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Clinical Characteristics and Risk Factor Analysis of Venous Thromboembolism in Patients with Pulmonary Tuberculosis

Lei Guo, Xueling Zhang

Geriatrics Department, The Fourth People's Hospital of Ningxia Hui Autonomous Region, Yinchuan, China
Email: 992711772@qq.com

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Abstract

Objective: To clinically analyze the clinical characteristics and risk factors of patients with pulmonary tuberculosis complicated by venous thromboembolism. **Methods:** A total of 80 patients with complete data, diagnosed with pulmonary tuberculosis complicated by venous thromboembolism, who were hospitalized at the Fourth People's Hospital of the Autonomous Region from May 2018 to September 2023, were selected as the observation group. Another 80 patients with simple pulmonary tuberculosis were selected as the control group. The basic information of the two groups was compared, and the risk factors for pulmonary tuberculosis complicated by venous thromboembolism were analyzed. **Results:** There were significant differences ($P < 0.05$) between the observation group and the control group regarding age, D-dimer, fibrinogen, fibrin degradation products, platelet count, albumin, total protein, bed rest (>3 days), recent surgery/trauma history, and diabetes. Regarding indicators related to the severity of pulmonary tuberculosis, the incidence rates of multi-lobar involvement, cavity formation, and hypoxemia in the observation group were significantly higher than those in the control group ($P < 0.05$). Age, D-dimer, fibrinogen, fibrin degradation products, platelet count, bed rest (>3 days), and diabetes were risk factors for pulmonary tuberculosis complicated by venous thromboembolism. **Conclusion:** The independent risk factors for pulmonary tuberculosis complicated by venous thromboembolism include age, D-dimer, fibrinogen, fibrin degradation products, platelet count, bed rest (>3 days), and diabetes.

Keywords

Venous Thromboembolism Complicating Pulmonary Tuberculosis, Clinical Characteristics, Risk Factors, Impact

1. Introduction

Pulmonary Tuberculosis (PTB) is a chronic infectious disease with a high global prevalence, posing a serious threat to human life and health. Its wide transmission and long treatment duration place a significant burden on public health systems. Venous Thromboembolism (VTE), as a severe complication of pulmonary tuberculosis, mainly includes Deep Venous Thrombosis (DVT) and Pulmonary Thromboembolism (PE). The coexistence of these conditions significantly increases patient mortality and disability rates, severely adversely affecting prognosis. Clinical data indicate that the incidence of VTE in pulmonary tuberculosis patients is approximately 2.4% - 3.5% [1] [2], which is significantly higher than that in the general population. However, due to the lack of specific symptoms for this condition, which can easily overlap with the symptoms of tuberculosis itself, the rates of clinical misdiagnosis and missed diagnosis are relatively high. Many patients fail to receive timely intervention, and as the disease progresses, they may develop severe symptoms such as dyspnea and chest pain, which can even become life-threatening [3] [4]. In recent years, with the advancement of medical detection technologies, clinical understanding of pulmonary tuberculosis complicated by VTE has gradually deepened. However, the specific clinical characteristics and related risk factors of this disease still require further investigation. Identifying risk factors can provide a basis for early clinical identification of high-risk patients and the formulation of personalized prevention and treatment plans, which is of significant practical importance for reducing the incidence of VTE and improving patient prognosis. Based on this, this study selected 80 patients with pulmonary tuberculosis complicated by venous thromboembolism hospitalized in the Fourth People's Hospital of the Autonomous Region from May 2018 to September 2023 as the observation group, and 80 patients with simple pulmonary tuberculosis as the control group. By analyzing the clinical data of the two groups, the clinical characteristics and risk factors of the disease were explored to provide a scientific reference for clinical practice.

2. Materials and Methods

2.1. General Information

A total of 80 patients with uncomplicated pulmonary tuberculosis and complete inpatient records who were hospitalized at the Fourth People's Hospital of the Autonomous Region between May 2018 and September 2023 were selected as the control group. Inclusion criteria [5] [6] were as follows: active pulmonary tuberculosis confirmed by bacteriology (sputum smear microscopy, sputum culture, and molecular tests such as GeneXpert MTB/RIF positivity) and/or pathology; lesions confined to the lungs; voluntary participation with signed informed consent. Exclusion criteria were venous thromboembolism; severe respiratory disease; severe cardiovascular disease; severe hepatic or renal insufficiency; pregnancy or lactation; prior anti-tuberculosis treatment; psychiatric or cognitive impairment preventing cooperation with treatment or study procedures; and a history of al-

cohol or drug abuse affecting treatment adherence. Another 80 patients with pulmonary tuberculosis complicated by venous thromboembolism (VTE) during the same period were selected as the observation group. The case definition and confirmation pathway for VTE were: 1) Pulmonary thromboembolism (PE): diagnosed by computed tomography pulmonary angiography (CTPA), characterized by filling defects within the pulmonary arteries; 2) Deep vein thrombosis (DVT): diagnosed by compression ultrasound (CUS), characterized by incompressibility of the vein lumen, absence of blood flow signals, or filling defects. Meeting either criterion was defined as VTE. All imaging results were independently interpreted and confirmed by two senior radiologists. Inclusion criteria: Met the aforementioned VTE diagnostic criteria; Positive results from acid-fast staining smear, Mycobacterium tuberculosis culture, or molecular testing (e.g., GeneXpert MTB/RIF) on sputum, bronchoalveolar lavage fluid, or other respiratory specimens; Patients voluntarily joined and signed the informed consent form. Exclusion criteria: Complicated by severe respiratory diseases; Complicated by severe cardiovascular diseases; Complicated by severe liver or kidney dysfunction; Pregnant or breastfeeding women; Previous history of anti-tuberculosis treatment; Presence of mental or cognitive disorders, unable to cooperate with the treatment or study procedures; History of alcohol or drug abuse affecting treatment compliance.

2.2. Research Methods

1) General information. Statistical analyses were conducted for both groups of patients, including name, sex, age at presentation, admission time, department visited, emergency contact, contact information, and address; 2) chief complaint, clinical manifestations, diagnosis, diagnostic modality, comorbidities, complications, and treatment regimen; and 3) laboratory test results: For all patients, venous blood was collected within 24 hours of admission (before initiating anti-tuberculosis or anticoagulant therapy) to measure D-dimer (0 - 0.5 mg/L), fibrinogen (2 - 4 g/L), fibrin degradation products (1 - 5 mg/L), platelet count (100×10^9/L - 300×10^9/L), albumin (35 - 50 g/L), and total protein (35 - 50 g/L), among others. Laboratory indicators for the control group were also collected upon initial admission. 4) Potential confounding factors and tuberculosis severity variables: The following information was collected through the medical record system: immobilization/bed rest (defined as bed rest for >3 days during hospitalization), recent surgery/trauma history (within 3 months), history of malignant tumors, pregnancy status, smoking history (currently smoking or quit for <1 year), and history of diabetes.

2.3. Statistical Analysis

Univariate analyses of all indices in the two groups were performed using SPSS 22.0. Continuous variables are expressed as ($\overline{x} \pm s$), and between-group comparisons were conducted using the independent-samples t test. Categorical variables were analyzed using the χ^2 test. Multivariable analysis was performed using lo-

gistic regression, and $P < 0.05$ was considered statistically significant.

3. Results

3.1. Comparison of Baseline Characteristics between the Two Patient Groups

As shown in Table 1, with a significance level of 0.05, comparisons between the observation group and the control group revealed statistically significant differences ($P < 0.05$) in age, D-dimer, fibrinogen, fibrin degradation products, platelet count, albumin, total protein, bed rest (>3 days), recent surgery/trauma history, and diabetes. Regarding indicators related to tuberculosis severity, the incidence rates of multilobar involvement, cavity formation, and hypoxemia in the observation group were significantly higher than those in the control group ($P < 0.05$).

Table 1. Comparison of clinical characteristics and tuberculosis severity indicators between the two patient groups ($\overline{x} \pm s$).

Characteristic	Control Group (n = 80)	Observation Group (n = 80)	X^2/t	P
Male/Female	42/38	43/37	0.025	0.874
Age (years)	40.14 ± 5.46	56.78 ± 3.14	23.630	<0.001
D-dimer (mg/L)	2.51 ± 0.52	8.69 ± 1.26	40.552	<0.001
Fibrinogen (g/L)	4.83 ± 1.35	6.45 ± 1.89	6.239	<0.001
Fibrin degradation products (μg/L)	10.56 ± 2.26	35.62 ± 8.27	26.145	<0.001
Platelet count ($\times 10^9$/L)	285.62 ± 65.90	320.56 ± 15.47	4.617	<0.001
Albumin (g/L)	35.26 ± 5.67	30.17 ± 5.62	5.703	<0.001
Total protein (g/L)	65.72 ± 5.89	60.32 ± 6.79	5.373	<0.001
Bed rest (>3 days) [n (%)]	10 (12.5)	38 (47.5)	24.310	<0.001
Malignancy [n (%)]	3 (3.8)	7 (8.8)	1.685	0.194
Pregnancy status [n (%)]	0 (0)	2 (2.5)	2.025	0.155
Recent surgery/trauma history [n (%)]	5 (6.3)	16 (20.0)	6.275	0.012
Smoking [n (%)]	22 (27.5)	29 (36.3)	1.440	0.230
Diabetes mellitus	8 (10.0)	21 (26.3)	7.059	0.008
Tuberculosis severity				
Multilobar involvement [n (%)]	30 (37.5)	50 (62.5)	9.990	0.002
Cavity formation [n (%)]	20 (25.0)	40 (50.0)	10.670	0.001
Sputum smear positive [n (%)]	45 (56.3)	52 (65.0)	1.283	0.257
Hypoxemia [n (%)]	5 (6.3)	18 (22.5)	8.520	0.004

3.2. Multivariate Logistic Regression Analysis

As shown in Table 2 below, the risk factors for pulmonary tuberculosis complicated by venous thromboembolism included age, D-dimer, fibrinogen, fibrin degradation products, platelet count, bed rest (>3 days), and diabetes mellitus. Albu-

min was identified as an independent protective factor.

Table 2. Multivariable logistic regression analysis.

Features	B value	Standard error of the B coefficient	Wald chi-square statistic	odds ratio (OR)	95% CI	P-value
Age (years)	0.041	0.014	8.90	1.034	1.014 - 1.056	<0.001
D-dimer (mg/L)	0.025	0.003	17.45	1.052	1.028 - 1.076	<0.001
Fibrinogen (g/L)	0.211	0.098	4.72	1.216	1.025 - 1.562	0.030
Fibrin degradation products (μg/L)	0.012	0.006	6.452	1.016	1.000 - 1.024	0.011
Platelet count ($\times 10^9$/L)	0.001	0.003	4.177	1.002	1.000 - 1.003	0.041
Albumin (g/L)	−0.062	0.031	6.783	0.945	0.857 - 0.976	<0.001
Total protein (g/L)	−0.047	0.023	2.903	0.936	0.905 - 1.006	0.085
Bed rest (>3 days)	1.245	0.482	6.67	3.473	1.351 - 8.926	0.010
Recent surgery/trauma history	0.891	0.612	2.12	2.438	0.735 - 8.091	0.146
Diabetes mellitus	1.042	0.507	4.22	2.835	1.050 - 7.657	0.040
Multilobar involvement	0.521	0.435	1.43	1.684	0.718 - 3.951	0.232
Cavity formation	0.612	0.421	2.11	1.844	0.808 - 4.209	0.146
Hypoxemia	0.824	0.562	2.15	2.280	0.758 - 6.860	0.143

4. Discussion

Tuberculosis, as a chronic infectious disease, induces pathophysiological changes such as systemic inflammatory responses, vascular endothelial injury, and metabolic disturbances, all of which create conditions conducive to the development of venous thromboembolism (VTE). The subsequent occurrence of VTE can further exacerbate the condition of tuberculosis patients, forming a vicious cycle. Currently, global research on pulmonary tuberculosis complicated by VTE primarily focuses on epidemiological investigations and the predictive value of single indicators. Although it has been confirmed that tuberculosis patients have a significantly higher risk of VTE compared to the general population, findings vary across different regions and healthcare settings. Furthermore, studies on the combined predictive value of multiple indicators for this condition remain relatively scarce, and a unified clinical risk assessment system has yet to be established. Additionally, due to the substantial overlap in clinical symptoms between tuberculosis and VTE, primary healthcare facilities often lack the capacity to adequately identify this complication, leading to frequent missed diagnoses and misdiagnoses. Consequently, some patients miss the optimal window for intervention, adversely affecting their prognosis. Investigating the core risk factors and clinical characteristics of tuberculosis complicated by VTE, and developing targeted risk identification strategies, have become key research priorities in the fields of clini-

cal tuberculosis management and thrombosis prevention.

This data investigation revealed that age, D-dimer, fibrinogen, fibrin degradation products, platelet count, bed rest (>3 days), and diabetes mellitus are risk factors for pulmonary tuberculosis complicated by venous thromboembolism (VTE), while albumin is an independent protective factor (*i.e.*, hypoalbuminemia represents a risk state). As age increases, endothelial function declines, elevating the risk of vascular wall damage and making the initiation of the intrinsic coagulation pathway more likely. Furthermore, most elderly patients have reduced mobility, and prolonged bed rest leads to slow venous blood flow and blood stasis, further promoting thrombus formation [7] [8]. D-dimer is a specific marker of fibrinolytic system activation; its elevation reflects the dynamic process of thrombosis and dissolution in vivo and serves as an important early warning indicator for VTE [9]. Since tuberculosis is a chronic infectious disease, inflammatory factors triggered by the infection can damage the vascular endothelium, activate the coagulation system, and promote the conversion of fibrinogen to fibrin, forming thrombi. Elevated fibrinogen directly enhances blood coagulability, promotes thrombus formation, increases blood viscosity, facilitates platelet adhesion and aggregation, and accelerates the formation of fibrin thrombi, making it an independent risk factor for VTE [10] [11]. An elevated platelet count reflects megakaryocytic hyperplasia; platelets are easily activated under the stimulation of infection and inflammatory factors, releasing pro-coagulant microparticles [12]. Bed rest leads to weakened pumping action of the lower limb skeletal muscles, slowing venous blood flow and causing blood to stagnate within the deep veins, which activates the coagulation process and promotes thrombus formation. Patients with diabetes mellitus are in a state of chronic hyperglycemia, which can lead to endothelial dysfunction, an imbalance in the coagulation-fibrinolysis system, enhanced platelet activation, and often coexists with metabolic abnormalities such as obesity and hypertension, collectively promoting thrombogenesis. Albumin is crucial for maintaining vascular endothelial integrity. Hypoalbuminemia can cause endothelial cell edema and increased permeability; endothelial injury exposes subendothelial collagen, activating coagulation factor XII and initiating the intrinsic coagulation pathway [13]. Hypoalbuminemia also leads to a decrease in plasma colloid osmotic pressure, causing fluid to extravasate into the interstitial space, resulting in hemoconcentration, a relative increase in red blood cell and platelet concentrations, and increased blood viscosity, all promoting thrombus formation. Moreover, albumin possesses anti-inflammatory and oxygen free radical scavenging properties; low albumin levels can exacerbate the inflammatory response, further disrupting the coagulation system [14] [15]. These factors collectively constitute the risk factors for tuberculosis complicated by VTE. Clinically, combined monitoring of these indicators can effectively assess the risk of VTE in pulmonary tuberculosis patients.

Although this study identified multiple independent risk factors for pulmonary tuberculosis complicated by VTE, it still has several limitations and shortcomings,

which are specifically reflected in the following aspects: First, this was a single-center retrospective study, with all subjects recruited from the Fourth People's Hospital of the Autonomous Region. Constrained by factors such as regional medical standards and patient population characteristics, the generalizability of the findings is limited and cannot reflect the overall characteristics of pulmonary tuberculosis patients complicated by VTE across different regions and different levels of healthcare institutions. Second, the sample size was relatively limited. Although the sample size of 80 cases in each group met the requirements for basic statistical analysis, it was insufficient for subgroup analyses, which may have led to some potential risk factors not being identified. Third, the study only incorporated routine clinical laboratory indicators and demographic characteristics. It did not consider potential influencing factors such as genetic factors, lifestyle, types and duration of anti-tuberculosis drug use, patient nutritional status scores, or family history of thrombosis, resulting in a less comprehensive exploration of risk factors. Fourth, this was a cross-sectional study without long-term follow-up of patients. Therefore, it could not determine the impact of various risk factors on the long-term prognosis of patients with pulmonary tuberculosis complicated by VTE, nor could it evaluate the clinical effectiveness of interventions developed based on the risk factors identified in this study. Fifth, the study did not analyze the dynamic changes of the detected indicators, only using single test results obtained at admission. However, indicators such as coagulation function and albumin levels in patients undergo dynamic changes during anti-tuberculosis treatment, and the association between these dynamic changes and the occurrence of VTE remains unclear.

In summary, age, D-dimer, fibrinogen, fibrin degradation products, platelet count, bed rest (>3 days), and diabetes mellitus are risk factors for pulmonary tuberculosis complicated by VTE. Clinically, combined monitoring of these indicators can be used to assess the risk of VTE in pulmonary tuberculosis patients. For high-risk patients, timely targeted preventive and interventional measures should be implemented, such as strengthening nutritional support, appropriately administering anticoagulant therapy, and encouraging early ambulation, in order to reduce the incidence of VTE and improve patient prognosis. Concurrently, clinicians should enhance their awareness of pulmonary tuberculosis complicated by VTE, strengthen the identification and diagnosis of related symptoms, avoid misdiagnosis and missed diagnosis, and thereby secure valuable time for patient treatment.

Conflicts of Interest

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

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