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# Waiting Time Outside the Hospital May be a Risk Factor for Preoperative Deep Venous Thrombosis in Elderly Patients with Hip Fracture

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**ABSTRACT**

**Objective:** To investigate the incidence and risk factors of preoperative deep vein thrombosis (DVT) in elderly patients with hip fractures (age ≥ 65 years).

**Methods:** The clinical data of 372 hip fracture patients over 65 years old who underwent surgery were retrospectively analyzed. Patients were divided into venous thrombosis group and non-venous thrombosis group. Logistic analysis was used to analyze the relationship between preoperative deep venous thrombosis and the possible factors.

**Results:** Logistic analysis displayed that waiting time outside the hospital (WTOH) was the unique and independent risk factor for DVT in elderly patients with hip fracture (OR=1.22, 95% CI=1.05-1.41, p=0.02). Furthermore, ROC curve was applied to detect the prediction effect of WTOH on DVT occurrence, and the area under the curve was 0.66, 95% CI (0.56-0.76). The critical value was 4.5 days, and the sensitivity and specificity were 50% and 78.4%, respectively. Moreover, WTOH was divided into three layers (WTOH≤24 hours, 24 hours<WTOH≤4.5 days, WTOH>4.5 days), and the incidence of preoperative DVT was 5.4% vs 5.7% vs 15.9% respectively.

**Conclusion:** WTOH was an independent risk factor for preoperative DVT occurrence in elderly patients with hip fracture. When WTOH exceeded 4.5 days, the incidence of DVT was significantly increased.

**Keywords:** Elderly; Hip fracture; Deep Vein Thrombosis (DVT); Waiting Time Outside the Hospital (WTOH)

**Abbreviations:** DVT: Deep Vein Thrombosis; PE: Pulmonary Embolism; VTE: Venous Thromboembolism; IVC: Inferior Vena Cava; WTOH: Waiting Time Outside the Hospital; COPD: Chronic Obstructive Pulmonary Disease; CR: Coefficient Regression; CHD: Coronary Heart Disease

## Introduction

With the prolongation of life expectancy and the increasing number of elderly people, the health problem of the elderly had become a global challenge. Hip fracture is one of the most common accidents in old people, it has become a key factor affecting the health of the elderly because of its serious adverse complications and high mortality [1]. Evidence showed that the incidence of hip fractures in the elderly to be steady, or even to decline, in developed countries and developed regions, on the contrary, in developing areas, such as Asia and Africa, the rate was continuing rising [2]. As the largest developing country, there were exceeded 150 million elderly people over 65 years old in China, the risk of hip fractures in these individuals' will bring huge medical pressure to society. Deep vein thrombosis (DVT) was

a serious complication of hip fracture, which is closely cared by surgeons owing to its adverse events such as pulmonary embolism(PE) and postoperative death [3]. Studies showed that venous thromboembolism (VTE) was responsible for the hospitalization of >250000 Americans annually, PE caused the third death from cardiovascular disease after heart attack and stroke [4,5]. The highest incidence of thrombosis with hip fracture was 61% in hospital [6], and the rate was five times out hospital [7]. Older, surgery delay and anesthesia etc. will increase the risk of postoperative DVT [8]. The high incidence and bad effect of postoperative DVT had been concerned by clinicians. However, as harmful as postoperative DVT, a few studies reported the incidence of preoperative DVT and it may be underestimated [9]. This retrospective study investigated the incidence and risk factors of preoperative DVT in elderly patients with hip fractures.

## Method

### Patients

This retrospective study was approved by the ethics committee of our institution (Xijing hospital, Fourth Military Medical University, Xi'an, China). Patients aged at least 65 years with hip fracture (femoral neck fractures and intertrochanteric fractures) caused by low energy injury were considered for inclusion. Exclusive criteria were as follows: traffic accidents, falling from high place, violence and other high-energy injuries caused fractures, bone neoplasms or bone metastases and other secondary fractures, multiple fractures, previous history of venous thromboembolism, anticoagulant treatments, incomplete imaging or laboratory test results. Finally, 372 consecutive patients were recruited for this study from January 1, 2017 to December 31, 2021.All patients received a bilateral color Doppler ultrasound examination 1 day before operation. Colour Doppler ultrasonography was conducted by experienced sonographer. All results of the ultrasonography were reviewed by senior ultrasonologist. The diagnostic criteria were in accordance with the Robinov group's criteria. DVTs were classified into 3 types: central, peripheral, and both central and peripheral thrombosis. According to the results of ultrasonography, patients were divided into deep venous thrombosis group (DVT group) and non-deep venous thrombosis group (non-DVT group). All the patients were assessed using the Caprini score for thromboembolism risk, and also evaluated the blood risk.

For patients without anticoagulation contraindications were treated with Rivaroxaban (10mg, once a day, Bayer Pharma AG Production, Germany) to prevent DVT. In addition, mechanical thrombo-prophylaxis (pressure pump, 20 min twice a day) was used. When ultrasonography results showed central or mixed thrombosis preoperatively, evaluation was performed by the department of vascular surgery and an inferior vena cava (IVC) filter was used to prevent fatal pulmonary embolism if needed. When patients were discharged, rivaroxaban 15mg once a day lasted until 35 days post operation. In order to understood the effect of preoperative waiting time on preoperative DVT, we divided the preoperative waiting time as follows: waiting time outside the hospital (WTOH) was from injury to admission, waiting time in hospital (WTIH) was from admission to operation, waiting time of preoperative (WTOP) was from injury to operation (waiting time outside the hospital and waiting time in hospital). As the same time, the clinical data obtained included age, sex, hypertension, diabetes, coronary heart disease, chronic kidney disease, chronic obstructive pulmonary disease (COPD), dementia, Parkinson's disease, tumor history and hemoglobin, total protein, albumin, globulin, the clinical characteristics were collected by clinicians who had received a standardized training. Statistical analysis was performed using SPSS 19.0 system software (SPSS Inc., Chicago, IL). Numeric variables were compared by Student t test and categorical variables were compared by the chi-square test.

A stepwise multiple logistic regression analysis was used to identify which independent variables contributed to the occurrence of DVT. Statistical variables were input in a logistic regression analysis to determine the coefficient regression (CR) of the independent variables. The DVT predictor value was calculated using a formula based on the coefficient regression and the independent variables. For all tests, $p < 0.05$ was considered statistically significant.

## Results

### Patient Characteristics and Univariate Analysis of preoperative Thrombosis

A total of 372 patients met the inclusion criteria, including 140 males and 232 females. The mean age was 78.9±7.4. Of the total patients, 124 individuals (33.3%) were occurred venous thrombosis (superficial vein thrombosis and deep vein thrombosis), and 34 patients (9.1%) developed DVT. All patients received standard anticoagulation after admission. Of the 34 patients with DVT, 23 individuals were underwent filter implantation before operation.

### Univariate Analysis of Preoperative Thrombosis

The results of univariate analysis showed that there were significant correlations between preoperative venous thrombosis and the factors of waiting time outside the hospital, waiting time of preoperative, hemoglobin, total protein and albumin ($P < 0.01$). While these factors of hypertension, diabetes, coronary heart disease, chronic kidney disease, chronic obstructive pulmonary disease, Parkinson's disease, tumor history, waiting time in hospital, lymphocyte globulin, etc. had no obvious effect on preoperative venous thrombosis (Table 1).

**Table 1:** Univariate analysis of preoperative thrombosis factors.

| | VT Group N=124 | Non-VT Group N=248 | X2/t Value | P Value |
|---|---|---|---|---|
| Age (x± SD) | 78.6 ± 7.4 | 79.147.4 | 0.57 | 0.57 |
| Sex<br>Male<br>Female | 46 (37.1%)<br>78 (62.9%) | 94 (37.9%)<br>154 (62.1%) | 0.02 | 0.88 |
| Hypertension (%) | 49 (39.5%) | 100 (40.3%) | 0.02 | 0.88 |
| Diabetes (%) | 22 (17.7%) | 50 (20.2%) | 0.31 | 0.58 |
| CHD (%) | 17 (13.7%) | 50 (20.2%) | 2.33 | 0.13 |
| Heart failure (%) | 2 (1.6%) | 2 (0.8%) | | 0.60* |
| Stroke (%) | 24 (19.4%) | 54 (21.8%) | 0.29 | 0.59 |
| Cancer (%) | 5 (4.0%) | 9 (3.6%) | | 1* |
| Renal diseases (%) | 4 (3.2%) | 2 (0.8%) | | 0.10* |
| COPD (%) | 8 (6.5%) | 16 (6.5%) | 0.00 | 1.00 |
| Dementia (%) | 5 (4.0%) | 8 (3.2%) | | 0.77* |
| Parkinson (%) | 4 (3.2%) | 6 (2.4%) | | 0.74* |
| Waiting time outside the hospital (day) | 4.6 ± 5.7 | 3.0+4.2 | -2.84 | <0.01 |
| Waiting time in hospital (day) | 3.3 ± 2.2 | 3.3 ± 2.7 | -0.14 | 0.89 |
| Waiting time of Preoperative (day) | 7.9 ± 5.7 | 6.1 ± 5.2 | -3.12 | <0.01 |
| Hemoglobin (g/L) | 108 ± 21 | 116 ± 21 | 3.41 | <0.01 |
| Lymphocyte (g/L) | 1.0 ± 0.4 | 11 ± 0.6 | 1.66 | 0.10 |
| TP (g/L) | 61.4 ± 6.8 | 64.1 ± 6.8 | 3.62 | <0.01 |
| ALB (g/L) | 34.5 ± 3.9 | 36.7 ± 4.3 | 4.69 | <0.01 |
| Globulin (g/L) | 26.8 ± 4.7 | 27.4 ± 4.8 | 1.15 | 0.61 |
| A/G | 1.3 ± 0.3 | 1.4 ± 0.3 | 1.46 | 0.15 |

Note: *Fisher exact test; CHD coronary heart disease; COPD Chronic obstructive pulmonary disease

TP: Total protein; ALB: Albumin; A/G: Albumin/Globulin

## Multivariate Analysis with Preoperative Venous Thrombosis

Logistic regression analysis displayed that the correlation was disappeared between these factors and preoperative DVT (Table 2 & Figure 1).

**Table 2:** Multivariate analysis of preoperative venous thrombosis.

| Risk factor | OR | 95% CI | P Value |
|---|---|---|---|
| Waiting time outside the hospital (day) | 1.05 | 0.94-1.17 | 0.37 |
| Waiting time of Preoperative (day) | 1.01 | 0.92-1.11 | 0.77 |
| Hemoglobin (g/L) | 0.99 | 0.98-1.00 | 0.17 |
| TP (g/L) | 0.98 | 0.93-1.03 | 0.35 |
| ALB (g/L) | 0.95 | 0.86-1.03 | 0.21 |

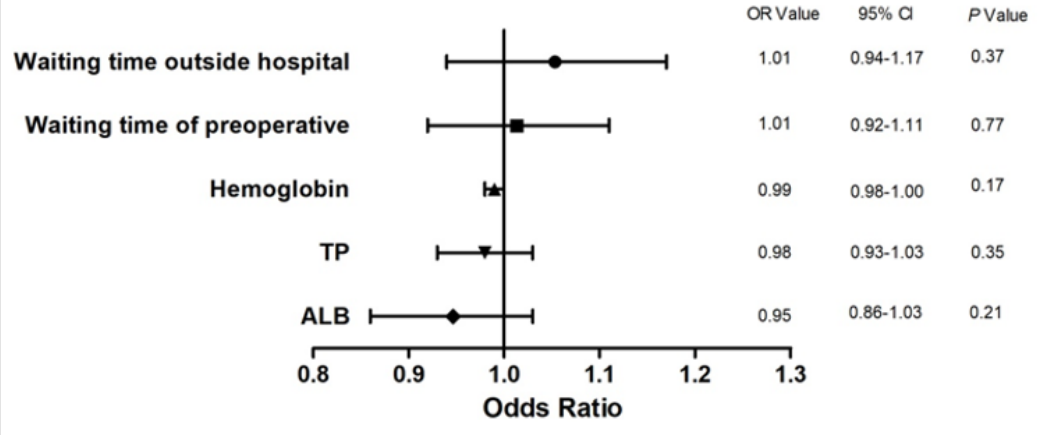


**Figure 1:** Multivariate analysis of preoperative venous thrombosis.

## Risk Factors of Preoperative DVT

Eliminated superficial vein thrombosis and analyzed risk factors of preoperative DVT. Outcomes exhibited that waiting time outside the hospital, waiting time of preoperative and coronary heart disease (CHD) were closely related to preoperative DVT. Hypertension, diabetes mellitus, chronic nephropathy, chronic obstructive pulmonary disease, dementia, Parkinson's disease, tumor history, waiting time in hospital, hemoglobin, lymphocyte, total protein, albumin, globulin had no clearly effect on DVT (Table 3). Logistic regression analysis showed that only waiting time outside the hospital was closely association with preoperative DVT ($p < 0.05$) (Table 4).

**Table 3:** Risk factors for preoperative deep venous thrombosis.

| | DVT Group N=34 | Non-DVT group N=338 | X2/t value | P value |
|---|---|---|---|---|
| Age (x± SD) | 77.6±7.4 | 79.0±7.4 | 0.57 | 0.57 |
| Sex<br>male<br>female | 16 (47.1%)<br>18 (52.9%) | 124 (36.7%)<br>214 (63.3%) | 1.42 | 0.23 |
| Hypertension (%) | 16 (47.1%) | 133 (39.3%) | 0.77 | 0.38 |
| Diabetes (%) | 6 (17.6%) | 66 (19.5%) | 0.07 | 0.79 |
| CHD (%) | 0 (0.00%) | 67 (19.8%) | 8.22 | <0.01 |
| Heart failure (%) | 1 (2.9%) | 3 (0.9%) | | 0.32* |
| Stroke (%) | 5 (14.7%) | 73 (21.6%) | 0.89 | 0.35 |
| Cancer (%) | 2 (5.9%) | 12 (3.6%) | | 0.37* |
| Renal diseases (%) | 2 (5.9%) | 4 (1.2%) | | 0.10* |
| COPD (%) | 4 (11.8%) | 20 (5.9%) | | 0.26* |
| Dementia(%) | 1 (2.9%) | 12 (3.6%) | | 1.00* |
| Waiting time outside the hospital (day) | 7.0 ± 7.9 | 3.2 ± 4.2 | -2.80 | <0.01 |
| Waiting time in hospital (day) | 2.7 ± 2.1 | 3.4 ± 2.5 | 1.46 | 0.14 |
| Waiting time of Preoperative (day) | 9.7 ± 7.4 | 6.4 ± 5.2 | -2.58 | 0.01 |
| Hemoglobin (g/L) | 111 ± 18 | 113 ± 22 | 0.64 | 0.53 |
| Lymphocyte (g/L) | 1.0 ± 0.4 | 1.1 ± 0.5 | 0.74 | 0.46 |

| | | | | |
|---|---|---|---|---|
| TP (g/L) | 61.7 ± 6.7 | 63.4 ± 6.9 | 1.32 | 0.19 |
| ALB (g/L) | 35.0 ± 3.9 | 36.0 ± 4.3 | 1.33 | 0.18 |
| Globulin (g/L) | 26.7 ± 4.6 | 27.3 ± 48 | 0.67 | 0.50 |
| A/G | 1.3 ± 0.2 | 1.4 ± 0.3 | 0.41 | 0.68 |

Note: *Fisher exact test; CHD, coronary heart disease; COPD Chronic obstructive pulmonary disease

TP: Total protein; ALB: Albumin; A/G: Albumin/Globulin

**Table 4:** Logistics regression analysis of risk factors for preoperative deep venous thrombosis.

| Risk factor | OR | 95% CI | P Value |
|---|---|---|---|
| Waiting time outside the hospital (day) | 1.21 | 1.03-1.40 | 0.02 |
| Waiting time of Preoperative (day) | 0.93 | 0.81-1.07 | 0.30 |
| CHD | 1.90 | - | 0.99 |

## Receiver Operating Characteristic Curve (ROC) of Waiting Time Outside the Hospital in Patients with Hip Fracture

A receiver operating characteristic curve (ROC curve) was used to examine the ability of cut off values to identify diseases. It was used to test the predictive effect of waiting time outside the hospital on DVT. Results displayed that the area under the curve was 0.66, 95% CI (0.56-0.76), the cut off value was 4.5 days, and the sensitivity and specificity were 50% and 78.4%, respectively (Figure 2 & Table 5).

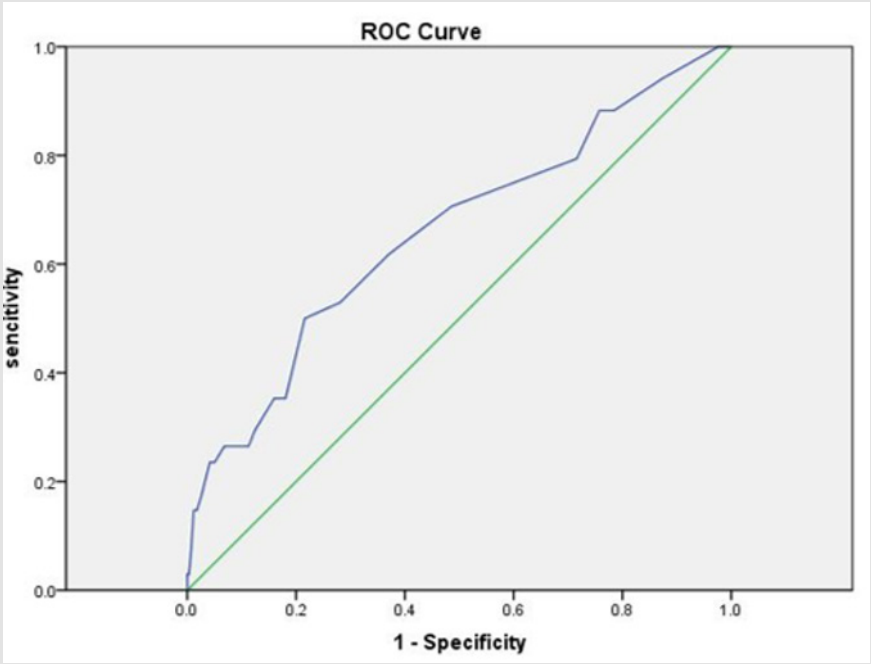


**Figure 2:** ROC of waiting time outside the hospital.

**Table 5:** Cut off value of ROC.

| | OR | 95% CI | P Value | Cut- off value | Sencitivity | Specificity |
|---|---|---|---|---|---|---|
| Waiting time outside the hospital (day) | 1.21 | 1.03-1.40 | 0.02 | 4.5 | 0.50 | 0.78 |
| Waiting time of Preoperative (day) | 0.93 | 0.81-1.07 | 0.30 | | | |

### Effect of Waiting Time Outside the Hospital on The Incidence of Thrombosis

According to the ROC outcomes, waiting time outside the hospital was divided into three layers (< 24 hours; ≤4.5 days; > 4.5 days). The results revealed that the incidence of thrombosis was 5.4% VS 5.7% VS 15.9% in different time periods (Figure 3).

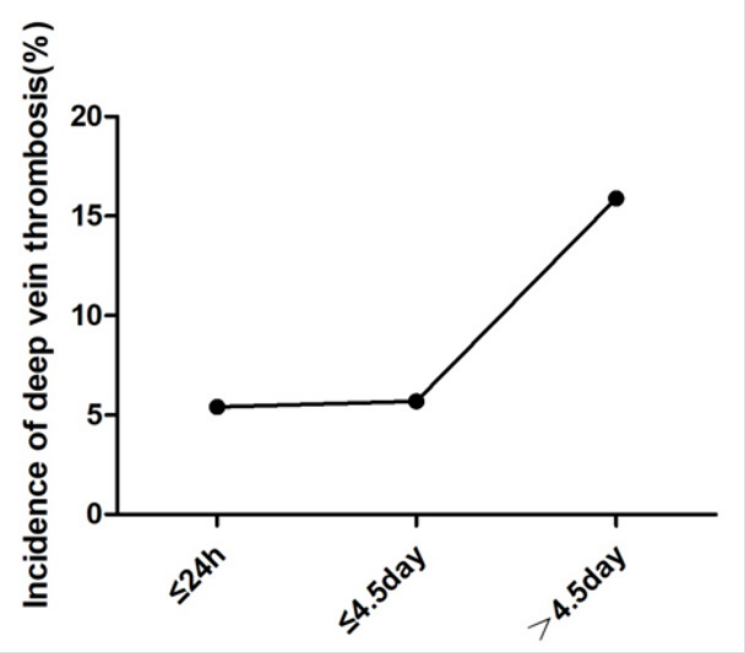


**Figure 3:** Trend of incidence of deep venous thrombosis with pre-hospital waiting time.

## Discussion

Deep vein thrombosis (DVT) is one of the most common complications of hip fracture in elderly. Previous studies on DVT of fracture were mainly focused on postoperative. However, it did not receive enough attention of preoperative DVT, despite it also led to poor prognosis and high mortality . Our results showed that the overall incidence of preoperative venous thrombosis and deep venous thrombosis was 33.3% and 9.1% in elderly patients with hip fractures. Univariate analysis displayed that waiting time outside the hospital, waiting time of preoperative, hemoglobin level, total protein and albumin level were significantly correlated with preoperative venous thrombosis (Table 1), and the association disappeared after logistic regression analysis (Table 2 & Figure 1). Eliminated patients with superficial vein thrombosis and multivariate analysis illustrated that only waiting time outside the hospital was an independent risk factor for preoperative DVT. ROC curve explained that the cut value of waiting time outside the hospital for preoperative DVT was 4.5 days, exceeded 4.5 days, the incidence of preoperative DVT was significantly increased (Figure 3). The pathogenesis of post-fracture DVT was a complex process. Many studies had shown that DVT of fracture influenced by internal and external factors [10,11]. Virchow's triad of thrombosis includes vascular endothelial injury, slow blood flow and increased blood viscosity.

Because of trauma, fixation and blood concentration, patients with hip fracture had all the conditions for thrombosis happened. Researchers found that age, preoperative waiting time, chronic kidney disease, and history of venous thrombosis were risk factors for deep venous thrombosis in hip fractures [9]. Studies had also revealed that the risk of vein thrombosis increases 14.5% when operation delayed

one day [12]. It was reported that the medical history of hypertension, diabetes, chronic obstructive pulmonary disease, and etc. factors were considered as risk factors for post-operative deep venous thrombosis [9,13]. Interestingly, none of those factors associated with preoperative DVT in our findings (Table 3), it was possible that a larger sample study need conducted or there were no correlation between these factors and preoperative DVT indeed. Our results were consistent with previous studies that preoperative waiting time was a risk factor for preoperative DVT occurrence [9,14]. Differently, we first divided waiting time of preoperative into waiting time outside the hospital (WTOH) and waiting time in hospital. Findings suggested that only WTOH was an independent risk factor for preoperative DVT. The possible reasons of the results were that all of the patients received standard anticoagulation and professional guidance after admission.

Perioperative DVT could lead to chronic pain, ulceration, what's worse, it was caused surgery delay and filter implantation, even pulmonary vein embolism [15]. It was reported that the incidence of preoperative DVT varies greatly among different countries [16,17]. Young-Ho Cho found that the incidence was 2.6% in Korea, and the earlier operation, the lower DVT rate [17]. A study conducted in British showed that the incidence of preoperative DVT was 62% in hip fracture patients [16]. Research from China revealed that the incidence of preoperative DVT was from 29.4% to 34.9% [9,14]. Although the incidence of preoperative DVT was varied in different countries and regions, there were common features that preoperative waiting time was the main risk factor for DVT. Lectures reported that the risk of deep venous thrombosis after fracture would obviously increase if preoperative waiting time exceeded 48 hours [18], when delayed 72 hours, the incidence raised significantly [17]. However, it was difficult for Chinese patients who received operation within 72 hours after fracture. Due to poor health awareness, shortage of medical staff, and more complications, patients in developing countries such as China were often unable to receive surgery within 72 hours. Therefore, we divided preoperative waiting time into outside the hospital and in hospital, and explored its correlation with DVT. We hoped to optimize the treatment process, easy for early therapy, finally improve the prognosis of elderly patients with hip fracture through this study. In our study, multivariate analysis showed that waiting time outside the hospital was an independent risk factor for DVT, and ROC curve was conducted to test its predictive effect. Results revealed that 4.5 days was the appropriate cut off value. Compared with previous studies, this waiting time was longer, and sensitivity only 50%. The results were not perfect, which may be due to the sample size too small, and then, the research center is the best medical institution in our region, mainly treatment of critically patients, consequently, there maybe existed selection bias. Therefore, the result of our findings could be used as a reference for the critically patients DVT occurrence. Of course, this study also had some limitations. The data were from a single center, which was not representative enough. The color Doppler ultrasound examination was not operated by a designated doctor or the same machine, so there may be errors. The results of the retrospective study needed further verification.

## Conclusion

Our results suggested that waiting time outside the hospital was an independent risk factor for preoperative DVT, and 4.5 days was a reasonable predictor. The incidence of thrombosis was significantly increased when waiting time exceeded 4.5 days. Therefore, we suggested that patients with fractures should be sent to hospital as soon as possible after injury and the waiting time outside the hospital should be shortened within 4.5 days in order to reduce the risk of preoperative DVT.

## Conflict of Interest

There is no conflict of interest between all authors.

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