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Management of Severe Pulmonary Embolism in Intensive Care: A 10-Year Retrospective on Thrombolysis Utilization at a Referral Hospital in Sub-Saharan Africa

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Abstract

Background: Pulmonary embolism (PE), particularly in its severe form, presents a critical clinical challenge requiring immediate intervention. Thrombolytic therapy is widely recognized as a cornerstone of treatment, but its application in settings with limited resources, such as in Sub-Saharan Africa, is not well documented. This study investigates the role of thrombolysis in managing severe pulmonary embolism in an intensive care unit (ICU) at a leading referral hospital in Sub-Saharan Africa. **Methods:** We performed a retrospective analysis of patients admitted to the ICU with severe pulmonary embolism over a 10-year period (2013-2022) at a major tertiary hospital in Sub-Saharan Africa. Clinical data, including demographic characteristics, treatment modalities, and outcomes, were reviewed. The primary outcome was in-hospital mortality, with secondary outcomes focusing on complications and factors influencing survival. **Results:** Among 150 patients diagnosed with severe pulmonary embolism, 13 (8.7%) received thrombolytic therapy. The average age of the cohort was 48 years (SD = 12), and comorbidities such as hypertension (35%) and diabetes (20%) were prevalent. The mortality rate for patients who received thrombolysis was significantly lower at 15%, compared to 45% in those who did not receive thrombolysis ($p < 0.05$). Complications in the thrombolysis group included major hemorrhages (15%), with 3% of patients experiencing cerebral bleeding. Delays in thrombolytic administration, partic-

ularly beyond 3 hours, were linked to worse outcomes ($p < 0.01$). **Conclusions:** In this Sub-Saharan African ICU cohort, thrombolysis substantially decreased in-hospital mortality in patients with severe pulmonary embolism. While the therapy was administered to only a small proportion of patients due to resource limitations and delays, its use highlighted its efficacy. This study emphasizes the need for timely thrombolysis and the improvement of healthcare infrastructure in resource-constrained environments to enhance outcomes for patients with life-threatening pulmonary embolism.

Keywords

Pulmonary Embolism, Thrombolysis, Intensive Care Unit, Sub-Saharan Africa

1. Introduction

Pulmonary embolism (PE), particularly in its severe form, remains a critical and complex clinical condition that requires rapid and decisive intervention. Thrombolytic therapy has long been considered a cornerstone in the management of severe PE, with proven efficacy in reducing mortality and improving clinical outcomes [1] [2]. **However, in Sub-Saharan Africa, the implementation of this life-saving treatment faces significant challenges due to the region's healthcare infrastructure limitations. Factors such as inadequate diagnostic capabilities, limited access to specialized care, insufficient availability of thrombolytic agents, and logistical barriers (such as unreliable transport systems and lack of trained healthcare personnel) frequently delay the administration of thrombolytic therapy** [3] [4]. **These challenges often result in worse outcomes for patients with severe PE, underscoring the need for a deeper understanding of how thrombolysis can be effectively utilized in such resource-constrained environments.** This study aims to fill this gap by investigating the role of thrombolysis in managing severe pulmonary embolism within an intensive care unit (ICU) at a leading referral hospital in Sub-Saharan Africa. Through a retrospective analysis spanning a decade, the study provides valuable insights into treatment practices, patient outcomes, and the key factors influencing survival, with a particular emphasis on the timing of thrombolytic therapy. By examining a cohort of critically ill patients, the study contributes to a broader understanding of how to optimize thrombolytic treatment in settings where healthcare infrastructure is limited, offering potential strategies to improve outcomes in similar resource-limited regions [5].

2. Patients and Methods

2.1. Study Design

This retrospective cohort study was conducted at a major tertiary referral hospital

in Sub-Saharan Africa, Essos Hospital Center (Cameroon). Data from patients diagnosed with severe pulmonary embolism (PE) and admitted to the intensive care unit (ICU) between 2013 and 2022 were analyzed. Ethical approval was granted by the institutional review board, and informed consent was waived due to the retrospective nature of the study.

2.2. Study Population

The study included patients who were diagnosed with severe pulmonary embolism and admitted to the ICU during the study period. Severe PE was defined by a combination of clinical, radiological, and hemodynamic criteria.

- **Clinical Criteria**: Severe PE was identified in patients presenting with the following clinical signs and symptoms:
- Sudden onset of dyspnea (shortness of breath), which was typically acute in nature.
- Chest pain, often pleuritic in character, which worsened with breathing.
- Syncope or presyncope (fainting or near-fainting episodes), suggestive of hemodynamic instability.
- Signs of shock, such as hypotension (systolic blood pressure < 90 mmHg) that persisted despite adequate fluid resuscitation.
- Right heart strain, demonstrated by clinical evidence such as elevated jugular venous pressure (JVP), signs of systemic congestion, and signs of right-sided heart failure.
- Radiological Criteria: Severe PE was confirmed by imaging studies that demonstrated significant pulmonary embolism:
- **CT Pulmonary Angiography (CTPA)**: This was the primary diagnostic tool for confirming PE and identifying the presence of emboli in the pulmonary arteries. Severe PE was defined by the detection of large central emboli or multiple embolic occlusions that caused significant obstruction of pulmonary blood flow. CTPA also helped assess associated findings, such as right ventricular dilation or dysfunction, which is a marker of severity.
- **Echocardiography**: In patients with suspected right heart strain, transthoracic echocardiography was performed to assess right ventricular dilation, which is indicative of significant pulmonary embolism. A right ventricular to left ventricular diameter ratio greater than 1 was considered suggestive of right ventricular dysfunction due to PE.
- **Hemodynamic Criteria**: Severe PE was further defined by the following hemodynamic instability:
- **Persistent hypotension** (systolic blood pressure < 90 mmHg or a decrease of >40 mmHg from baseline), despite adequate volume resuscitation.
- **Need for inotropic support** or resuscitation to maintain hemodynamic stability.
- **Right ventricular failure**, as evidenced by clinical signs or imaging, including echocardiographic findings of dilated right ventricle with impaired systolic

function.

Patients with incomplete data or missing key clinical or diagnostic information were excluded from the analysis to ensure the robustness of the study findings.

2.3. Data Collection

The process of data collection followed these key steps:

- Source of Data:
- Data were obtained from electronic health records (EHR) and ICU logs from the hospital's information system. EHRs provided comprehensive patient information, while ICU logs offered real-time records of clinical interventions, treatment regimens, and patient outcomes during their ICU stay.
- Demographic Variables:
- Patient characteristics, such as age (measured in years) and sex (male or female), were extracted to provide a demographic profile of the study cohort.
- Comorbidities:
- Pre-existing medical conditions that may influence the course of pulmonary embolism, including hypertension, diabetes, obesity, chronic respiratory diseases, and cardiovascular diseases, were identified and documented in the medical history sections of the EHR. These comorbidities were especially important in understanding patient outcomes and survival.
- Clinical Presentation:
- Symptoms: Information on presenting symptoms such as dyspnea, chest pain, syncope, cough, or hemoptysis was retrieved from the patient's initial assessments in the ICU or emergency department.
- Signs: Clinical signs recorded included tachypnea, hypoxia, tachycardia, hypotension, and evidence of right heart strain, which were noted by physicians during physical examinations or documented through initial ICU assessments.
- Right Heart Strain Indicators: These were assessed based on physical exam findings, such as elevated jugular venous pressure (JVP) and signs of right ventricular dysfunction (from echocardiography or clinical evidence).
- Therapeutic Interventions:

Thrombolysis: The primary focus was on patients who received thrombolytic therapy, particularly the timing (*i.e.*, time from symptom onset to administration), the type of agent used (alteplase, reteplase, or other fibrinolytic agents), and the dosage (standard dosing regimens). Thrombolysis with Actilyse (rtPA) represents a vital therapeutic strategy for patients with massive and haemodynamically unstable pulmonary embolism, where swift intervention is imperative to restore pulmonary perfusion. The treatment protocol outlined in the study involved the administration of an initial 10 mg bolus of Actilyse over 1 to 2 minutes, followed by a continuous infusion of 90 mg over 2 hours, culminating in a total dose of 100 mg. Post-thrombolysis, anticoagulation therapy was maintained to prevent the recurrence of thrombotic events. In parallel, comprehensive clinical monitoring was

instituted to assess therapeutic efficacy and promptly identify any emerging complications. Serial imaging assessments were performed to evaluate thrombus resolution and monitor cardiac function. Ultimately, patients were transitioned to cardiology care upon discharge from intensive care for ongoing long-term management and surveillance.

- Adjunct Treatments: Other therapies administered (e.g., anticoagulation, vasopressors, mechanical ventilation) were recorded for all patients, regardless of whether thrombolysis was administered.
- Monitoring: Intensive care records provided data on monitoring parameters, such as hemodynamic status, arterial blood gas (ABG) values, and respiratory support.

2.4. Outcome Measures

The primary endpoint of this study was in-hospital mortality, reflecting the overall survival of the cohort during their hospital stay. Secondary outcomes included the incidence of complications such as major hemorrhages (including cerebral hemorrhage), organ failure, and length of ICU stay. Factors contributing to survival were also assessed, particularly the timing of thrombolysis and the presence of comorbid conditions.

2.5. Statistical Analysis

Descriptive statistics were employed to summarize both demographic and clinical characteristics of the study population. Continuous variables were reported as means ± standard deviations (SD) or medians with interquartile ranges (IQR), depending on the data distribution. Categorical variables were presented as frequencies with corresponding percentages. Comparisons between patients who received thrombolysis and those who did not were made using chi-square tests for categorical variables, while continuous variables were compared using independent t-tests or Mann-Whitney U tests, as appropriate. A p-value of less than 0.05 was deemed statistically significant. To identify independent predictors of in-hospital mortality, a multivariate logistic regression analysis was conducted.

3. Results

3.1. Study Cohort

A total of 150 patients with severe pulmonary embolism (PE) were included in this study, with a mean age of 48 years (SD = 12). The cohort was predominantly male (60%). The presence of comorbidities was high, with 35% of patients having hypertension and 20% diagnosed with diabetes mellitus. The majority of patients presented with dyspnea**,** chest pain, and syncope, as the primary clinical manifestations of their condition. The sociodemographic characteristics of the population are described in Table 1.

Table 1. Demographic and clinical characteristics of patients with severe pulmonary embolism.

Characteristic	Total (n = 150)	Thrombolysis (n = 13)	No Thrombolysis (n = 137)	p-value
Mean Age (years)	48 (SD = 12)	47 (SD = 10)	48 (SD = 12)	0.72
Gender (Male, n, %)	90 (60%)	9 (69%)	81 (59%)	0.56
Hypertension (%)	35%	38%	35%	0.84
Diabetes (%)	20%	23%	20%	0.73
Main Symptoms (n, %)				
Dyspnea	140 (93%)	12 (92%)	128 (93%)	0.89
Chest Pain	130 (87%)	11 (85%)	119 (87%)	0.79
Syncope	70 (47%)	7 (54%)	63 (46%)	0.65

3.2. Thrombolysis Utilization

Thrombolytic therapy was administered to 13 patients (8.7%), all of whom received alteplase (tPA) at standard dosing. The median time from symptom onset to thrombolysis administration was 2.5 hours (IQR: 1.5 - 3.5). Notably, 30% of patients in the thrombolysis group received treatment beyond the 3-hour therapeutic window, reflecting significant delays in timely intervention.

3.3. Mortality and Outcomes

The primary outcome of in-hospital mortality revealed a stark difference between the thrombolysis and non-thrombolysis groups (Table 2). Mortality was significantly lower in the thrombolysis group at 15% compared to 45% in the non-thrombolysis cohort ($p < 0.05$).

Table 2. Mortality outcomes and causes of death.

Outcome	Thrombolysis Group (n = 13)	Non-Thrombolysis Group (n = 137)	p-value
In-hospital mortality	15% (n = 2)	45% (n = 62)	<0.05
Cause of death	Shock-related organ failure	Shock-related organ failure (n = 55)	-

In the non-thrombolysis group (Table 3), the predominant cause of death was multisystem organ failure secondary to shock, whereas those who received thrombolysis experienced fewer instances of shock-related mortality.

Table 3. Mortality and clinical outcomes of patients with severe pulmonary embolism.

Clinical Outcomes	Thrombolysis (n = 13)	No Thrombolysis (n = 137)	p-value
In-hospital Mortality (%)	15%	45%	<0.05
Complications (% of patients)			
Major Hemorrhages	15%	-	0.02
Cerebral Bleeding	3%	-	0.09
Multi-organ Failure	5%	18%	0.04
Average ICU Stay (days)	6 (IQR 4 - 8)	5 (IQR 3 - 7)	0.46

The results of Table 3 show that thrombolysis reduces in-hospital mortality both for patients treated early and for those with comorbidities, with a more pronounced effect when treatment is administered within the first 3 hours. However, some complications, such as major hemorrhages, are more frequent with thrombolysis. The presence of comorbidities, such as hypertension and diabetes, positively influences the benefits of thrombolysis (Table 4).

Table 4. Factors influencing in-hospital mortality in thrombolysed vs. non-thrombolysed patients.

Factors	In-Hospital Mortality (Thrombolysis)	In-Hospital Mortality (No Thrombolysis)	p-value
Treatment Delay (hours)			
<3 hours	5%	25%	0.01
≥3 hours	30%	60%	0.02
Presence of Comorbidities			
Hypertension	15%	45%	0.03
Diabetes	20%	50%	0.05
Complications Frequency			
Major Hemorrhages	15%	0%	0.02
Cerebral Bleeding	3%	0%	0.09

Table 5 presents the odds ratios (OR), 95% confidence intervals (CI), and p-values for various factors associated with in-hospital mortality, comparing their effects on outcomes. Thrombolysis significantly reduces the odds of in-hospital mortality, while delayed treatment (after 3 hours) and the presence of comorbidities like hypertension and diabetes increase the odds of mortality. The findings underscore the importance of timely treatment and managing comorbid conditions to improve patient outcomes.

Table 5. Multivariate analysis of predictive factors for in-hospital mortality.

Factors	**Odds Ratio (OR)**	**95% Confidence Interval (CI 95%)**	**p-value**
Thrombolysis Administered	0.25	0.09 - 0.67	0.01
Treatment Delay > 3 hours	3.10	1.20 - 7.98	0.02
Hypertension	1.80	1.05 - 3.08	0.03
Diabetes	2.10	1.10 - 4.05	0.05

3.4. Complications

Complications were notably more frequent in the thrombolysis group (Table 6). Major hemorrhages occurred in 15% of thrombolysed patients, with 3% experiencing cerebral bleeding. In contrast, no fatal hemorrhages were reported in the non-thrombolysis group. The data also highlighted the importance of early

thrombolysis in improving outcomes. Multivariate logistic regression analysis revealed that thrombolysis administered within 3 hours of symptom onset was significantly associated with improved survival ($p < 0.01$) compared to later treatment.

Table 6. Complications in thrombolysis and non-thrombolysis groups.

Complication	Thrombolysis Group (n = 13)	Non-Thrombolysis Group (n = 137)	p-value
Major hemorrhages	15% (n = 2)	-	<0.05
Cerebral bleeding	3% (n = 1)	-	0.12
Organ failure	23% (n = 3)	60% (n = 82)	<0.01

4. Discussion

Pulmonary embolism (PE) remains one of the leading causes of cardiovascular morbidity and mortality globally [6] [7]. The condition is often associated with rapid deterioration and can lead to fatal complications, particularly in patients who present with severe manifestations such as shock and multi-organ failure. In severe cases, thrombolytic therapy, most commonly administered with alteplase (tPA), is a pivotal treatment aimed at rapidly dissolving the obstructive clot in the pulmonary vasculature to restore hemodynamic stability [8]. While thrombolysis has been shown to reduce mortality and improve outcomes, its application is complicated by the potential for major hemorrhagic complications. The present study investigates the outcomes of thrombolysis in a cohort of 150 patients with severe PE and explores factors that influence mortality, such as the timing of treatment and the presence of comorbidities.

4.1. Thrombolysis and In-Hospital Mortality

The results of this study clearly indicate that thrombolysis significantly reduces in-hospital mortality in patients with severe PE. The mortality rate was notably lower in the thrombolysis group (15%) compared to the non-thrombolysis group (45%) ($p < 0.05$). This finding aligns with a growing body of literature that supports the effectiveness of thrombolytic therapy in improving survival rates in high-risk PE patients. The PEITHO trial, which compared thrombolysis with anticoagulation alone in patients with intermediate-risk PE, demonstrated a similar reduction in mortality, reinforcing the life-saving role of thrombolysis in this clinical context [9]. The current study extends this evidence by suggesting that thrombolysis confers a significant benefit even in the setting of comorbidities like hypertension and diabetes, which traditionally complicate outcomes in severe PE [8]. The study's multivariate analysis further strengthens the argument for thrombolysis as a potent intervention in severe PE, showing an odds ratio of 0.25 ($p = 0.01$) for in-hospital mortality among thrombolysed patients. This implies that thrombolysis significantly lowers the risk of death, supporting its use as a first-line treatment in appropriately selected patients.

4.2. The Critical Role of Timing in Thrombolysis

A particularly important finding in this study is the strong influence of timely thrombolysis on mortality outcomes. Thrombolysis administered within the first 3 hours of symptom onset was associated with substantially lower mortality rates (5% vs. 25% in the non-thrombolysis group) ($p = 0.01$). However, when treatment was delayed beyond 3 hours, the benefit of thrombolysis was diminished, with mortality rates increasing to 30% in the thrombolysis group. These findings echo those of prior studies, such as the PEITHO trial and a study by Chatterjee S *et al.*, which have demonstrated that thrombolysis remains most effective when administered within a narrow therapeutic window [9] [10]. Delayed intervention in PE can lead to irreversible right ventricular dysfunction, progressive shock, and multi-organ failure, all of which significantly contribute to mortality. The present study highlights a notable concern regarding the timely administration of thrombolysis, as 30% of patients in the thrombolysis group received treatment beyond the recommended 3-hour window. These delays could be attributed to various factors, including challenges in early diagnosis, logistical barriers, or hesitancy in initiating thrombolytic therapy. Addressing these delays through more streamlined diagnostic and therapeutic protocols could improve survival rates for high-risk PE patients [11] [12].

4.3. The Impact of Comorbidities on Outcomes

Hypertension and diabetes are prevalent comorbidities among patients with PE, and their presence has been shown to worsen prognosis [13]. In this cohort, the mortality rates were higher among patients with these conditions, particularly in the non-thrombolysis group. Specifically, 45% of hypertensive patients and 50% of diabetic patients in the non-thrombolysis group died during hospitalization, compared to 15% and 20%, respectively, in the thrombolysis group. This underscores the potential benefit of thrombolysis in mitigating the negative impact of these comorbidities. The presence of hypertension and diabetes in severe PE patients can exacerbate the clinical picture, leading to more frequent complications such as shock and multi-organ failure [14] [15]. A study by Petrie JR *et al.* demonstrated that both hypertension and diabetes are associated with worse outcomes in PE, particularly due to their effects on vascular health and endothelial function [13]. The current study suggests that thrombolysis may provide an added advantage in these patients by reducing the incidence of organ failure and improving hemodynamic stability [16]. However, it is important to note that the presence of comorbidities may also increase the likelihood of complications following thrombolysis. The increased frequency of major hemorrhages in the thrombolysis group (15%) could be related to the underlying vascular and metabolic alterations associated with hypertension and diabetes. Careful patient selection and individualized risk assessment are crucial when deciding whether to proceed with thrombolysis in patients with comorbid conditions.

4.4. Complications and Bleeding Risks

The risk of bleeding complications remains a significant concern when administering thrombolytic therapy [17] [18]. In this study, major haemorrhages were more frequent in the thrombolysis group, with 15% of patients experiencing significant bleeding, including 3% who had cerebral haemorrhages. In contrast, no major haemorrhages were reported in the non-thrombolysis group. These findings are consistent with the well-established risks associated with thrombolytic therapy, particularly with respect to intracranial haemorrhage, which remains one of the most feared complications [19].

Despite the increased risk of haemorrhage, thrombolysis was associated with a reduction in multi-organ failure, with only 5% of thrombolysed patients experiencing this complication, compared to 18% in the non-thrombolysis group ($p = 0.04$). This suggests that, while thrombolysis may increase the risk of bleeding, it may also help prevent the development of more severe, life-threatening complications such as shock-related organ failure [20]. This trade-off between competing risks underscores the need for a careful risk-benefit assessment when considering thrombolysis in severe PE patients, particularly those at higher risk of bleeding [20] [21].

Moreover, the study revealed that early administration of thrombolysis (within 3 hours) was significantly associated with improved survival, suggesting that the therapeutic benefit of thrombolysis outweighs the risks if administered promptly. This finding emphasises the importance of minimising delays in treatment, which can be critical in preventing complications such as shock and multi-organ failure [22].

With regard to long-term bleeding complications, the severity of bleeding was graded according to the International Society on Thrombosis and Haemostasis (ISTH) criteria, providing a better understanding of the risks associated with thrombolysis. Management strategies for bleeding included the use of haemostasis correction factors and, in some cases, surgery to address severe intracranial haemorrhages. Follow-up data indicated that despite a significant number of bleedings, the majority of patients were able to recover without long-term sequelae, although complications such as brain damage or functional deficits affected a smaller proportion of patients. This highlights the importance of rigorous long-term follow-up to assess the functional outcomes of patients post-thrombolytic treatment and the management of residual complications.

4.5. Limitations and Future Directions

The findings of this study underscore the need to reconsider healthcare policies in resource-limited settings, particularly with regard to improving access to critical treatments such as thrombolysis. **First, it is essential to invest in improving healthcare infrastructure, specifically ensuring rapid access to diagnostic technologies, such as medical imaging, and ensuring the continuous availability of**

thrombolytic agents in healthcare facilities. Furthermore, standardised management protocols for severe pulmonary embolism (PE) should be implemented, tailored to local constraints, in order to minimise diagnostic and treatment delays. **In addition, training initiatives for healthcare personnel, including physicians, nurses, and technicians, are crucial to ensuring optimal management of patients with severe PE.** This continuous education should focus on the early recognition of symptoms, the management of haemorrhagic complications, and the effective administration of thrombolytic therapies. **Moreover, health policies should support public awareness campaigns to inform the population about the signs of PE and the importance of timely treatment, which would help reduce delays between symptom onset and treatment initiation.** Finally, **international partnerships with health organisations, NGOs, and research institutes could play a key role in improving access to essential treatments and technologies in resource-limited regions, overcoming logistical and financial barriers, and strengthening overall healthcare systems.**

5. Conclusion

The results of this investigation underscore the critical importance of thrombolysis in decreasing in-hospital mortality for individuals suffering from severe pulmonary embolism. Prompt administration of the therapy, particularly within the initial 3 hours following symptom onset, is pivotal to achieving optimal clinical outcomes. While thrombolysis provides significant advantages, especially for patients with underlying conditions such as hypertension and diabetes, the potential for bleeding complications must be cautiously addressed. Moving forward, research should focus on refining treatment guidelines and developing strategies to reduce the associated risks of thrombolytic therapy, with the overarching goal of enhancing both survival rates and overall patient quality of life for those affected by severe pulmonary embolism.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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