICU=intensive care union

Table 3. Preoperative and postoperative echocardiograph datus of RV

	Pre n=41	1week Post. n=38	3moths Post. n=35	1 years Post. n=19
Size of RV (mm)	32.8±9.34	25.6±4.32*	24.1±5.08	23.1±4.61
Pressure of PA (mmHg)	73.3±25.9	38.6±10.2*	32.9±11.5	31.2±9.76
Grade of TR	3.86±1.33	2.62±1.43*	2.13±1.35	1.21±0.86

Pre=preoperation; Post=postoperation; RV=right ventricle; PA=pulmonary artery; TR=tricuspid valve regurgitation; \* P value < 0.05 Compare to "Pre group",

## Discussion

Acute PE is the third most common cause of cardiovascular death in the USA<sup>(1)</sup> The symptom is often presented with poorly predictive such as dyspnea,chest pain, haemoptysis, syncope and arterial hypotension. Because of the clinical manesfestation being low characteristic and low sensitive,

especially for those massive PE cases, patients would be deteriorated within short time rapidly, therefore rapid diagnosis is very important. In clinical practice, pulmonary artery computed tomography angiography (PACTA) was most common useful tool for making a rapid diagnosis and risk stratification. PACTA has sensitivity of 83% and a specificity of 96%<sup>[27]</sup>. By PACTA surgeons have very a visualization of thrombosis clots location in the main pulmonary arteries and down to at least the segmental level. Acute PE was categorized as massive, submassive and non-massive PTE. Massive PE<sup>(2)</sup> was defined as a PACTA finding of thrombosis clots in the main pulmonary artery or more than 2 lobar arteries. In our study, 38 patients were diagnosed by PACTA of pulmonary artery, but 2 cases did not receive CTA because of impossibility of receiving PACTA due to critical illness with cardiac arrest. In the case of patients with severe hemodynamic instability and inability to travel for PACTA, transthoracic echocardiography (TTE) should be considered a critical useful tool for making diagnosis. TTE provides not only location of thrombi clot but also assessment of right ventricle structure and function as well. In our study, all patients were diagnosed of PE by TTE.

For massive PE patients if hemodynamic unstable, the therapeutic window is very narrow, it was reported that about 10% of patients with symptomatic PE died within 1 hour of onset<sup>(12)</sup>. There are several options of treatment for massive PE such as: systemic thrombolysis (ST), catheter-directed thrombolysis or embolectomy and ST.<sup>(1)</sup> According to traditional view, surgical embolectomy (SE) would not be first choice but to be the last resort treatment when patients were contraindication to ST or CDL or ST failed to work even though patients were critical illness. SE was considered as very dangerous treatment for PE due to its high operative mortality with 27.2% to 59%<sup>(13)</sup>. However, in 2005, Leacche M et al<sup>(4)</sup> firstly reported that pulmonary embolectomy mortality was only 6%, encouraged by the favorable result, the idea of extend indication for PE has evolved to patients whose hemodynamic are stable but intermediate and severe right ventricle dysfunction. The mortality of pulmonary embolectomy has gradually decreased. Lehnert P<sup>(14)</sup> reported 33 cases of surgical treatment with 2 deaths, the mortality was 6%. Worku B<sup>(15)</sup> reported 20 cases surgical treatment for PE with only 1 case death, the mortality was 5%. Yalamanchili<sup>(16)</sup> reported with 8% mortality of surgical treatment, Edelman JJ<sup>(17)</sup> reported 37 cases pulmonary embolectomy with 2 case death, the mortality was 5.4%. Aymard T<sup>[18]</sup> reported 28 cases pulmonary embolectomy with 2 cases death, mortality was only 3.6%. Cho<sup>(19)</sup> reported SE had lower cardiac mortality risk than thrombolysis in PE patients with hemodynamic stable. More and more good results of SE indicated SE should not only to be a rescue therapy for those patients who ST failed to work, but could be considered as to be first line treatment choice for PE. But there is still controversial about the outcome of SE. Jiye<sup>(20)</sup> reported 14.8% of surgical treatment mortality rate, Reza<sup>(21)</sup> recently reported 36 cases surgical treatment for massive PE with 10 death cases, the mortality was 27.8%. In our study, from 2007 to 2019, there were 41 cases of acute PE who received surgical embolectomy, of whom, 3 patients died postoperatively, the operative mortality rate was 7.32%, consideration of 3 cases cardiac arrest preoperatively, the result was accepted, if cases of cardiac arrest was excluded, the operative mortality rate was 5.26% [2/38], which is very favorable. In our study, there were only 2 patients accepted ST as first

choice treatment but both of them failed to work and were transferred to surgical treatment. The other 39 cases of PE patients, SE were first-line treatment choice, the mortality was low, only 2.56%(1/39).

Stein<sup>(22)</sup> performed a meta-analysis of 1300 patients in 46 reports and found a linear relationship between mortality and the prevalence of cardiac arrest before pulmonary embolectomy in each report. The most risk factor of surgical treatment is preoperative cardiac arrest which causing mortality up to 59%. Keeling<sup>23</sup> reported that the in-hospital mortality of patients with preoperative cardiopulmonary resuscitation (CPR) was significantly higher (9/28,32.8%) than in those without CPR (16/186,8.6%). Takahashi<sup>24</sup> reported that 73% of patients who received CPR for longer than 30 minutes died after pulmonary embolectomy. In our study, there were 3 patients who suffered from cardiac arrest before operation, 2 received surgical embolectomy as first line treatment even after continued CPR lasting more than 40 minutes, and got very good recovery without any brain damage. But the other one patient suffered from about 3mins CPR and then was treated with thrombolysis firstly, but failed and resorted to surgical embolectomy. This patient died of surgical site bleeding lead to multiple organ function failure postoperatively. Even though there were reports of successful thrombolysis therapy for PE patient after long time CPR<sup>(25)</sup>. In the light of our limited experience, it seemed to be more effectient to select surgical embolectomy as be the first choice treatment for PE patients with cardiac arrest. Aymard<sup>(8)</sup> did research for massive pulmonary embolism therapy between surgical embolectomy and thrombolytic therapy, and found that SE had lower mortality rate with 17.9% vs 23.1% in thrombolytic group. Compared with thrombolysis, surgical embolectomy would take less time in removal of clots in pulmonary artery and relieve afterload of RV rapidly. Another reason is that postoperative bleeding also is a critical problem for those patients who failed in thrombolysis treatment.

Massive lung hemorrhage was severe operative related complication of SE which accounted for main cause of mortality in our study. There were 3 cases of massive lung hemorrhage postoperatively in the study. One patient died during operation because of uncontrolled great amount of bleeding in the lung. Another 2 patients were survival. Massive lung hemorrhage was often due to pulmonary arterial vasculature injured. During operation, in case of pulmonary massive hemorrhage, it is necessary to open pleural cavity, and locate the responsible pulmonary artery and repair rupture pulmonary artery with 6-0 polypropylene suture. In order to avoid damage to the infarcted smaller pulmonary artery, we modified surgical technique, when doing removal of thrombus clot in the distal pulmonary arterial branches, it is forbidden to perform extraction without visualization. It is hard to extract smaller clots deep in the distal pulmonary arterial branches, we used heparine saline to irrigate vigorously the pulmonary arterial branches and aspirated till flesh red blood flew out from distal pulmonary arterial branch. Alternative option<sup>(14,26)</sup> was retrograde pulmonary venous perfusion with heparine saline, which was useful to removal very smaller clot in the distal pulmonary arterial branches.

Because all cases received anticoagulation therapy after discharge and lasted at least 2 years, there was no reoccurrent PE cases in the follow-up. However there was a case with cerebral intracranial bleeding at 1 year after SE.

## Conclusion

In the study, there was no mortality for submassive PE. For massive PE patients, if the first choice treatment was surgical embolectomy, the mortality was low, only 2.56% (1/39), even though there were 3 cases suffering from cardiac arrest preoperatively. However, if 2 cases, who received systemic thrombolysis as first treatment, were included in the data of SE, the mortality rate of SE increased to 12.5%. It seems that the clinical mortality rate of PE depended on not only the selection of PE patient but also treatment choice. The study showed that SE presented with a low mortality rate when it was rendered as the first line treatment in selected patients for massive and submassive acute pulmonary embolism. SE should play the same role as ST in the treatment for acute PE. But the study was retrospective, not contrasted, and the sample was rather small, further study is needed to assess the role of SE in the treatment algorithm for acute PE.

## Abbreviations

PE pulmonary embolism

SE surgical embolectomy

ST systemic thrombolysis

RV right ventricle

RVD right ventricle dysfunction

CPR cardiopulmonary resuscitation

CPB cardiopulmonary bypass

ARDS adult respiratory distress syndrome

ECOM extracorporeal oxygenated membrane;

DVT deep venous thrombosis

ICU intensive care unit

PACTA Pulmonary arterial CT angiography

SD standard deviation

LVEF left ventricle ejection fraction ;

SPAP systolic pulmonary artery pressure ;

CVE cerebrovascular event

IVC inferior vena cava

TR tricuspid valve regurgitation

PA pulmonary artery

## Declaration

### **-Ethical Approval and Consent to participate:**

This study was approved by the ethics committee of our hospital and conformed to the declaration of Helsinki

### **- Consent for publication:**

No applicable

### **- Availability of supporting data:**

Please contact author for data requests

### **- Competing interests:**

No potential conflicts of interest with respect to the research, authorship, and publication of the article

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### **- Authors' contributions:**

Wang Qimin designed the study and wrote the manuscript. Chen Liangwan reviewed the manuscript and made change in the manuscript. Chen Huabin collected clinical follow- up datus and analyzed data. Chen Daozhong, Qiu Hanfan, Huang Zhongyao, Dai Xiaofu, Huang XueShan and LinFeng made supplement of patients datua and changed parts of manuscript. All authors read and the approved the manuscript

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