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Research Article

# Clinical Features and Risk Factors of 134 HA-PTE Patients

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## Abstract

*Objective*: The objective of this study was to determine the clinical features and risk factors for hospital-associated pulmonary thromboembolism (HA-PTE) in Taizhou Hospital of Zhejiang Province. *Methods*: The clinical data of 513 pulmonary thromboembolism (PTE) patients who were admitted to Taizhou Hospital of Zhejiang Province in from January 1st, 2020, to December 31st, 2022, were retrospectively analyzed. The HA-PTE group and the community-associated PTE (CA-PTE) group were classified according to whether these disorders occurred during hospitalization or within a 90-day period of admission to the hospital (including inpatients with at least two days of hospitalization stay or a surgical procedure under or regional anesthesia). Differences in clinical features, risk factors and other indicators were also analyzed between the two groups. *Results*: A total of 513 patients with acute PTE were analyzed in the present study. Among them, 134 patients had HA-PTE, and 379 patients had CA-PTE. Patients in the HA-PTE group had less dyspnea or hemoptysis and more fever and chest pain. The all-cause mortality rate in the HA-PTE group was greater than that in the CA-PTE group, but it was not statistically significant. In comparison to community-acquired pulmonary thromboembolism (CA-PTE), long-term bed rest, active malignancy, lung infection, acute cerebral infarction, and fracture were observed as more prevalent risk factors in the hospital-acquired pulmonary thromboembolism (HA-PTE) group. Additionally, recent surgery (within one month post-operation) and central venous catheterization were identified as independent risk factors in the HA-PTE group. According to the subgroup analysis of the HA-PTE group, the all-cause mortality rate of patients who experienced HA-PTE in the hospital was lower than that of patients who experienced HA-PTE which in 90 days after admission (1.56% versus 2.85%, respectively); however, the difference was not statistically significant. *Conclusion*: More than half of the HA-PTE events were associated with recent hospitalization. HA-PTE and CA-PTE have different risk factors; when combined with different clinical symptoms, they have a higher incidence of HA-PTE occurring in the hospital. More attention should be given to inpatients to reduce the incidence of HA-PTE.

## Keywords

Pulmonary Thromboembolism, Clinical Feature, Risk Factor, Hospitalization

## 1. Introduction

PTE is the result of the interaction between genetic factors and acquired factors [1]. PTE is considered now as the third most common cardiovascular pathology. PTE can be asymptomatic, passing misdiagnosed, or detected incidentally during routine investigations making its epidemiology hard to be properly characterized [2]. On the other hand, PTE may be presented with more serious symptoms ranging from tachycardia, tachypnea up to the sudden cardiovascular collapse,

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and death [3]. It also may result in some serious long-term complications such as chronic thromboembolic pulmonary hypertension. Hence, the clinical suspicion is the main factor in proper and early detection. Clinically, PE is a common complication of deep venous thrombosis (DVT), which has many risk factors including prior history of DVT/PE, recent surgery, prolonged immobilization, cardiac diseases, autoimmune diseases, cancer, and conditions associated with hypercoagulability (such as antiphospholipid antibody syndrome and NS) [4]. Due to the different incidence environment and conditions, PTE varies in clinical features and risk factors [5]. At present, there are few complete research data on this topic in China, and these data do not reflect the differences among people in different regions. To further explore the clinical characteristics and risk factors for HA-PTE patients, the archived medical records of local patients hospitalized in Taizhou Hospital of Zhejiang Province in the past three years were selected for statistical analysis.

# 2. Materials and Methods

## 2.1. Subjects Who Were Investigated

### 2.1.1. Subjects

Patients were selected on January 1, 2020, to December 31, 2022, at the Research Center. Patients younger than 14 years (including pediatric surgery, pediatric medicine and neonatology patients, among others) were excluded, and day ward patients were found to meet the exclusion criteria.

### 2.1.2. Inclusion Criteria

(i) Patients at least 14 years of age;

(ii) Confirmation of PTE events via CT pulmonary angiography (CTPA), magnetic resonance pulmonary angiography (MRPA), pulmonary ventilation/perfusion (V/Q) imaging, or pulmonary angiography.

### 2.1.3. Exclusion Criteria

(i) Patients with chronic PTE (PTE diagnosis for more than 1 month);

(ii) Patients who were hospitalized within 90 days prior to admission and who had confirmed PTE during the previous hospitalization;

(iii) This study collected only archived data and did not involve patient consent; thus, no cases were excluded due to refusal to provide informed consent.

(iv) Outcome: death and non-healing were considered as adverse outcomes, whereas transfer to hospital and home treatment were not considered as adverse outcomes.

## 2.2. Methods

### 2.2.1. Group Method

Patients who experienced new PTE events during hospitalization or within 90 days of the previous admission (excluding those patients diagnosed with PTE after their previous admission) were included in the HA-PTE group. The remaining PTE patients, who had no medical or surgical hospitalization within 90 days prior to admission were included in the CA-PTE group,

### 2.2.2. Data Collection

Basic Information on the patients, underlying diseases, clinical manifestations and related risk factors were exported and recorded in the medical record room and the Hi-His system of the Research Center. Moreover, information on laboratory examinations, imaging examinations and outcome events were collected.

### 2.2.3. Indicator Analysis

Basic data, including clinical manifestations, risk factors, outcome events, and other data, were compared between the two groups.

### 2.2.4. Statistical Methods

Statistical analysis was performed by using SPSS28.0 software. Count data are expressed as percentage (%) and were compared between two groups by using the $X^2$ test, which was calculated with the correction chi-square test formula when $1 \leq T\ min \leq 5$, $N \geq 40$. The Fisher's exact test was used when T min <1 or N <40. The normally distributed data are expressed by $\overline{X} \pm S$, and the independent sample t test was used to compare two groups; additionally, non-normally distributed data are expressed as M (Q1, Q3), and the rank-sum test was used for comparison between two groups. P-values less than 0.05 were considered to indicate statistical significance.

# 3. Results

## 3.1. General Data

A total of 513 patients with acute PTE were included after the exclusion criteria were applied. A total of 134 patients were in the HA-PTE group. In this cohort, 64 patients experienced PTE during hospitalization, and 70 patients experienced PTE within 90 days after the last admission. The other 379 patients, excluding patients with existing pulmonary embolism during the previous hospitalization, were in the CA-PTE group. There were no significant differences in sex, age or type of PTE diagnosis between the two groups (P> 0.05) (Figure 1).

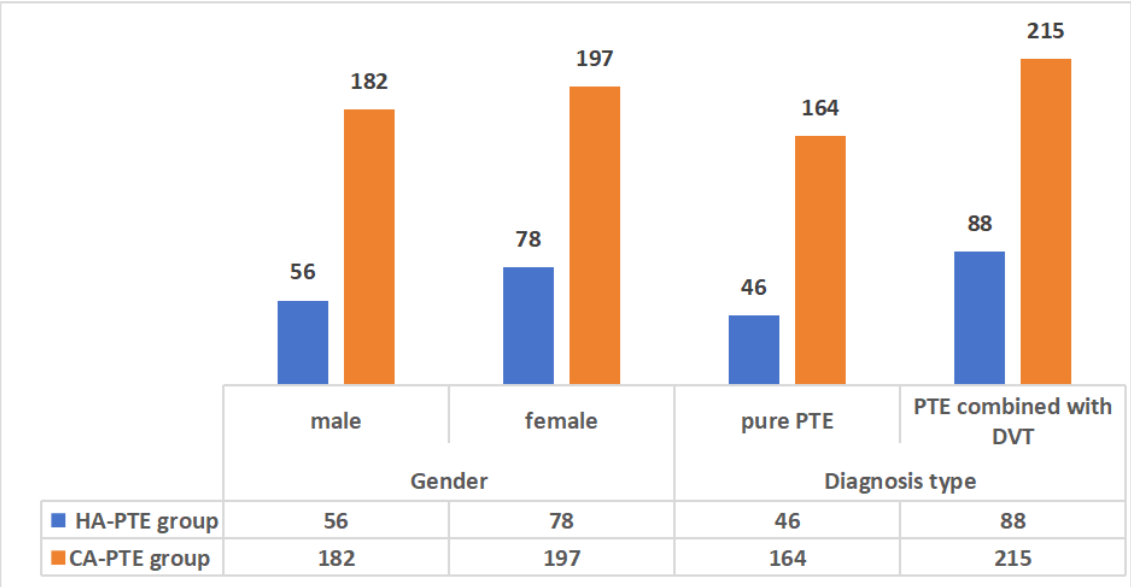



***Figure 1.*** *Comparison of general clinical data of the two groups.*

## 3.2. Clinical Features

The incidence of dyspnea and/or hemoptysis in the HA-PTE group was lower than that in the CA-PTE group (P< 0.05), but the incidence of fever and chest pain was greater than that in the CA-PTE group (P< 0.05). The incidence of lower limb pain was lower in the HA-PTE group than that in the CA-PTE group, but it was not statistically significant (P> 0.05). The incidence of lower extremity edema was greater in the HA-PTE group, however, the difference was not significant (P> 0.05). While tachycardia and hypoxia are commonly associated with pulmonary thromboembolism (PTE), we did not focus on them as distinguishing features in this study. (Table 1).

***Table 1.*** *Comparison of clinical features between the two groups [Case (%)].*

| Clinical manifestation | HA-PTE group | CA-PTE group | P |
|---|---|---|---|
| Dyspnea or hemoptysis | 49 (36.57%) | 216 (56.99%) | <0.01* |
| Lower limb pain | 7 (5.22%) | 41 (10.82%) | 0.056* |
| Edema of lower extremity | 62 (46.27%) | 145 (38.26%) | 0.104* |
| Chest pain | 15 (11.19%) | 10 (2.64%) | <0.01* |
| Fever | 53 (39.55%) | 108 (28.50%) | 0.018* |

Note: * calculated with Chi-square test formula

## 3.3. Risk Factors

Significant risk factors observed in the hospital-acquired pulmonary thromboembolism (HA-PTE) group included prolonged bed rest (bedridden for more than 1 month), active malignancies, acute cerebral infarctions, fractures, and lung infections (P < 0.05). Conversely, recent surgery (within one month post-operation) and central venous catheterization emerged as independent risk factors for PTE events during hospitalization, with incidences of 32.83% and 23.13%, respectively, in the HA-PTE group. These two risk factors were absent in the CA-PTE group, thus considered as independent risk factors during the study period. Varicosity and sedentary behavior (sitting for more than 2 hours at a time or 8 hours in a day) were slightly less prevalent in the HA-PTE group compared to the CA-PTE group; however, the difference between the two groups was not statistically significant (P > 0.05). (Table 2).

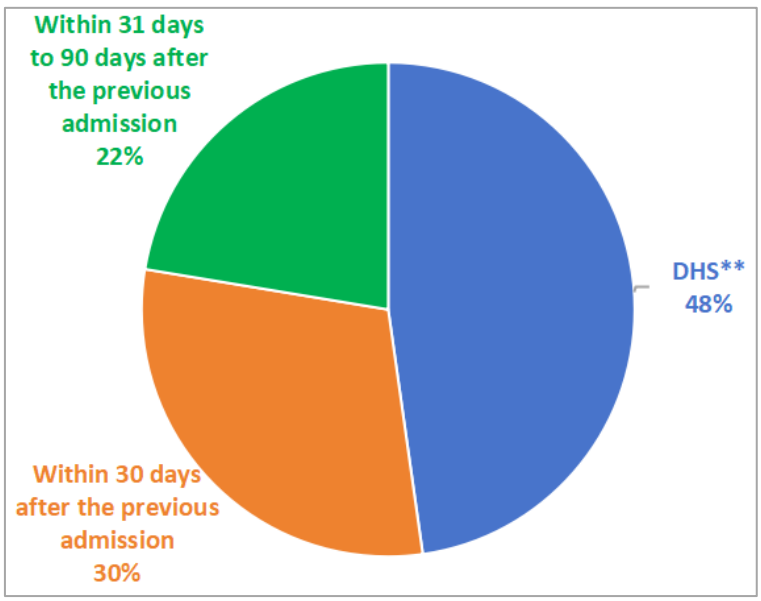
*Table 2. Comparison of the two groups of risk factors [case (%)].*

| Risk factor | HA-PTE group | CA-PTE group | P |
|---|---|---|---|
| Long-term lying in bed | 78 (58.21%) | 30 (7.92%) | <0.01 |
| Active malignancy | 54 (40.30%) | 77 (20.32%) | <0.01 |
| Acute cerebral infarction | 25 (18.66%) | 31 (8.18%) | <0.01 |
| Pulmonary infection | 41 (30.60%) | 76 (20.05%) | 0.020 |
| Recent surgery (in less than 1 month after surgery) | 44 (32.83%) | 0 (0.00%) | -* |
| Fracture | 32 (23.88%) | 27 (7.12%) | <0.01 |
| Central venous catheterization | 31 (23.13%) | 0 (0.00%) | -* |
| Varicosity | 8 (5.97%) | 31 (8.18%) | 0.407 |
| Sedentary sitting | 15 (11.19%) | 45 (11.87%) | 0.833 |

Note: * calculated with Fisher's exact test

## 3.4. Occurring Time of HA-PTE

In the HA- PTE group, 64 PTE events occurred during the hospital day (Due to limited data availability, we were unable to determine the average or mean number of days after admission. However, this aspect could be addressed in future studies to provide a more comprehensive understanding of the timeline of events related to pulmonary thromboembolism.), and 70 PTE events occurred within 90 days after the previous admission. Of the 70 patients with HA- PTE that developed after the previous admission, 40 patients had HA- PTE within 30 days after the previous admission, and the remaining 30 patients had HA-PTE within 31 days to 90 days after the previous admission. There was no difference between the two subgroups (HA- PTE occurred within 30 days after the previous admission and within 31 days to 90 days after the previous admission, respectively)(29.85% versus 22.39%, P> 0.05); however, the number of patients in both HA- PTE subgroups was significantly less than that in the PTE group which occurred during the hospitalization (P< 0.05) (Figure 2).




(Note: **DHS stands for during hospital stay)

*Figure 2. Occurrence time of HA-PTE.*

## 3.5. Department of Hospital Discharge

The hospital discharge departments of HA-PTE group patients included 19 departments. In the first 9 departments that had more PTE patients, 6 departments were involved in surgery. Three departments were involved in internal medicine (respiratory medicine, oncology, neurology). The CA-PTE group patients were discharged from 24 departments. In the first 11 departments that had more CA-PTE patients, 9 departments were involved in internal medicine. (Table 3).

*Table 3. PTE distribution of departments [case (%)].*

| Department | HA-PTE group | CA-PTE group | P |
|---|---|---|---|
| Respiratory Medicine | 53 (39.55%) | 230 (60.69%) | <0.01 |
| Cardiothoracic Surgery | 14 (10.45%) | 2 (0.53%) | <0.01** |
| Medical Oncology | 9 (6.72%) | 16 (4.22%) | 0.249 |
| Vascular Surgery | 8 (5.97%) | 50 (13.19%) | 0.023 |
| Orthopedics | 8 (5.97%) | 5 (1.32%) | <0.01 |
| Hepatobiliary and Pancreatic Surgery | 8 (5.97%) | 0 (0.00%) | -* |
| Neurology | 6 (4.48%) | 2 (0.53%) | <0.01** |
| Urinary Surgery | 6 (4.48%) | 2 (0.53%) | <0.01** |
| Neurosurgery | 5 (3.73%) | 2 (0.53%) | 0.02** |
| ED*** | 4 (2.99%) | 13 (3.43%) | 0.973** |
| Gynecology | 3 (2.24%) | 0 (0.00%) | -* |
| Rehabilitation | 2 (1.49%) | 3 (0.79%) | 0.842** |
| Hematology | 2 (1.49%) | 3 (0.79%) | 0.842** |
| Intensive Care Units | 1 (0.75%) | 11 (2.90%) | 0.277** |
| General Medicine | 1 (0.75%) | 7 (1.85%) | 0.632** |
| Cardiovascular Medicine | 1 (0.75%) | 8 (2.11%) | 0.519** |
| Radiotherapy | 1 (0.75%) | 5 (1.32%) | 0.950** |
| Gastroenterology | 1 (0.75%) | 5 (1.32%) | 0.950** |
| Infectious Disease | 1 (0.75%) | 1 (0.26%) | -* |
| Geriatric Medicine | 0 (0.00%) | 5 (1.32%) | -* |
| Special Needs Ward | 0 (0.00%) | 3 (0.79%) | -* |
| Nephrology | 0 (0.00%) | 2 (0.53%) | -* |
| other departments | 0 (0.00%) | 4 (1.06%) | -* |

Note: * is calculated with Fisher's exact probability method; ** is calculated with the corrected chi-square test; ***ED: Emergency Department

## 3.6. Comorbidity

### 3.6.1. Patients Combined with Venous Thrombosis

In the HA-PTE group, 88 patients had concurrent deep venous thrombosis, including 15 patients with inter-muscle venous thrombosis. In the CA-PTE group, 215 patients were complicated with intermuscular venous thrombosis. There were more HA-PTE-treated patients than the CA-PTE-treated patients; however, the difference was not significant (P> 0.05). The ratio of patients with inter-muscle venous thrombosis was significantly greater in the HA-PTE group than in the CA-PTE group (P< 0.05).

### 3.6.2. Patients with Inherited Thrombophilia or Antiphospholipid Antibody Syndrome

There were 7 patients combined with inherited thrombophilia and antiphospholipid antibody syndrome in the two

groups, all of which were clearly diagnosed in the respiratory medicine department of our hospital. Three inherited thrombophilia cases were confirmed in the HA-PTE group. Four antiphospholipid antibody syndrome cases were confirmed in the CA-PTE group. The rate of diagnosed inherited thrombophilia or antiphospholipid antibody syndrome in the HA-PTE group was higher than the CA-PTE group (2.24%: 1.06%), but no difference between the two groups (P> 0.05) (Table 4).

*Table 4. Occurrence of comorbidity [case (%)].*

| Comorbidity | HA-PTE group | CA-PTE group | P |
|---|---|---|---|
| deep venous thrombosis | 88 (65.67%) | 215 (56.73%) | 0.0703 |
| intermuscular Venous thrombosis | 15 (11.19%) | 15 (3.96%) | 0.002 |
| inherited thrombophilia/antiphospholipid antibody syndrome | 3 (2.24%) | 4 (1.06%) | 0.560* |

Note: * calculated with Correctional chi-square test

### 3.6.3. Patients with Malignant Tumors

In the HA-PTE cohort, 69 patients had confirmed active malignancy or cancer, 7 patients had a personal history of malignancy alone and 1 patient had elevated carcinoembryonic antigen (CEA) alone. In the CA-PTE cohort, 77 patients had confirmed active malignancy or carcinoma, 10 patients had a personal history of malignancy alone and 3 patients had elevated CEA alone. The rate of confirmed active malignancy or cancer was significantly greater in the HA-PTE group than in the CA-PTE group (51.49% versus 20.32%, respectively), with significant differences between groups (P< 0.01); however, the distribution of personal history of malignancy and elevated CEA alone in the two groups (all P> 0.05) (Table 5).

*Table 5. Distribution of malignant tumors and related medical history [Case (%)].*

| Kind of abnormal | HA-PTE group | CA-PTE group | P |
|---|---|---|---|
| Active malignancy or carcinoma | 69 (51.49%) | 77 (20.32%) | <0.01 |
| Personal history of the malignancy | 7 (5.22%) | 10 (2.64%) | 0.248 |
| Elevated CEA** alone | 1(0.75%) | 3 (0.79%) | 0.603* |

Note: * calculated with correctional chi-square test formula; **CEA stands for carcinoembryonic antigen

## 3.7. End-point Events

### 3.7.1. All-cause Mortality

During the study period, 7 patients with PTE died during hospitalization, and the all-cause mortality rate was 1.36%. There were 3 deaths in the HA-PTE group and 4 deaths in the CA-PTE group. All-cause mortality rate was greater in the HA-PTE group than that in the CA-PTE group (2.24%versus 1.06%, respectively); however, the difference was not significant (P> 0.05).

### 3.7.2. Poor Prognosis Rate

There were 3 patients died and 4 patients unhealed in the HA-PTE group. There were 4 deaths and 11 patients unhealed in the CA-PTE group. The poor prognosis rate in HA-PTE group was greater than that in CA-PTE group (5.22% versus 4.22%, respectively); however, there was no significant difference between the two groups (P> 0.05).

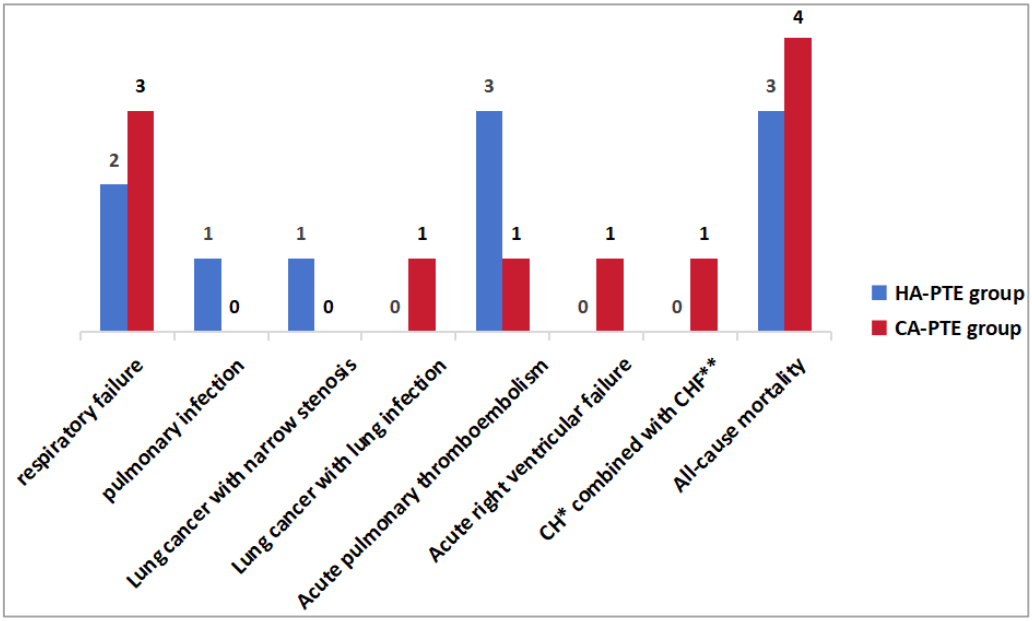
### 3.7.3. Subgroup Analysis of the HA-PTE Group

This study analyzed the number of deaths from new PTE occurring during hospitalization and within 90 days after discharge. one death occurred in the subgroup in which new PTE occurred during hospitalization, and 2 deaths occurred in the subgroup in which new PTE occurred within 90 days after discharge. The all-cause mortality rate of patients with new PTE occurred during hospitalization was lower than that of patients with new PTE occurred within 90 days after dis-

charge (1.56% versus 2.86%, respectively, P> 0.05).

### 3.8. Causes of Death

Three patients in HA-PTE group died during hospitalization, all of whom had PTE as the main cause of death; one patient had lung cancer with large airway stenosis, and 1 patient had lung infection. These two patients had respiratory failure. The causes of death in four patients with CA-PTE were lung cancer progression bound with lung infection, acute pulmonary embolism bound with obstructive shock, acute right heart failure, and cerebral hemorrhage bound with cerebral herniation, three of which were combined with respiratory failure. There were no significant differences in all-cause mortality, respiratory failure or acute pulmonary thromboembolism (P> 0.05). (Figure 3).




(Note: *CH stands for "Cerebral hemorrhage"; *CHF stands for "Cerebral herniation formation")

***Figure 3.*** *Cause of death.*

## 4. Discussion

Pulmonary thromboembolism (PTE) and deep vein thrombosis (DVT) are both venous thromboembolism (VTE) types. VTE is an important cause of unexpected death in hospitals and is also a preventable cause of disability. It is characterized by high morbidity, a high disability rate and high mortality, which seriously endangers patient safety [6]. This study demonstrated that the median age of individuals in both groups was 70 years, which is consistent with the previous perception that PTE is a disease that occurs mainly in the elderly population [7].

Multiple studies show that approximately 70% of all VTE events occur after hospital discharge [8, 9]. Spencer et al. [10] found that two-thirds of the HA-VTE events occurred during hospitalization and within 30 days after hospital discharge; moreover, one-third of the HA-VTE events occurred within 2-3 months after hospital discharge. This study demonstrated that the number of patients with new HA-PTEs during hospitalization was slightly less than that with new HA-PTEs occurring after hospital discharge; however, the incidence of HA-PTE occurring during hospitalization was lower than that occurring within 30 days and within 31days to 90 days after hospital discharge. This finding suggested that the hospitalization period was associated with a high incidence of HA-PTE, and our study indicated the risk of HA-PTE is still high within 90 days after hospital discharge. Moreover, hospitalization itself or iatrogenic factors might affect the incidence of HA-PTE, therefor, additional attention should be given to the influence of iatrogenic factors, especially the prevention and treatment of PTE in patients who undergo invasive operation. In this study, 77.61% of HA-PTEs occurred during hospitalization or within 30 days after the previous admission, which was higher than that reported in foreign studies. Due to the limitation of this study, in which only PTE was selected as the research object, further studies are needed to confirm the statistical results.

This study revealed that the prevalence of chest pain and fever was greater in the HA-PTE group than the CA-PTE group, whereas the incidence of dyspnea or hemoptysis was lower. As symptomatic indicators of HA-PTE, fever and chest pain should be focused on patients hospitalized during or within 90 days after hospital discharge. Dyspnea or hemoptysis may be the focus of screening for CA-PTE in the com-

munity. Lower limb edema and lower limb pain, as typical VTE clinical symptoms, can be used as a beneficial clue for PTE screening [11].

In this study, long-term lying in bed, active malignancy, acute cerebral infarction, lung infection, fracture, recent surgery and central venous catheterization were common risk factors in the HA-PTE group, whereas varicose vein and sedentary time were not significantly different between the two groups. Infection is a common exposure factor in hospitalized patients, and some studies have shown that respiratory tract infections are more strongly associated with VTE than non-respiratory tract infections [12, 13]. In this study, it was also found that the proportion of pulmonary infections in both groups was great, and the proportion of pulmonary infections was greater in HA-PTE group. Therefore, special attention should be given to the risk of PTE in pulmonary infections in these hospitalized patients, and measures should be taken to identify the diagnosis of PTE or to prevent the occurrence of PTE. Studies have shown that sedentary sitting is a risk factor for VTE in the general population [14]. This study demonstrated that the proportion of sedentary sitting patients was more than 11% of all PTE patients, thus suggesting that PTE screening should be performed in such populations. In addition, excessive exercise should also be prevented because high-intensity exercise injury can also induce PTE [15]; this phenomenon was not observed in the present study.

Multiple studies have suggested that 1 in 4 patients with HA-VTE have malignancies [16]. This study demonstrated that more than half of the patients in the HA-PTE group had active malignancies; this number was much greater than that in foreign countries and significantly greater than that in the CA-PTE group. This finding suggested a greater tendency for HA-PTE findings in patients with active malignancies. This study demonstrated that the proportion of active malignancy patients in the CA-PTE group was greater than that in HA-PTE group, but the difference between the groups was not significant, thus suggesting that these patients may not be an independent risk factors for HA-PTE. These findings need to be further confirmed by subsequent studies. Other studies have shown that the occurrence of PTE is related to the secondary susceptibility to nephrotic syndrome [17, 18]. The sample in this study was relatively small, and no cases of PTE in nephrotic syndrome were found.

This study demonstrated that most patients in the HA-PTE group were from the surgical system, whereas most patients in the CA-PTE group were from the internal medical system. This study suggests that the occurrence of HA-PTE is mostly related to trauma, fracture and surgery. These findings are consistent with the results of previous studies [19]. The distribution pattern of discharged patients in the CA-PTE cohort suggested that the occurrence of PTE was related to infection, physical factors and genetic factors (such as hereditary susceptibility). Due to the fact that most patients in both groups were discharged from the respiratory medicine department (which indicates that the occurrence of PTE is related to pulmonary infection and chronic lung disease), we should be aware of the possibility of PTE onset in winter and spring. This was consistent with the opinions of Perincek et al. [20].

In all of the patients in the two groups, all-cause mortality in the HA-PTE group is more than the CA-PTE group; however, the difference was not significant and failed to suggest a greater risk of death from HA-PTE, which was inconsistent with the findings of previous study [21]. Subgroup analysis also demonstrated no significant differences between the two subgroups during hospitalization or after discharge. Due to the sample size, the conclusion that HA-PTE had a greater risk of all-cause death after discharge cannot be denied. Although this study failed to conclude that HA-PTE patients are at high risk of death, additional attention should be given to the prevention and treatment of HA-PTE.

## 5. Conclusion

Overall, this study indicated that inpatients (especially those who underwent invasive procedures or surgery) are at high risk of PTE, whether during hospitalization or within 90 days after discharge. Clinicians should assess the VTE risk of patients during hospitalization and after discharge. DVT prophylaxis is a routine in the hospital and nearly half of these patients were given medical or pharmacological prophylaxis. This study suggests standardized preventive measures, early detection, early diagnosis and early treatment may effectively reduce the incidence and mortality of PTE and benefit patients. We hope that our future studies can provide further data to answer this question.

## Abbreviations

| | |
|---|---|
| VTE | Venous Thromboembolism |
| PTE | Pulmonary Thromboembolism |
| HA-PTE | Hospital-Associated Pulmonary Thromboembolism |
| CA-PTE | Community-Associated PTE |
| NS | Nephropathy Syndrome |
| CEA | Carcinoembryonic Antigen |
| CH | Cerebral Hemorrhage |
| CHF | Cerebral Herniation Formation |
| ED | Emergency Department |

## Conflicts of Interest

There is no conflict of interest to any person or organization. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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