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Original Article

Efficacy and influencing factors of thrombolytic therapy in patients with pulmonary embolism complicated y pulmonary arterial hypertension

Hui Wei[1,2*], Jingsong An[3*], Haijun Yin[4], Huizhao Liu[2], Fang Sun[2], Yanli Wang[5], Jie Cao[1]

[1]Department of Respiratory and Critical Care Medicine, Tianjin Medical University General Hospital, Tianjin 300052, China; [2]Department of Respiratory and Critical Care Medicine, Inner Mongolia People's Hospital, Hohhot 010010, Inner Mongolia Autonomous Region, China; [3]Department of Cardiovascular Medicine, Inner Mongolia People's Hospital, Hohhot 010010, Inner Mongolia Autonomous Region, China; [4]Department of Ultrasound Medicine, Inner Mongolia People's Hospital, Hohhot 010010, Inner Mongolia Autonomous Region, China; [5]Department of Nursing, Inner Mongolia People's Hospital, Hohhot 010010, Inner Mongolia Autonomous Region, China. [*]Equal contributors.

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Abstract: Objective: To evaluate the therapeutic efficacy of thrombolysis in patients with pulmonary embolism (PE) and pulmonary hypertension (PH), and identify factors influencing therapeutic outcomes. Methods: A retrospective analysis was conducted on 148 patients diagnosed with PE complicated by PH who received thrombolytic treatment at Tianjin Medical University General Hospital and Inner Mongolia People's Hospital between January 2022 and August 2024. Changes in inflammatory markers, blood gas parameters, and coagulation function indicators before and after treatment were compared, and the overall treatment efficacy rate was calculated. Patients were stratified based on therapeutic response, and a binary logistic regression model was employed to analyze factors associated with treatment effectiveness. The predictive value of these factors was assessed using receiver operating characteristic (ROC) curve analysis. Results: Within 24 hours post-thrombolysis, primary symptoms and clinical signs significantly improved. Specifically, respiratory rate (RR), heart rate (HR), and partial pressure of carbon dioxide ($PaCO_2$) decreased significantly, whereas oxygen saturation (SaO_2) and partial pressure of oxygen (PaO_2) increased significantly. Additionally, there was a significant improvement in mean pulmonary artery pressure (MPAP) and right ventricular end-diastolic diameter (RVEDD). Among the patients, 27 demonstrated marked improvement, 81 showed improvement, and these were categorized as the effective group (n=108). The remaining 40 patients showed no improvement and were classified into the ineffective group (n=40). Binary Logistic regression analysis identified $PaCO_2$ <35 mmHg, D-dimer (D-D) ≥11 mg/L, interleukin-6 (IL-6) ≥24 pg/mL, and C-reactive protein (CRP) ≥16 mg/L as independent risk factors for ineffective thrombolysis in patients with PE and PH (all P<0.05). The areas under the curve (AUCs) for $PaCO_2$, D-D, IL-6, and CRP in predicting thrombolysis efficacy were 0.684, 0.655, 0.634, and 0.629, respectively. Conclusion: Thrombolytic therapy effectively improves clinical symptoms, physical signs, hemodynamic parameters, and cardiac function in patients with PE complicated by PH. Furthermore, in clinical practice, early monitoring of inflammatory markers such as $PaCO_2$, D-D, IL-6, and CRP is crucial for timely adjustment and optimization of individualized therapeutic strategies.

Keywords: Pulmonary embolus, pulmonary hypertension, thrombolytic therapy, efficacy, risk factors, inflammatory factors

Introduction

Pulmonary embolus (PE) is a life-threatening cardiopulmonary vascular disorder caused by the obstruction of the pulmonary artery due to exogenous or endogenous thrombi, resulting in impaired pulmonary circulation [1]. Common thrombi associated with PE include blood clots, fat droplets, air, amniotic fluid, and incompletely dissolved particles from intravenous infusions, with blood clots being the most prevalent [2]. PE is typically characterized by sudden onset and rapid progression, ranking among the three most acute cardiovascular emergen-

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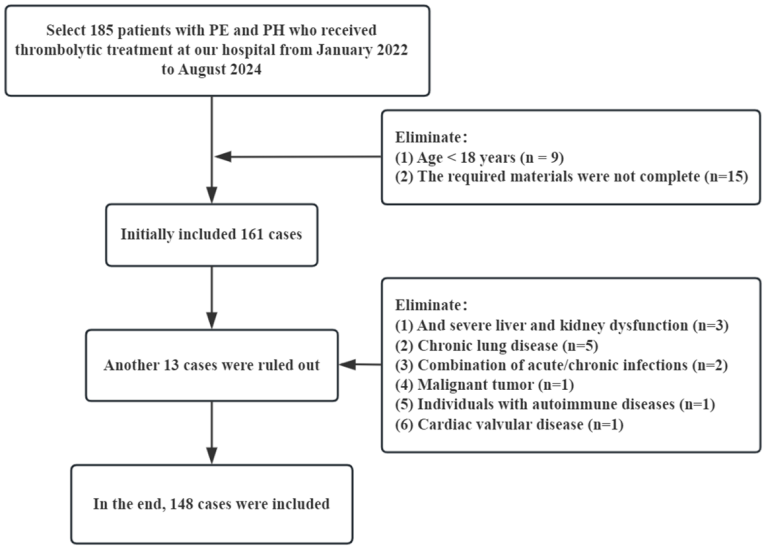

Figure 1. Flowchart of patient screening process.

cies, with a risk level second only to myocardial infarction and stroke [3]. Clinical data indicate that 11.7 per 100,000 emergency department patients are diagnosed with PE, with a hospital mortality rate of 17.4% [4].

Pulmonary hypertension (PH) is a severe complication of PE, resulting from the vascular obstruction or pulmonary bed spasm, which impairs blood flow, increases pulmonary vascular resistance, and elevates pulmonary artery pressure [5]. The symptoms of PH are often non-specific and insidious. The coexistence of PE and PH exacerbates pulmonary ventilation and gas exchange, causing severe dyspnea, hypoxemia, and respiratory failure. Additionally, it increases the cardiac workload. Prolonged exposure to elevated pressures can induce structural changes in the heart, such as right ventricular hypertrophy and dilation, ultimately progressing to heart failure, one of the leading causes of mortality in PE patients [6, 7].

Thrombolytic therapy serves as a critical intervention for PE complicated by PH, aiming to rapidly dissolve thrombi, restore pulmonary perfusion, lower pulmonary artery pressure, and mitigate right ventricular dysfunction. However, the pathogenesis and pathophysiological mechanisms of PE with PH are complex, and the therapeutic effect is influenced by multiple factors. For instance, previous studies have demonstrated that thrombotic events and hemodynamic disturbances in PE with PH trigger complex inflammatory responses, leading to abnormal vascular contraction and dilation, which accelerate pulmonary vascular remodeling and right ventricular hypertrophy, further worsening the condition [8, 9].

To enhance the clinical understanding of thrombolytic therapy in PE complicated by PH, this study aims to evaluate its therapeutic efficacy and investigate the factors influencing treatment outcomes. By addressing a critical research gap, this study seeks to provide a theoretical foundation for optimizing clinical management, refining treatment protocols, and offering new directions for future research.

Objects and methods

Study population

This retrospective study included 148 patients diagnosed with PE complicated by PH who received thrombolytic treatment at Tianjin Medical University General Hospital and Inner Mongolia People's Hospital between January 2022 and August 2024. Inclusion criteria: (1) Patients who met the diagnostic standards for PE and PH as outlined in the *Draft Guidelines for Pulmonary Embolism Diagnosis and Treatment in China* and the *2021 Guidelines for Diagnosis and Treatment of Pulmonary Arterial Hypertension*, with all diagnoses clinically confirmed; (2) Patients who underwent thrombolytic therapy via catheter-directed thrombolysis; (3) Patients with an age of 18 years or older; (4) Patients with complete data available for analysis. Exclusion criteria: (1) Patients with severe liver or kidney dysfunction, valvular heart disease, atrial fibrillation, or chronic lung diseases; (2) Patients with a history of bleeding disorders; (3) Patients presenting concurrent acute/chronic infections, malignancies, vasculitis, or autoimmune conditions; (4) Pregnant or lactating women; (5) Patients who died during hospitalization or were lost to follow-up. The detailed patient inclusion screening process is illustrated in **Figure 1**. This study was approved by the

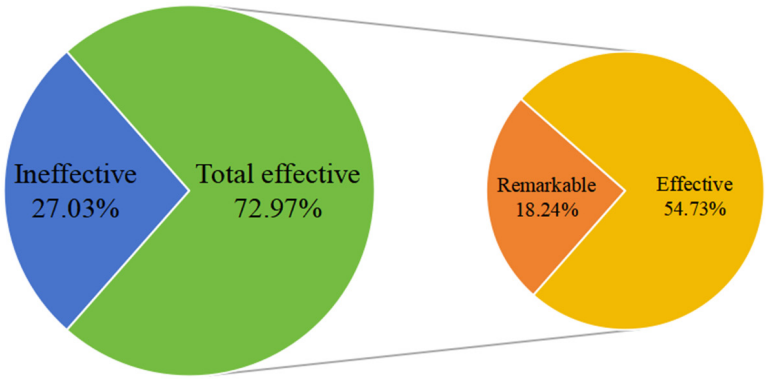

Figure 2. Effect of thrombolytic therapy in patients with PE complicated by PH. PE: pulmonary embolus; PH: pulmonary hypertension.

Ethics Committee of Inner Mongolia People's Hospital.

Analysis of therapeutic effect

Therapeutic efficacy was evaluated based on the following criteria [10]. Markedly effective: Seven days post-thrombolysis, pulmonary angiography showed that the defect involves fewer than one lung segment, pulmonary artery pressure decrease by at least 15 mmHg, and clinical symptoms such as chest pain and hemoptysis completely resolve. Effective: Pulmonary angiography indicates a reduction in defect size of more than 60%, pulmonary artery pressure decreases by at least 10 mmHg, and clinical symptoms partially improve. Ineffective: Neither of the above criteria is met. The overall effective rate was calculated as: (markedly effective cases + effective cases)/total number of cases ×100%. Changes in key physiological parameters, including respiratory rate (RR), heart rate (HR), blood oxygen saturation (SaO_2), partial pressure of carbon dioxide ($PaCO_2$), and partial pressure of arterial oxygen (PaO_2), were analyzed from 24 hours pre-thrombolysis to 24 hours post-thrombolysis. Additionally, cardiac ultrasound was used to measure the mean pulmonary artery pressure (MPAP), right ventricular end-diastolic diameter (RVEDD), and left ventricular end-diastolic diameter (LVEDD). Additionally, all adverse reactions occurring during thrombolytic therapy were documented.

Analysis of factors influencing therapeutic outcomes

Patients were subsequently classified into an effective group (n=108) and an ineffective group (n=40). Univariate and multivariate analyses were performed to assess the general information (age, gender, smoking history, history of pre-existing conditions) and laboratory parameters within 24 hours of admission [interleukin-6 (IL-6), interleukin-1β (IL-1β), tumor necrosis factor-α (TNF-α), C-reactive protein (CRP), $PaCO_2$, PaO_2, prothrombin time (PT), activated partial thromboplastin time (APTT), D-dimer (D-D), MPAP, miller score, dietary inflammatory index (DII)].

Statistical methods

Statistical analyses were conducted using SPSS version 26.0. Quantitative data following normal distribution were presented as means ± standard deviations (means ± SD), with paired t-tests used for within-group comparisons. Qualitative data were presented as frequencies and percentages [n (%)] and analyzed using the chi-square test. Binary logistic regression analysis was employed to identify factors influencing therapeutic outcomes in patients with PE complicated by PH. The clinical significance of these factors was further evaluated using receiver operating characteristic (ROC) curve analysis. A $P<0.05$ was deemed statistically significant.

Results

Efficacy analysis

Upon completion of the treatment, 27 patients (18.24%) exhibited a remarkable response, while 81 patients (54.73%) demonstrated an effective response. The remaining 40 patients (27.03%) were classified as ineffective. The total effective rate was 72.97%, as illustrated in **Figure 2**.

Predominant symptoms and findings

The most common symptoms of PE included difficulty breathing, shortness of breath, coughing, and chest pain. Key clinical findings include increased respiratory rate (>22/min), tachycardia (>100/min), bilaterally increased breath sounds, and lower extremity swelling. All these symptoms and clinical findings were significant-

Table 1. Main symptoms in patients with PE complicated by PH [n (%)]

Symptoms/Findings	24 hours after admission	24 hours after thrombolysis
Difficulty in breathing	131 (88.51)	62 (35.14)[a]
Shortness of breath	124 (83.78)	69 (22.97)[a]
Chest pain	95 (64.19)	48 (32.43)[a]
Coughing	108 (72.97)	76 (51.35)[a]
Fever	62 (41.89)	28 (18.92)[a]
Coughing up blood	30 (20.27)	17 (11.49)[a]
Palpitations	56 (37.84)	22 (14.86)[a]
Breathing rate increases (>22/min)	78 (52.70)	30 (20.27)[a]
Pulse quickens (>100/min)	74 (50.00)	25 (16.89)[a]
Bilateral increased breath sounds	65 (43.92)	27 (18.24)[a]
Wet rales in both lungs	58 (39.19)	19 (12.84)[a]
Bronchial rales	32 (21.62)	11 (7.43)[a]
Pleural effusion	47 (31.76)	31 (20.95)[a]
Lower extremities swelling	60 (40.54)	35 (23.65)[a]

Note: PE: pulmonary embolism; PH: pulmonary hypertension. [a]indicates $P<0.05$, compared with 24 hours after admission.

Table 2. Changes in key monitoring parameters before and after thrombolysis treatment (means ± SD)

Parameter	24 hours before thrombolysis	24 hours after thrombolysis	*t*	*P*
RR	27.40±3.16	21.47±1.73	20.195	<0.001
HR	105.41±7.21	89.12±6.67	17.836	<0.001
SaO_2	87.47±4.92	93.18±3.78	-4.833	<0.001
$PaCO_2$	58.34±3.78	43.07±3.86	16.175	<0.001
PaO_2	78.54±3.72	85.10±4.64	-5.572	<0.001

Note: RR: respiratory rate; HR: heart rate; SaO_2: blood oxygen saturation; $PaCO_2$: partial pressure of carbon dioxide; PaO_2: partial pressure of arterial oxygen.

ly improved 24 hours after thrombolysis ($P<0.05$), as presented in **Table 1**.

Changes in key parameters before and after thrombolysis

Following thrombolysis, RR, HR, and $PaCO_2$ all decreased significantly, while SaO_2 and PaO_2 increased significantly (all $P<0.05$), as detailed in **Table 2**.

Echocardiographic parameters before and after thrombolysis

At 24 hours post-thrombolysis, the MPAP and RVEDD decreased significantly (both $P<0.05$). However, there was no significant change in the LVEDD ($P>0.05$), as illustrated in **Figure 3**.

Adverse reactions during thrombolytic treatment

During thrombolytic therapy, four patients developed subcutaneous ecchymosis, one patient experienced gingival bleeding, and two patients exhibited gross hematuria. The hematuria resolved after reducing the urokinase dosage. No fatal complications occurred during the treatment period.

Univariate analysis of therapeutic efficacy

The ineffective group exhibited significantly higher proportions of patients with $PaCO_2$ <35 mmHg, D-D ≥11 mg/L, IL-6 ≥24 pg/mL, and CRP ≥16 mg/L in comparison to effective group (all $P<0.05$; **Table 3**).

Multivariate analysis of therapeutic efficacy

Therapeutic efficacy of thrombolytic treatment in patients with PE and PH was designated as the dependent variable, while $PaCO_2$, D-D, IL-6, and CRP were included as independent variables. The variable assignment details are provided in **Table 4**. Binary logistic regression analysis identified $PaCO_2$ <35 mmHg, D-D ≥11 mg/L, IL-6 ≥24 pg/mL, and CRP ≥16 mg/L as independent risk factors for ineffective thrombolytic therapy in patients with PE and PH (all $P<0.05$; **Table 5**).

ROC curve analysis

ROC curve analysis revealed that the area under the curve (AUC) for $PaCO_2$, D-D, IL-6, and CRP in predicting thrombolytic treatment efficacy in patients with PE and PH was 0.684, 0.655, 0.634, and 0.629, respectively. Importantly, the AUC for the combined evaluation utilizing these four biomarkers reached 0.807, indicating improved predictive accuracy (**Figure 4**; **Table 6**).

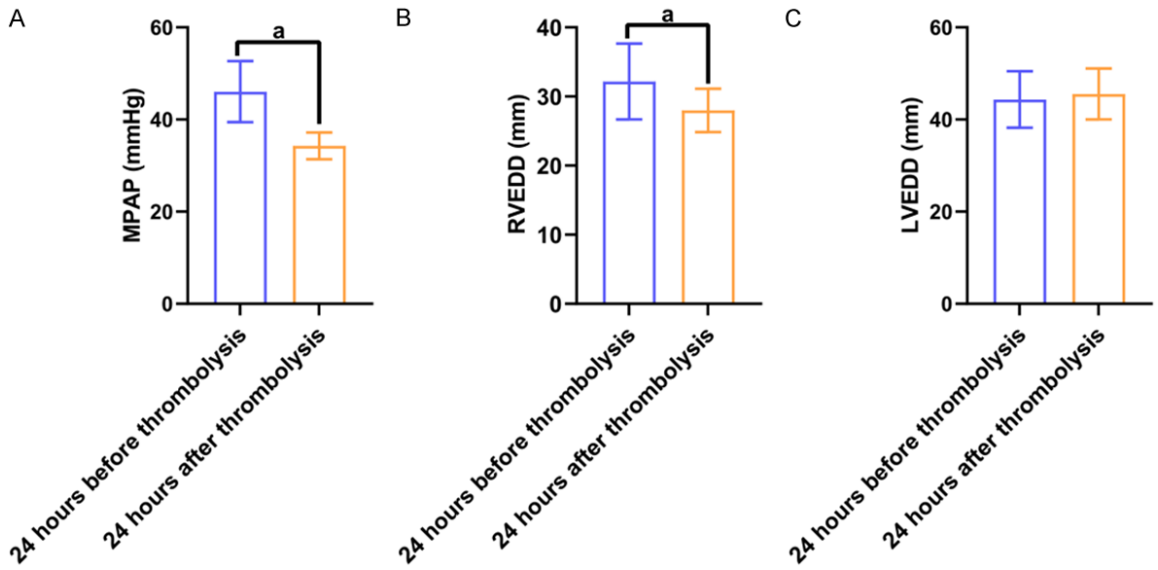

Figure 3. Changes in echocardiographic parameters before and after thrombolysis. A: Comparison of MAPA 24 hours before thrombolytic therapy and 24 hours after thrombolytic therapy; B: Comparison of RVEDD 24 hours before thrombolytic therapy and 24 hours after thrombolytic therapy; C: Comparison of LVEDD 24 hours before thrombolytic therapy and 24 hours after thrombolytic therapy; a, $P<0.05$, compared with 24 hours before thrombolysis. MAPA: mean pulmonary artery pressure; RVEDD: right ventricular end-diastolic diameter; LVEDD: left ventricular end-diastolic diameter.

Discussion

Thrombosis is the primary cause of pulmonary embolism (PE), with the persistence and gradual organization of thrombi within the pulmonary artery serving as a key mechanism in the development of secondary pulmonary hypertension (PH) [11, 12]. Epidemiological studies show that the incidence of PH among survivors of acute PE ranges from 2% to 4% [13, 14]. Currently, diagnosing PH in patients with PE necessitates invasive hemodynamic evaluation [15]. However, due to its insidious onset and nonspecific clinical manifestations, delayed diagnosis is common, particularly in some primary care settings where diagnostic capabilities and understanding of pathophysiology may be limited. Such delays contribute to disease progression and elevated mortality rates [16]. Unlike other forms of PH, timely and effective intervention can significantly improve long-term outcomes in patients with both PE and PH, and in some cases, even lead to complete resolution [17]. Consequently, advancing diagnostic and therapeutic strategies is essential for optimizing the management of PE complicated by PH.

Varies treatment modalities are available for PE; however, current management primarily focuses on anticoagulation therapy and thrombolytic interventions. Clinical guidelines explicitly recommend immediate systemic thrombolysis for high-risk PE patients, while intermediate-risk individuals should initially receive anticoagulation therapy, with thrombolysis reserved for cases of clinical deterioration in the absence of contraindication, and low-risk patients are advised to undergo anticoagulation treatment alone [18]. In cases where PE coexists with PH, thrombolytic therapy has been shown to more effectively reverse hemodynamic impairment than anticoagulation alone by reducing pulmonary vascular resistance and improving pulmonary arterial pressure [19]. While thrombolysis is effective for most patients, traditional systemic thrombolysis has raised concerns regarding increased bleeding risk, unnecessary systemic drug exposure, and delayed therapeutic onset (often several hours). In contrast, catheter-directed thrombolysis (CDT) enables direct administration of thrombolytic agents into the pulmonary artery system, achieving higher local drug concentrations. This method not only facilitates rapid clot dissolution but also reduces the required thrombolytic drug dosage, thereby minimizing the risk of major complications such as hemorrhage [20].

Table 3. Univariate analysis of therapeutic efficacy [n (%)]

Data	Ineffective group (n=40)	Total effective group (n=108)	χ^2	*P*
Age			1.336	0.248
<46 years	15 (37.50)	52 (48.15)		
≥46 years	25 (62.50)	56 (51.85)		
Gender			0.706	0.401
Male	18 (45.00)	57 (52.78)		
Female	22 (55.00)	51 (47.22)		
Smoking history	11 (27.50)	46 (42.59)	2.808	0.094
Underlying disease				
Hypertension	16 (40.00)	44 (40.74)	0.007	0.935
Diabetes	8 (20.00)	27 (25.00)	0.404	0.525
Family history of PE	0 (0.00)	4 (3.70)	0.440	0.507
Formation of DVT	5 (12.50)	15 (13.89)	0.048	0.826
Right ventricular dysfunction	5 (12.50)	4 (3.70)	2.564	0.109
DII			2.975	0.085
<0.8	14 (35.00)	55 (50.93)		
≥0.8	26 (65.00)	53 (49.07)		
Miller score			1.396	0.237
<21	16 (40.00)	55 (50.93)		
≥21	24 (60.00)	53 (49.07)		
MPAP			0.285	0.593
<35 mmHg	19 (47.50)	46 (42.59)		
≥35 mmHg	21 (52.50)	62 (57.41)		
$PaCO_2$			15.780	<0.001
<35 mmHg	31 (77.50)	44 (40.74)		
≥35 mmHg	9 (22.50)	64 (59.26)		
PaO_2			1.171	0.279
<66 mmHg	24 (60.00)	54 (50.00)		
≥66 mmHg	16 (40.00)	54 (50.00)		
PT			0.292	0.589
<11 s	22 (55.00)	54 (50.00)		
≥11 s	18 (45.00)	54 (50.00)		
APTT			1.117	0.291
<35 s	25 (62.50)	57 (54.81)		
≥35 s	15 (37.50)	51 (49.01)		
D-D			12.770	<0.001
<11 mg/L	12 (30.00)	68 (62.96)		
≥11 mg/L	28 (70.00)	40 (37.04)		
IL-6			8.374	0.004
<24 pg/mL	13 (32.50)	64 (59.26)		
≥24 pg/mL	27 (67.50)	44 (40.74)		
IL-1β			0.450	0.502
<4 pg/mL	19 (47.50)	58 (53.70)		
≥4 pg/mL	21 (52.50)	50 (46.30)		
TNF-α			1.624	0.203
<2 ng/mL	8 (20.00)	33 (30.56)		
≥2 ng/mL	32 (80.00)	75 (69.44)		
CRP			7.798	0.005
<16 mg/L	13 (32.50)	63 (58.33)		
≥16 mg/L	27 (67.50)	45 (41.67)		

Note: PE: pulmonary embolus; DVT: deep vein thrombosis; DII: dietary inflammatory index; MPAP: mean pulmonary artery pressure; $PaCO_2$: partial pressure of carbon dioxide; PaO_2: arterial oxygen partial pressure; PT: prothrombin time; APTT: activated partial thromboplastin time; D-D: D-dimer; IL-6: interleukin-6; IL-1β: interleukin-1β; TNF-α: tumor necrosis factor-α; CRP: C-reactive protein.

Table 4. Assignment table

Variable	Assignment
Therapeutic efficacy	1= total effective, 2= ineffective
$PaCO_2$	1= ≥35 mmHg, 2= <35 mmHg
D-D	1= <11 mg/L, 2= ≥11 mg/L
IL-6	1= <24 pg/mL, 2= ≥24 pg/mL
CRP	1= <16 mg/L, 2= ≥16 mg/L

Note: $PaCO_2$: partial pressure of carbon dioxide; D-D: D-dimer; IL-6: interleukin-6; CRP: C-reactive protein.

The findings of this study indicate that in patients with PE complicated by PH, symptoms such as dyspnea, shortness of breath, cough, chest pain, increased respiratory rate, tachycardia, enhanced bilateral breath sounds, and lower extremity swelling are more prevalent, reflecting the complexity of the condition. If left untreated, PE can lead to lung ischemia, hypoxia, and decreased left ventricular output, giving rise to severe conditions such as massive pulmonary embolism and cardiogenic shock, posing a life-threatening risk. After thrombolytic therapy, patients exhibited significant improvement in symptoms and clinical signs. Additionally, hemodynamic parameters such as RR, HR, $PaCO_2$, SaO_2, PaO_2, MAPA, and RVEDD, as well as cardiac function indicators, also improved rapidly. Notably, no major bleeding events or fatal complications occurred during the thrombolytic treatment process. Piazza et al. reported findings from the SEATTLE II study, which included 150 patients from 22 states with massive or submassive PE diagnosed within 14 days, all presenting with an RVEDD/LVEDD ratio of ≥0.9. After 48 hours of CDT, the RV/LV diameter decreased by 25%, pulmonary artery obstruction reduced by 30%, and pulmonary artery systolic pressure decreased by 30%. No patients experienced fatal or intracranial hemorrhage, though the incidence of major bleeding events within 30 days after thrombolysis was 10% [21]. Nevertheless, it is important to note that approximately 27.03% of patients in our study did not respond to thrombolytic therapy. Despite the clinical utility and growing research support for thrombolysis, its unpredictable bleeding risk and significant individual variability make patient selection and treatment management highly challenging. Thus, rigorous patient screening and precise prediction of therapeutic efficacy are crucial for optimizing treatment strategies and improving patient prognosis.

This study examined five specific inflammatory markers and found that post-treatment levels of IL-6, IL-1β, TNF-α, and CRP were significantly lower than pre-treatment levels. Moreover, the total effective group exhibited lower values compared to the ineffective group, suggesting a correlation between inflammatory marker reduction and thrombolytic therapy efficacy in PE-PH patients. These findings indicate that thrombolytic treatment may enhance clinical outcomes by alleviating the thrombus burden and mitigating inflammatory responses. Additionally, binary logistic regression analysis identified $PaCO_2$ <35 mmHg, D-Dimer ≥11 mg/L, IL-6 ≥24 pg/mL, and CRP ≥16 mg/L as independent risk factors for treatment failure in PE-PH patients. The underlying mechanisms are as follows: (1) In patients with PE complicated by PH, the levels of alveolar surface active factors in alveoli are significantly reduced compared to those in normal alveoli. This reduction leads to alveolar collapse and atrophy, reducing lung compliance and diffusion capacity, thereby impairing gas exchange and carbon dioxide excretion. However, compensatory mechanisms within the body and hyperventilation induced by pulmonary embolism often result in lower $PaCO_2$ [22, 23]. In healthy adults, $PaCO_2$ typically ranges from 35 to 45 mmHg; when it falls below 35 mmHg, it suggests insufficient compensatory capacity to maintain normal carbon dioxide levels, indicating severe illness and significant impairment of lung function. In such cases, the extent of dysfunction may render thrombolytic therapy ineffective in resolving the thrombus burden. (2) In abnormal coagulation, the degradation of cross-linked fibrin generates fragments that subsequently form D-D through the linkage of D fragments. Elevated D-D levels reflect coagulation-fibrinolysis system dysregulation and serves as a key biomarker for thrombus formation [24]. Keller et al. reported that thrombus burden in PE is associated with elevated D-D levels, and multivariate logistic regression identified D-D >1.18 mg/L as a predictor of right ventricular dysfunction [25]. Following PE, the body enters a hypercoagulable state, and PH exacerbates microvascular occlusion, further disrupting the balance of the coagulation-fibrinolysis system and creating a vicious cycle [26]. This leads to persistently elevated D-D levels, significantly complicating treatment efforts. (3) Vascular remodeling resulting from

Table 5. Multivariate analysis of therapeutic efficacy

Independent variables	*B*	*SE*	*Wald*	*P*	*OR*	*95% CI*
$PaCO_2$	1.673	0.467	12.809	<0.001	5.327	2.131-13.316
D-D	1.131	0.447	6.397	0.11	3.099	1.290-7.446
IL-6	1.101	0.441	6.232	0.013	3.007	1.267-7.136
CRP	1.015	0.450	5.090	0.025	2.760	1.142-6.666

Note: $PaCO_2$: partial pressure of carbon dioxide; D-D: D-dimer; IL-6: interleukin-6; CRP: C-reactive protein.

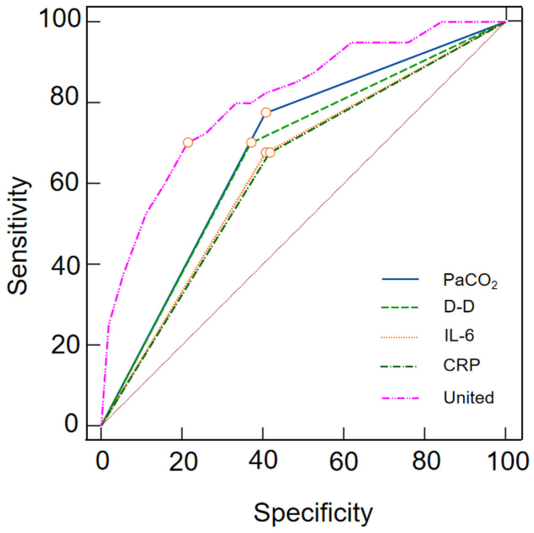

Figure 4. ROC curves for each independent risk factor in predicting therapeutic outcome. $PaCO_2$: partial pressure of carbon dioxide; D-D: D-dimer; IL-6: interleukin-6; CRP: C-reactive protein.

inflammation and recurrent thrombosis-embolism plays a crucial role in the development of PH, with multiple interwoven inflammatory factors contributing to disease progression [27]. A meta-analysis by Ding et al., which involved 25 studies, demonstrated that activated inflammatory biomarkers such as IL-6 and CRP are not only associated with an increased risk of venous thromboembolism (VTE) but may also serve as predictive markers for VTE occurrence in clinical settings [28]. In the combination of PE and PH, inflammatory infiltration and immune system dysregulation usually precede vascular remodeling in the pulmonary microvasculature. IL-6 is a key cytokine in thrombosis and disease progression, promoting coagulation by inducing the expression of tissue factor, fibrinogen, factor VIII and von Willebrand factor, while inhibiting anticoagulation by reducing the concentration of thrombin, protein S and thrombomodulin. Under hypoxic conditions, IL-6 expression is upregulated, contributing to

Table 6. ROC curve analyses of independent influencing factors for therapeutic outcomes

Independent variables	AUC	*SE*	*P*	*95% CI*
$PaCO_2$	0.684	0.0410	0.001	0.602-0.758
D-D	0.665	0.0435	<0.001	0.583-0.740
IL-6	0.634	0.0444	0.003	0.551-0.711
CRP	0.629	0.0444	0.004	0.546-0.707
United	0.807	0.0405	<0.001	0.734-0.867

Note: $PaCO_2$: partial pressure of carbon dioxide; D-D: D-dimer; IL-6: interleukin-6; CRP: C-reactive protein.

vascular remodeling and right ventricular hypertrophy in PH [29]. Zhang et al. demonstrated that IL-6 induces endothelial cell activation and enhances leukocyte activity, further amplifying inflammatory responses in PH [30]. Additionally, dysregulated signaling pathways, immune dysfunction, and interactions among inflammatory cells significantly influence disease progression [31]. CRP can promote the expression of P-selectin, increase the expression of tissue factor, reduce prostacyclin release, and upregulate cyclooxygenase-2, all of which enhance platelet adhesion and activation. Persistent inflammation leads to sustained CRP elevation, which reflects a more severe inflammatory response and contributes to pulmonary endothelial damage and functional impairment. This process promotes sustained increases in pulmonary artery pressure and may activate the coagulation cascade, facilitating thrombus formation and stabilization, while rendering clots more resistant to dissolution [32, 33].

In this study, ROC curve analysis was employed to evaluate the predictive value of $PaCO_2$, D-D, IL-6, and CRP for thrombolytic treatment efficacy in patients with PE complicated by PH. The AUC values for all indicators exceeded 0.5, demonstrating certain predictive capability. Notably, the AUC for their combined detection reached 0.807, indicating improved diagnostic value.

Based on these findings, the following clinical strategies are recommended: Protective pulmonary ventilation strategies should be implemented prior to thrombolytic therapy to mitigate excessive ventilation-induced reductions in $PaCO_2$. For patients exhibiting elevated D-D levels, intensified anticoagulation therapy may help prevent thrombosis formation and progression. Additionally, for those with increased IL-6 and CRP levels, anti-inflammatory medications or other intervention strategies aimed at controlling inflammation should be considered.

This study has several limitations. First, as a single-center retrospective study with a limited sample size, potential selection bias may affect the generalizability of the findings. Second, although multiple influencing factors were analyzed, unmeasured confounders may still exist, potentially affecting the treatment outcomes. Additionally, significant individual differences among patients may lead to variations in the implementation of the treatment plan, further impacting the study results. Future research should expand the sample size and adopt a multi-center prospective study design to more accurately assess the efficacy of thrombolytic therapy and its influencing factors. Moreover, exploring other potential influencing factors, such as genetic polymorphisms and underlying diseases, could provide a more comprehensive understanding of the reasons for individual differences in treatment response. Finally, with the continuous advancement of medical technology, new thrombolytic drugs and treatment strategies are emerging. Future studies should evaluate their clinical application, efficacy, and safety in patients with PE complicated by PH, aiming to optimize treatment outcomes and improve patient quality of life.

Conclusion

Thrombolytic therapy has a significant therapeutic effect in patients with PE combined by PH, leading to notable improvements in clinical symptoms, blood gas parameters, and pulmonary artery pressure. However, its efficacy is influenced by multiple factors, with $PaCO_2$ <35 mmHg, D-D ≥11 mg/L, IL-6 ≥24 pg/mL, and CRP ≥1 mg/L identified as independent risk factors for predicting ineffective treatment. ROC curve analysis further verified their predictive value in evaluating the therapeutic outcomes. Therefore, in clinical practice, these indicators should be carefully evaluated prior to thrombolytic therapy to guide personalized treatment plans, ultimately enhancing treatment success rates and improving patient prognosis.

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Disclosure of conflict of interest

None.

Address correspondence to: Jie Cao, Department of Respiratory and Critical Care Medicine, Tianjin Medical University General Hospital, No. 154, Anshan Road, Heping District, Tianjin 300052, China. Tel: +86-8622-60361612; E-mail: 1868608-5727@163.com

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