

# Outcomes Post Thrombolysis for Acute Pulmonary Embolism

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## Abstract

### Background

Pulmonary embolism (PE) remains a significant cause of mortality in Europe<sup>1</sup>. Thrombolytic therapy is often utilised as a therapeutic strategy in massive and sub-massive PE. There is a dearth of research on short term complications and subsequent outcomes in patients who have received thrombolysis for PE in Ireland.

### Methods

This retrospective study examined patients who underwent thrombolysis for acute sub massive PE whilst under the care of the respiratory service in Cork University Hospital (CUH) from 2010-2018. All patients had CTPA done for diagnosis of PE. Alteplase was used as a thrombolytic agent. Patient records were perused. Follow-up pulmonary functions tests (PFTs) and trans-thoracic echocardiogram (TTE) results were assessed for evidence of impairment of diffusing capacity (DLCO) and pulmonary hypertension (PH) respectively.

### Results

Twenty five patients were included in the study. Nine patients (36%) were women and 64% men. Average age was 55.1 years. Four patients suffered complications related to thrombolysis (average age 63.3 years). Twenty-Two patients (88%) underwent a follow-up echocardiography (mean 30 weeks post PE). Three patients (13%) had echocardiographic evidence of possible mild PH (i.e. RVSP >40mmhg) at initial follow-up. Fourteen patients (56%) who underwent thrombolysis had follow-up PFTs (mean 11.8 months post PE). The diffusing capacity (DLCO) was normal in all patients.

### Conclusion

Thrombolysis was a relatively safe intervention in this small study.

## Introduction

Pulmonary embolism remains a significant cause of mortality in Europe<sup>1</sup>. Approximately 10% of all patients with acute PE die within 3 months of the event<sup>2</sup>.

Thrombolytic therapy for PE is of proven benefit in patients with haemodynamic compromise<sup>3</sup>. The role of fibrinolysis in individuals with sub-massive PE (acute PE without systemic hypotension but with either right ventricular or myocardial dysfunction<sup>4</sup>) remains controversial as it is associated with a significant risk of major bleeding<sup>5</sup>. These complications are more common in older individuals<sup>6</sup>.

This increased risk of haemorrhagic complications prompted Investigators in the landmark PEITHO study to advise caution when considering fibrinolytic therapy for haemodynamically stable patients<sup>5</sup>. Subsequent American College of Chest Physician (ACCP) guidelines no longer recommend thrombolysis in sub-massive PE<sup>7</sup>.

Chronic thrombo-embolic pulmonary hypertension (CTEPH) has been reported to occur in up to 4% of individuals post PE<sup>8</sup>. Evidence concerning the impact of thrombolysis on subsequent likelihood of developing elevated pulmonary artery pressures is conflicting. Routine screening for CTEPH after PE is not currently recommended by the European Society of Cardiology (ESC)<sup>9</sup>. Guidelines concerning follow up of thrombolysed PE are lacking. Furthermore, there is a dearth of research on short term complications and subsequent outcomes in patients who are thrombolysed for PE in Ireland.

## Methods

This was a retrospective study of patients who underwent thrombolysis for acute sub massive PE whilst under the care of the Respiratory service in CUH from 2010-2018. All patients had CTPA done for diagnosis of PE. We set out to identify patients who underwent thrombolysis with Alteplase for sub massive PE during this period and to determine the complication rate associated with this intervention. We sought to calculate the frequency with which follow up investigations, in particular PFTs and TTE, were performed and to assess results.

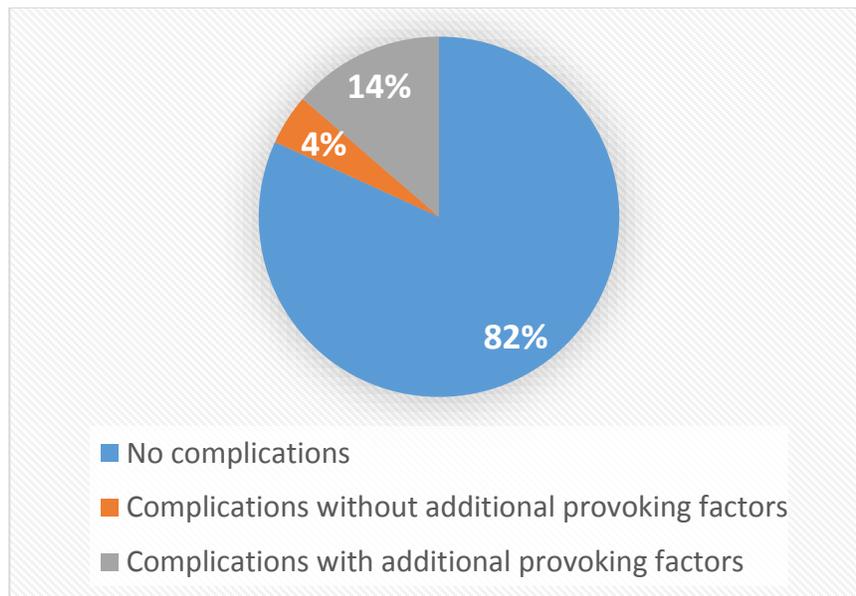
The study population was identified using the hospital electronic patient discharge and database system. Follow-up PFT and TTE results were assessed for DLCO and evidence of residual pulmonary hypertension (PH) respectively. Pulmonary hypertension was defined as a right ventricular systolic pressure (RVSP) of greater than 40mmHg on TTE. Complications associated with thrombolysis were recorded.

## Results

Twenty five patients were included in the study. Patient characteristics can be viewed in Table 1. Nine patients (36%) were women and 64% men. Average age was 51.1 years (SD=17.8). Four patients (Figure 1) suffered complications related to thrombolysis (average age 63.3 years). All complications comprised extracranial bleeding which, in 2 of 4 cases, was minor in nature. Twenty-Two patients (88%) underwent a follow-up echocardiography (mean 30 weeks post PE). Three patients (13%) had evidence of possible mild PH (i.e. RVSP >40mmHg) on TTE. Fourteen patients (56%) who underwent thrombolysis had follow- up PFTs (mean 11.8 months post PE). DLCO was normal in all patients tested.

<b>Male/Female Gender (%)</b>	<b>16/9 (64%/36%)</b>
<b>Age (years)</b>	26-88 (55.11)
<b>Number of patients experiencing Thrombolysis Related Complication</b>	4/25 (16%)
<b>Number of patients undergoing TTE (%)</b>	22/25 (88%)
<b>Number of patients undergoing PFTs (%)</b>	14/25 (56%)
<b>RSVP &gt;40 mmHg</b>	3/22 (13%)

**Table 1.** Characteristics of 25 patients undergoing thrombolysis for acute pulmonary embolism. Male preponderance (64%) in our cohort. Most (88%) underwent follow up echocardiography.



**Figure 1.** Complications Associated with thrombolysis. Four patients experienced complications, all of which comprised extracranial bleeding, 2 of these were minor.

## Discussion

All complications in this small study comprised extracranial bleeding which, in 2 of 4 cases, was minor in nature. Two patients developed retroperitoneal haematomas, one of which required surgical evacuation. Three of the 4 patients who experienced bleeding had additional predisposing factors, namely recent surgery or, in the case of two patients, coronary angiography and administration of dual antiplatelet therapy. In the PEITHO study the reported bleeding rate was 11.5%<sup>5</sup>. Major bleeding rate in this study was 8%. Two patients died during the follow up period from unrelated events.

Previous studies have quoted a prevalence of pulmonary hypertension of 16% in thrombolysed populations<sup>11</sup>. In one large study, not limited to patients who had undergone thrombolysis, the cumulative incidence of symptomatic CTEPH was 1.0% at six months, 3.1% at one year, and 3.8% at two years<sup>8</sup>. A more recent study has reported CTEPH in 2.1% of patients who underwent thrombolysis at a median follow-up of 3 years<sup>10</sup>. In our patient cohort, 13% of patients who underwent echocardiography had possible mild PH. None of our patients have, as yet, had confirmatory right heart catheterisation. They remain under active surveillance. In all patients who underwent PFTs with a DLCO, the DLCO was normal, suggesting no residual impairment in gas transfer as a consequence of their pulmonary embolism.

In summary, the findings from our study suggest that thrombolysis for acute PE is generally safe and appears to have good clinical outcomes for patients at initial follow up, in terms of pulmonary vascular dysfunction and gas transfer.

## Declaration of Conflicts of Interest:

There are no conflicts of interest to disclose.

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