# Clinical Characteristics and Risk Factors of Intermediate-High Risk Pulmonary Embolism with Secondary Pulmonary Infarction Misdiagnosed as Pneumonia: A Postprint Study

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## Abstract

Background Although cases of pulmonary infarction secondary to pulmonary embolism have been increasingly reported in recent years, misdiagnosis of this condition remains common, with pneumonia being the most frequent misdiagnosis. Particularly in patients with intermediate-to-high risk, delayed diagnosis and failure to receive timely treatment can affect patient prognosis. Objective To summarize the clinical characteristics of intermediate-to-high risk pulmonary embolism patients with secondary pulmonary infarction misdiagnosed as pneumonia, analyze related risk factors, and construct an early diagnostic model. Methods Clinical data of hospitalized patients diagnosed with intermediate-to-high risk pulmonary embolism with secondary pulmonary infarction at the First Affiliated Hospital of University of Science and Technology of China from 2017 to 2023 were retrospectively collected. The misdiagnosis status of patients was analyzed, and based on diagnostic circumstances, patients were divided into a misdiagnosis group (discharged home after being misdiagnosed with pneumonia) and a control group (correctly diagnosed at first visit in outpatient or emergency department). Multivariate binary Logistic regression analysis was used to explore influencing factors for misdiagnosis of intermediate-to-high risk pulmonary embolism with secondary pulmonary infarction as pneumonia, receiver operating characteristic (ROC) curves were plotted to analyze the predictive value of each indicator for such misdiagnosis, and Delong' s test was used to compare the areas under the ROC curves (AUC). Results A total of 101 patients were included, of which 70 intermediate-to-high risk pulmonary embolism patients with secondary pulmonary infarction were misdiagnosed as pneumonia. The incidence of misdiagnosis of intermediate-to-high risk pulmonary embolism with secondary pulmonary infarction as pneumonia showed a decreasing trend from 2017

to 2023 (100.0%, 83.3%, 74.1%, 71.4%, 63.2%, 66.7%, and 50.0% sequentially, P=0.010). Multivariate binary Logistic regression analysis revealed that age $ $60 years (OR=18.271, 95%CI=4.373~76.339, P<0.001), fever (OR=16.073, 95%CI=3.510~73.786, P<0.001), chest pain (OR=6.660, 95%CI=1.571~28.233, P=0.010), and absence of dyspnea (OR=9.027, 95%CI=2.049~30.249, P=0.003) were independent influencing factors for misdiagnosis of intermediate-to-high risk pulmonary embolism with secondary pulmonary infarction as pneumonia. The multivariate combined model = -6.624 + 0.095 × age + 2.510 × fever + 2.683 × absence of dyspnea; the AUC of the combined model for predicting misdiagnosis of intermediate-to-high risk pulmonary embolism with secondary pulmonary infarction as pneumonia was 0.880 (95%CI=0.802~0.959), with an optimal cutoff value of 0.854, sensitivity of 0.871, and specificity of 0.806. The predictive value of the combined model was superior to single-factor indicators such as age (Z=2.771, P=0.006), fever (Z=4.653, P<0.001), and absence of dyspnea (Z=4.014, P<0.001). Conclusion Although the proportion of intermediate-to-high risk pulmonary embolism patients with secondary pulmonary infarction misdiagnosed as pneumonia decreased from 2017 to 2023, clinicians should pay attention to the differential diagnosis between pulmonary infarction and pneumonia when elderly pulmonary embolism patients present with fever, chest pain, and absence of dyspnea.

## Full Text

# Clinical Characteristics and Risk Factors of Patients with Pulmonary Infarction Secondary to Intermediate and High-risk Pulmonary Embolism Misdiagnosed as Pneumonia

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## Abstract

**Background:** Although case reports of pulmonary infarction (PI) secondary to pulmonary embolism (PE) have increased in recent years, misdiagnosis remains

common, most frequently as pneumonia. In patients with intermediate and high-risk PE, delayed diagnosis and treatment can adversely affect prognosis.

**Objective:** To summarize the clinical characteristics of patients with intermediate and high-risk PE complicated by PI who were misdiagnosed as having pneumonia, analyze related risk factors, and construct an early diagnostic model.

**Methods:** We retrospectively collected clinical data from hospitalized patients diagnosed with intermediate and high-risk PE complicated by PI at the First Affiliated Hospital of University of Science and Technology of China from 2017 to 2023. Patients were divided into a misdiagnosis group (discharged home after misdiagnosis as pneumonia) and a control group (correctly diagnosed at first outpatient or emergency department visit). Multivariate binary logistic regression analysis was used to identify factors associated with misdiagnosis of PI as pneumonia. Receiver operating characteristic (ROC) curves were constructed to evaluate predictive performance.

**Results:** Among 101 included patients, 70 with intermediate and high-risk PE complicated by PI were misdiagnosed as having pneumonia. The misdiagnosis rate showed a declining trend from 2017 to 2023 (100.0%, 83.3%, 74.1%, 71.4%, 63.2%, 66.7%, and 50.0%, respectively; P=0.010). Multivariate analysis revealed that age \$ $60 years (OR = 18.271,95 \times age + 2.510 \times fever + 2.683 \times$ \$absence of dyspnea. This model achieved an AUC of 0.880 (95%CI=0.802-0.959) for predicting misdiagnosis, with an optimal cutoff of 0.854, sensitivity of 0.871, and specificity of 0.806. The combined model demonstrated superior predictive value compared to single factors including age (Z=2.771, P=0.006), fever (Z=4.653, P<0.001), and absence of dyspnea (Z=4.014, P<0.001).

**Conclusion:** Although the misdiagnosis rate of intermediate and high-risk PE complicated by PI has decreased from 2017 to 2023, clinicians should remain vigilant for differential diagnosis between PI and pneumonia when elderly PE patients present with fever, chest pain, and particularly without dyspnea.

**Keywords:** Pulmonary infarction; Pulmonary embolism; Intermediate and high-risk; Misdiagnosis; Pneumonia; Prediction

## Introduction

Pulmonary embolism (PE) is a group of diseases or clinical syndromes characterized by obstruction of pulmonary arteries and their branches by various emboli, leading to pulmonary circulatory dysfunction [1-2]. Pulmonary infarction (PI) occurs when PE obstructs pulmonary vessels, causing hemorrhage and necrosis of lung tissue. Traditionally considered rare, PI has gained increasing clinical attention, with multiple studies reporting that 20-40% of PE patients develop secondary PI [3-6].

Due to its nonspecific clinical features, PI is frequently misdiagnosed as pneumonia, preventing timely administration of standard anticoagulation therapy [7-9]. This is particularly concerning in intermediate and high-risk PE patients, where delayed treatment significantly impacts prognosis [10-11]. Guidelines from European and American cardiac associations indicate that intermediate-risk PE patients have 4.0% in-hospital mortality and 6.0% 30-day post-discharge mortality, while high-risk patients have mortality rates exceeding 20%. Failure to promptly treat this population may lead to disease progression, cardiopulmonary dysfunction, and even sudden death. Therefore, early identification of clinical characteristics and risk factors is crucial for accurate diagnosis and precise treatment.

This study retrospectively analyzed data from patients with intermediate and high-risk PE complicated by PI at our institution to summarize clinical features, identify risk factors, and construct a predictive model to aid clinical diagnosis.

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## Methods

### Clinical Data

We retrospectively collected clinical data from patients diagnosed with intermediate and high-risk PE complicated by PI at the First Affiliated Hospital of University of Science and Technology of China from 2017 to 2023.

**Inclusion Criteria for PI [12]:** (1) Occlusion of distal pulmonary arteries or branches causing necrosis of the supplied lung parenchyma, appearing as wedge-shaped consolidation; (2) Pulmonary consolidation distributed along vessels; (3) Meeting any of three conditions: peripheral consolidation with central cavitation, peripheral consolidation with ground-glass opacity, or peripheral ground-glass opacity; (4) Exclusion of other diagnoses such as vasculitis, malignancy, and sepsis besides acute PE with secondary PI.

**Exclusion Criteria:** (1) Incomplete clinical data (especially lacking CTPA); (2) Repeated hospitalizations; (3) No thrombus identified on CTPA; (4) Non-thrombotic embolic diseases; (5) Misdiagnosis as diseases other than pneumonia.

This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of University of Science and Technology of China (Approval No.: 2024-RE-14). As a retrospective study without involvement of personal privacy or biological sample testing, the requirement for written informed consent was waived.

### Data Collection and PE Risk Stratification

We retrospectively extracted data from the hospital' s electronic medical record system, including baseline characteristics, laboratory tests, and imaging findings. General data comprised age, sex, height, smoking/alcohol history, and clinical

manifestations (fever, dyspnea, chest pain, hemoptysis). Laboratory tests included white blood cell count, troponin, NT-proBNP, D-dimer, and blood gas analysis. Imaging studies included echocardiography, lower extremity venous ultrasound, and CTPA. Smoking history was defined as having smoked >100 cigarettes or continuous/cumulative smoking for $ $6 months; alcohol history was defined as any alcohol consumption [1-2].

PE risk stratification followed the 2018 Guidelines for Diagnosis, Treatment and Prevention of Pulmonary Thromboembolism [2], classifying patients into low-, intermediate-, and high-risk groups. After excluding low-risk patients, we identified intermediate and high-risk PE cases with PI based on chest CT findings. Patients were divided into a misdiagnosis group (discharged after misdiagnosis as pneumonia) and a control group (correctly diagnosed at first outpatient or emergency visit).

### Statistical Analysis

SPSS 24.0 software was used for statistical analysis. Normality and homogeneity tests were performed on continuous variables. Normally distributed data were expressed as mean±standard deviation and compared using two-sample t-tests; non-normally distributed data were expressed as median (P25, P75) and compared using Wilcoxon rank-sum tests. Categorical variables were expressed as percentages and compared using $^2$ tests. Multivariate binary logistic regression was used to identify factors associated with misdiagnosis as pneumonia. ROC curves were constructed to evaluate diagnostic performance, with AUC values compared using the DeLong test. $P<0.05$ was considered statistically significant.

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## Results

### Misdiagnosis Rate

From 2017 to 2023, the misdiagnosis rate of intermediate and high-risk PE complicated by PI as pneumonia showed a significant declining trend (P=0.010) . A total of 101 patients were included, with 70 misdiagnosed as pneumonia. Among misdiagnosed patients, 45 (64.3%) were aged $ $60 years. Imaging findings of misdiagnosed cases are shown in [Figure 1: see original paper].

### Comparison of Clinical Characteristics

Compared with the control group (n=31), the misdiagnosis group (n=70) was older and had higher proportions of fever, chest pain, dyspnea, and wedge-shaped infarct lesions on imaging ($P<0.05$). No significant differences were observed between groups in sex, smoking history, alcohol history, cough, hemoptysis, unilateral leg swelling, white blood cell count, troponin, D-dimer, NT-

proBNP, infarct location, lobar distribution, central lucency sign, vascular sign, air bronchogram sign, or prognosis (P>0.05) .

### Multivariate Logistic Regression Analysis

Using misdiagnosis of intermediate and high-risk PE with PI as pneumonia as the dependent variable (no=0, yes=1), we included significant variables from Table 2 as independent variables: age$ 60$years(no = 0, yes = 1), fever(no = 0, yes = 1), chestpain(no = 0, yes = 1), andabsenceofdyspnea(no = 0, yes = 1).Multivariateanalysisidentifiedage $60 years, fever, chest pain, and absence of dyspnea as independent risk factors for misdiagnosis (P<0.05) .

### Predictive Value of Risk Factors

ROC curves were constructed for age, fever, absence of dyspnea, and the combined model [Figure 2: see original paper]. The combined model, expressed as Y=-6.624+0.095×age+2.510×fever+2.683×absence of dyspnea, achieved an AUC of 0.880 (95%CI=0.802-0.959) for predicting misdiagnosis, with an optimal cutoff of 0.854, sensitivity of 0.871, and specificity of 0.806. The combined model demonstrated significantly superior predictive performance compared to single factors: age (Z=2.771, P=0.006), fever (Z=4.653, P<0.001), and absence of dyspnea (Z=4.014, P<0.001) .

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## Discussion

This study demonstrated a declining trend in misdiagnosis of intermediate and high-risk PE with PI as pneumonia from 2017 to 2023, with elderly patients comprising 64.3% of misdiagnosed cases. Multivariate analysis identified age ($ $60 years), fever, chest pain, and absence of dyspnea as independent risk factors for misdiagnosis.

PI results from emboli originating in the venous system and right heart that obstruct pulmonary circulation, causing ischemia, hemorrhage, and necrosis of lung parenchyma [6]. Beyond the classic triad of chest pain, hemoptysis, and dyspnea, PI often presents with respiratory symptoms similar to pulmonary infections such as cough, sputum production, and fever, leading to frequent misdiagnosis as pneumonia. Recent domestic reports have described multiple cases of PI misdiagnosed as pneumonia due to fever, hemoptysis, chest pain, and pulmonary infiltrates [13-14].

Approximately 60% of patients in the misdiagnosis group presented with fever, consistent with reports from Spanish [17] and recent Chinese studies [18]. Acute PE patients commonly develop low-grade fever (37.5-38.0°C) within one week, with reported incidence of 6-33%; similar rates are observed in PI [19]. The pathophysiology involves inflammatory reactions from lung tissue necrosis and

vascular irritation, possibly representing immune responses secondary to vascular and pleural remodeling. This can be confused with the fever mechanism in pneumonia, which results from pathogen stimulation, thermoregulatory center dysfunction, and compromised immunity.

Chest pain may arise from pleural inflammation, irritation, and necrosis due to alveolar hemorrhage. ELODIE et al. [3] reported chest pain in approximately one-third of PI patients, while a recent Chinese observational study documented high incidence (30/64) [4]. Notably, the misdiagnosis group had lower rates of dyspnea. The mechanism remains unclear, but dyspnea severity and duration correlate positively with thrombus size [20]; most misdiagnosed patients had small vessel occlusion with minimal and transient dyspnea. Our multivariate findings align with TORRES-MACHO et al. [17], though the non-significant association with hemoptysis may reflect limited sample size.

Predictive models serve as valuable tools for describing diagnostic or prognostic probabilities and are increasingly used in clinical medicine. YANG et al. [21] developed a PE prognostic model through multicenter research including 4,196 patients, while Song et al. [22] demonstrated that a combined protein model (AUC=0.924, sensitivity=0.75, specificity=0.94) effectively predicted tuberculosis treatment outcomes. Few studies have modeled multi-factorial influences on PI. MINIATI et al. [23] used binary logistic regression in a multicenter Italian study, finding PI risk peaked at age 40. Our study employed ROC analysis to examine relationships between multiple variables and pneumonia misdiagnosis in PI. Based on regression-identified risk factors, we selected three predictors (age, fever, and absence of dyspnea) to construct an ROC predictive model, validating its clinical utility through AUC values. Results confirmed all three single variables and the combined model as influential factors, with the combined model showing the largest AUC and highest diagnostic efficacy. Age warrants particular attention as a feasible clinical indicator for PI diagnosis [24]. However, given our limited sample size, future prospective multicenter studies are needed to further validate these variables' reliability and clinical utility.

While clinician awareness of PI has improved, reducing misdiagnosis rates, elderly PE patients presenting with fever, chest pain, and particularly without dyspnea should prompt immediate CTPA evaluation to exclude PI and avoid misdiagnosis as pneumonia. This study has limitations: its retrospective design with limited sample size introduces potential bias and missing data; additionally, insufficient follow-up compliance may have underestimated mortality rates, requiring further research for definitive prognostic conclusions.

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## Author Contributions

Guangyu Lü: conceptualization, data analysis, statistical processing, and manuscript writing. Guangyu Lü and Wanjun Sun: data collection and organization. Xiaowen Hu, Qianqian Zhou, and Xianmeng Chen: study

implementation and manuscript revision. Xuehan Liu: statistical methodology design and feasibility analysis. Xiaowen Hu: supervision of study design, quality control, manuscript revision, and overall oversight.

**Conflict of Interest:** The authors declare no conflict of interest.

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*Note: Figure translations are in progress. See original paper for figures.*