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Original Contribution

# Comparison between systemic and catheter thrombolysis in patients with pulmonary embolism☆

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ABSTRACT

*Background:* Although systemic thrombolysis (ST) or catheter-directed therapy (CDT) is performed in patients with acute massive or submassive pulmonary embolism (PE), clinical data comparing between both therapies remain limited. We compared clinical outcomes between ST and CDT in patients with acute massive and submassive PE.

*Methods:* From January 2005 to June 2015, clinical outcomes of patients with acute massive or submassive PE receiving ST or CDT were evaluated and compared retrospectively.

*Results:* Of 72 patients, 44 were treated with ST; and 28, with CDT. The mean age was 63.9 ± 17 years old. The proportion of male sex was higher in patients receiving CDT compared to that with ST (46.4% vs 20.5%; $P = .02$). Half of patients presented with massive PE, and cardiac arrest occurred in 11 patients (15.3%). No difference was observed between the 2 groups with respect to 7-day mortality (13.6% in ST vs 10.7% in CDT), inhospital mortality (13.6% in ST vs 14.3% in CDT), and major bleeding complication (16.7% in ST vs 16.7% in CDT). Cardiac arrest (odds ratio, 6.286; 95% confidence interval, 1.081-36.555; $P = .041$) was associated with 14-day mortality.

*Conclusions:* Similar clinical outcomes were shown between ST and CDT in patients with acute massive or submassive PE.



## 1. Introduction

Acute massive pulmonary embolism (PE) resulting in hemodynamic instability has been known as having high mortality [1,2]. Submassive PE, which right ventricular dysfunction develops without shock, was also associated with poor prognosis [3]. Systemic thrombolysis (ST) has been administered to rescue patients with massive PE [4,5], but clinical benefits of thrombolysis have remained controversial in patients with submassive PE [6,7]. Current guidelines recommend the administration of thrombolytic agents be selectively administered for submassive PE patients with high risk of clinical deterioration [8,9]. Although ST reduces mortality in patient with massive or submassive PE, major hemorrhagic complication is an obstacle to its routine widespread clinical application [4,5,7]. Catheter-directed therapy (CDT) using pharmacomechanical thrombolysis combined with low-dose thrombolytic infusion is known as an alternative method in replacement of ST in patients with massive or submassive PE. Several studies have shown significant clinical benefits of CDT in patients with massive or submassive PE [10–12]. However, there are few clinical data comparing treatment outcomes between ST and CDT in massive or submassive PE.

The aim of this study was to compare treatment outcomes between ST and CDT in patients with acute massive and submassive PE.

## 2. Methods

### 2.1. Patients

From February 2005 to June 2015, patients 18 years or older were included if they were diagnosed with acute massive or submassive PE and treated with either ST or CDT as a rescue therapy. Pulmonary embolism was diagnosed within 14 days of symptoms and confirmed by computed tomography (CT) of the chest showing filling defects of at least 1 main or lobar pulmonary artery or visible thrombus within the pulmonary artery by echocardiography. *Massive PE* is defined as acute PE with systolic blood pressure less than 90 mm Hg or pressure drop by at least 40 mm Hg for more than 15 minutes or requirement

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of inotropes or signs of shock, and *submassive PE* is defined as acute normotensive PE accompanied by right ventricular dysfunction (RVD) (right ventricular dilatation, hypokinesis, paradoxical septal systolic motion confirmed) on echocardiography and/or chest CT scan [8,13].

### 2.2. Systemic thrombolysis and CDT

The choice of thrombolytic modalities was decided at the discretion of the attending physicians. Two types of thrombolytic agents for ST were used: urokinase or alteplase. Urokinase was used at a dose rate of 4400 IU/kg bolus injection followed by a 4400 IU/kg per hour maintenance for 12 to 24 hours. Alteplase was used as 10-mg bolus, followed by a 90-mg intravenous infusion over a period of 2 hours. Pharmacomechanical thrombolysis was performed as CDT. Local thrombolysis via infusion catheter on pulmonary artery with/without mechanical maceration with standard pigtail catheter and continuous infusion of urokinase overnight was performed by experienced interventional radiologists.

### 2.3. Outcomes

We evaluated mortalities such as 7-, 14-, or 28-day mortality as treatment outcomes. We also analyzed bleeding complications (major or minor) from ST or CDT as measure of its safety profile. *Major bleeding* was defined as fatal bleeding, hemorrhagic stroke confirmed by CT, or a drop in the hemoglobin concentration by at least 2 g/dL, with or without the need for packed red cell transfusion [14]. This study was performed retrospectively and was approved by the institutional review board. Informed consent was waived due to the retrospective nature of the study. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the Helsinki Declaration and its later amendments or comparable ethical standards.

### 2.4. Statistical analysis

Categorical data are expressed as percentages, and continuous variables are expressed as means ± SD. Differences between groups were assessed using $\chi^2$ test or Fisher exact test for categorical variables, as appropriate. For continuous variables, differences between 2 groups were assessed by the Mann-Whitney *U* test. Logistic regression analysis was used to identify factors associated with mortality. All tests were 2 sided, and $P < .05$ was considered statistically significant. All statistical analyses were performed using SPSS 18 (Chicago, IL).

## 3. Results

### 3.1. Baseline characteristics of the enrolled patients

During the study period, a total of 72 patients were diagnosed with either massive or submassive PE and received ST (n = 44, 43 urokinase and 1 alteplase) or CDT (n = 28) using pharmacomechanical thrombolysis. The overall baseline characteristics of the enrolled patients are described in Table 1. The mean age was 63.9 ± 17 years old, and 22 patients (30.6%) were male. The proportion of men was higher in the group receiving CDT compared to the group that received ST. There was no difference between the 2 groups in terms of risk factors. Concomitant deep vein thrombosis was confirmed in approximately two-thirds of patients. Fifteen percent of patients presented with cardiac arrest, but the fraction was not significantly different between 2 groups. More patients with massive PE were treated with standard thrombolytics than CDT, but there was no significant difference (54.5% in ST vs 42.9% in CDT, $P = .334$).

**Table 1**
Comparison of baseline and clinical characteristics between patients treated with ST and catheter-directed thrombolysis

| | Total (n = 72) | ST (n = 44) | CDT (n = 28) | *P* |
|---|---|---|---|---|
| Mean age | 63.9 ± 17.0 | 65.5 ± 16.8 | 61.5 ± 17.3 | .290 |
| Male sex, n (%) | 22 (30.6) | 9 (20.5) | 13 (46.4) | .020 |
| Hypertension | 28 (38.9) | 17 (38.6) | 11 (39.3) | .956 |
| DM | 10 (13.9) | 6 (13.6) | 4 (14.3) | 1 |
| Surgery within 30 d | 13 (18.1) | 8 (18.2) | 5 (17.9) | .972 |
| Immobilization within 30 d | 16 (22.2) | 9 (20.5) | 7 (25) | .651 |
| Malignancy within 3 mo | 3 (4.2) | 3 (6.8) | 0 (0) | .277 |
| DVT | 36/53 (67.9) | 22/34 (64.7) | 14/19 (73.7) | .502 |
| Cardiac arrest | 11 (15.3) | 6 (13.6) | 5 (17.9) | .740 |
| Severity of PE | | | | .334 |
| Massive PE | 36 (50) | 24 (54.5) | 12 (42.9) | |
| Submassive PE | 36 (50) | 20 (45.5) | 16 (57.1) | |

Data are expressed as number (percentages) in categorical variable and mean ± SD. Abbreviations: DM, diabetes mellitus; DVT, deep vein thrombosis.

### 3.2. Management and outcomes

Table 2 compares the management and outcomes of the 2 groups. Thirty-five patients (48.6%) were admitted to intensive care unit (ICU), and 17 received invasive mechanical ventilation. Extracorporeal life support system was applied in 4 patients without differences between the 2 groups. Overall 7, 14, and 28-day mortalities were the same at 12.5%, and inhospital mortality was 13.9%. No significant difference was observed between the 2 groups in terms of mortalities. Seven of the total 9 deaths were patients with massive PE. In patients with submassive PE, 2 deaths (10%) occurred in 20 patients with submassive PE receiving thrombolysis, whereas there was no death in 16 patients with submassive PE treated with CDT ($P = .492$). In patients with massive PE, 4 (16.7%) and 3 (25%) deaths occurred in 24 patients with ST and 12 with CDT, respectively ($P = .664$). There was a trend toward longer ICU stay in patients receiving CDT. Eighteen patients (25%) experienced bleeding complications. Among them, 3 (2 in ST and 1 in CDT) have major bleeding complications. Hemorrhagic stroke and huge central line insertion site hematoma requiring packed red blood cell transfusion occurred in 2 patients receiving ST. Patients with hemorrhagic stroke died. Massive bleeding from extracorporeal membrane oxygenation catheter insertion site occurred in 1 patient receiving CDT. Other 5 minor bleeding complications were associated with catheter puncture site for CDT, and all of them were controlled by manual compression.

**Table 2**
Comparison of management and outcomes between patients treated with ST and those with catheter-directed thrombolysis

| | Total (n = 72) | ST (n = 44) | CDT (n = 28) | *P* |
|---|---|---|---|---|
| ICU admission | 35 (48.6) | 22 (50) | 13 (46.4) | .768 |
| Invasive mechanical ventilation | 17 (23.6) | 9 (20.5) | 8 (28.6) | .429 |
| ECLS application | 4 (5.6) | 1 (2.3) | 3 (10.7) | .292 |
| IVC filter insertion | 4 (5.6) | 1 (2.3) | 3 (10.7) | .292 |
| Mean ICU stay (d) | 5.7 ± 7.9 | 4.5 ± 7.9 | 7.8 ± 7.7 | .079 |
| Mean hospital stay (d) | 15.9 ± 28.8 | 18.4 ± 36.1 | 12 ± 8.66 | .594 |
| 7-d mortality | 9 (12.5) | 6 (13.6) | 3 (10.7) | 1 |
| 14-d mortality | 9 (12.5) | 6 (13.6) | 3 (10.7) | 1 |
| 28-d mortality | 9 (12.5) | 6 (13.6) | 3 (10.7) | 1 |
| Inhospital mortality | 10 (13.9) | 6 (13.6) | 4 (14.3) | 1 |
| Bleeding complication | 18 (25) | 12 (27.3) | 6 (21.4) | .577 |
| Major bleeding | 3 (16.7) | 2 (16.7) | 1 (16.7) | 1 |

Data are expressed as number (percentages) in categorical variable and mean ± SD. Abbreviations: ECLS, extracorporeal life support; IVC, inferior vena cava.