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The Correlation Between Preoperative Lower Extremity Deep Vein Thrombosis (DVT) and the Time from Injury to Surgery (TFITS)

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Abstract

Objective: To investigate the correlation between preoperative DVT and the time from injury to surgery (TFITS), and provide a clinical reference for the prevention of preoperative DVT.

Patients and methods: We collected the clinical data of patients with lower extremities fractures between September 1, 2014, and May 31, 2019. Doppler ultrasonography was used to diagnose DVT. Patients were divided into the 0-2d group, 3-4d group, 5-7d group, and >7d group according to TFITS. The correlation between TFITS and preoperative DVT was assessed using logistic regression according to the adjusted model.

Result: A total of 2831 patients were included in the study. The mean（+/-SD） TFITS was 6.11 ± 3.76 (0 to 21 d). A total of 821 (29.0%) cases had preoperative DVT, with the incidence of DVT being 8.0% in the 0-2d group, 23.8% in the 3-4d group, 32.0% in the 5-7d group, and 36.2% in the >7d group, with statistically significant differences(P＜0.05) among all the groups. The incidence of preoperative DVT increased with prolonged preoperative time. In the fully adjusted model, TFITS was positively correlated with the incidence of preoperative DVT (OR: 1.093; 95% CI: 1.068-1.118; P = 0.000), and the strength of the association increased with increasing time.

Conclusion: TFITS was an independent risk factor on the incidence of preoperative DVT. After excluding the effect of other factors, each 1d increases in TFITS was correlated with a 9.3% increase in the risk of preoperative DVT. The TFITS should be decreased to reduce the risk of preoperative DVT.

Keywords

deep vein thrombosis, time from injury to surgery, fracture, risk factor

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Introduction

Deep vein thrombosis (DVT) of the lower extremities is a common complication in trauma patients. The incidence of DVT after trauma was reported to be approximately 9.1% to 11.1%.[1,2] DVT can result from the stagnation of blood in the lower extremities by the pain and subsequent immobility due to fracture,[3] the hypercoagulability state induced by blood loss secondary to the fracture and the body's inflammatory immune response.[4] Deep vein thrombosis can lead to chronic pain, secondary varicose veins, or ulcers, which seriously affect patients' quality of life. Fatal pulmonary embolism can also occur in some cases.[5] In recent years, orthopaedists have paid increasing attention to the prophylaxis of DVT.

A 6–9% incidence of preoperative DVT has been reported in patients receiving surgery within 48h.[6,7] Delay in surgical care for patients due to acute trauma, whereas the rate raised to 54.5–62% when there was a delay for more than 48h.[7,8]

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Takaomi's report[9] found that a longer time from injury to admission and from injury to surgery significantly correlated with a high DVT risk. Song[10] identified that long-time immobilization increased the risk of preoperative DVT. A longer TFITS had been reported to be a relevant factor even for patients who are undergoing antithrombotic prophylaxis during their hospital stay.[11–13] Therefore, preoperative prevention and management of DVT were likely to reduce the incidence of DVT.

TFITS can be reduced by the management during hospitalization. Previous literature has limited research on preoperative time, and the correlation between TFITS and the risk factor of preoperative DVT occurrence is still uncertain. Therefore, in this study, we perform a retrospective study on patients with lower extremity fractures, analyze the incidence of DVT in different TFITS groups. We want to discover the correlation between the preoperative DVT incidence and the increasing preoperative time by the adjust model, hoping that it can serve as a reference for the prevention of preoperative DVT in clinical work.

Methods

Ethics Statement

This study analyzed the data of patients with lower extremity fractures admitted to the Honghui Hospital of Xi'an Jiaotong University from September 1, 2014, to May 31, 2019. The study was approved by the Ethics Committee of Xi'an Jiaotong University.

Inclusion and Exclusion Criteria

Inclusion criteria: ① closed fractures of the lower extremities (including pelvic fractures, acetabular fractures, femoral neck fractures, intertrochanteric fractures, subtrochanteric fractures, femoral shaft fractures, distal femoral fractures, patellar fractures, tibial plateau fractures, tibia and fibula fractures, distal tibial fractures, ankle fractures, and foot fractures); ② fractures requiring surgical treatment; ③ age 16 years or older; ④ patients signed an informed consent form, were able to receive anticoagulation and could complete preoperative ultrasound and other relevant examinations.

Exclusion criteria: ① preoperative combination of lower limb vascular diseases; ② patients requiring anticoagulation therapy before injury; patients contraindicated to anticoagulation; ③ patients with combined serious medical or surgical diseases （injury of head, chest, abdomen, etc） that make patients unsuitable for surgery; ④ open fractures, old fractures (time between injury and surgery >21 d), patients requiring multiple surgeries such as bone nonunion and bone infection.

Treatment

All the patients who were admitted to the hospital were routinely assessed using the Risk Assessment Profile for Thromboembolism score for thromboembolism risk.[14] At the same time, we also assessed whether the patients had anticoagulation contraindications. For patients without anticoagulation contraindications, low-molecular-weight heparin (LMWH) (3800 IU/0.4 mL once per day, Fraxiparine; Glaxo Wellcome Production, GlaxoSmithKline) was subcutaneously injected to prevent DVT. Then, Doppler ultrasonography was performed to screen for DVT. The patients with DVT received subcutaneous injections of LMWH (3800 IU/0.4 mL, twice per day). The therapeutic anticoagulation protocol was guided by hospital consultation from the department of vascular surgery.

When the results of the preoperative ultrasonography performed by the department of vascular surgery showed central or mixed thrombosis, an inferior vena cava filter was used to prevent fatal pulmonary embolism if needed. The anticoagulant therapy was discontinued 12h before surgery and resumed 24h after surgery. In addition, mechanical thromboprophylaxis (foot intermittent pneumatic compression sleeve, 20min twice a day) was used. Blood samples were collected on admission (within 24h after admission). The aim testing indexes included D-dimer level, Hematocrit(Hct) level and Hemoglobin(HGB) level.

We used Doppler ultrasonography to diagnose DVT. Experienced ultrasonography radiologists who were blind to any laboratory results conducted the scanning on bilateral lower extremities. The diagnostic criteria were in accordance with the Robinov group's criteria,[15] which was confirmed based on the detection of venous lumen obstruction or filling defect. The DVT cases were classified into 3 types as follows: central (femoral and iliac veins), peripheral (calf muscle, fibular, and anterior/posterior tibial veins), and mixed thrombosis (both central and peripheral thromboses).

General information, TFITS, DVT diagnostic results, and laboratory test data were collected from all patients. Patients were divided into four groups of 0-2d, 3-4d, 5-7d, and >7d according to the time from injury to surgery.

Statistics Analyses

Statistical analysis was performed using the SPSS (Version 19.0, SPSS Inc., Chicago, IL, USA). The measurement data were assessed for normal or non-normal distribution. An independent sample t-test was used in the statistical analysis. For the enumeration data, the chi-square test was used. A univariate analysis was first performed, and the risk factors were put into a logistic regression model (crude and multivariate-adjusted models were listed in the text, and the results of crude, minimally adjusted, and fully adjusted analyses were also shown) to identify risk factors for DVT. The difference was statistically significant (P,0.05).

Results

Patient Demographic and Clinical Characteristics

A total of 2831 patients who met the inclusion criteria between September 1, 2014, and May 31, 2019, were included in the

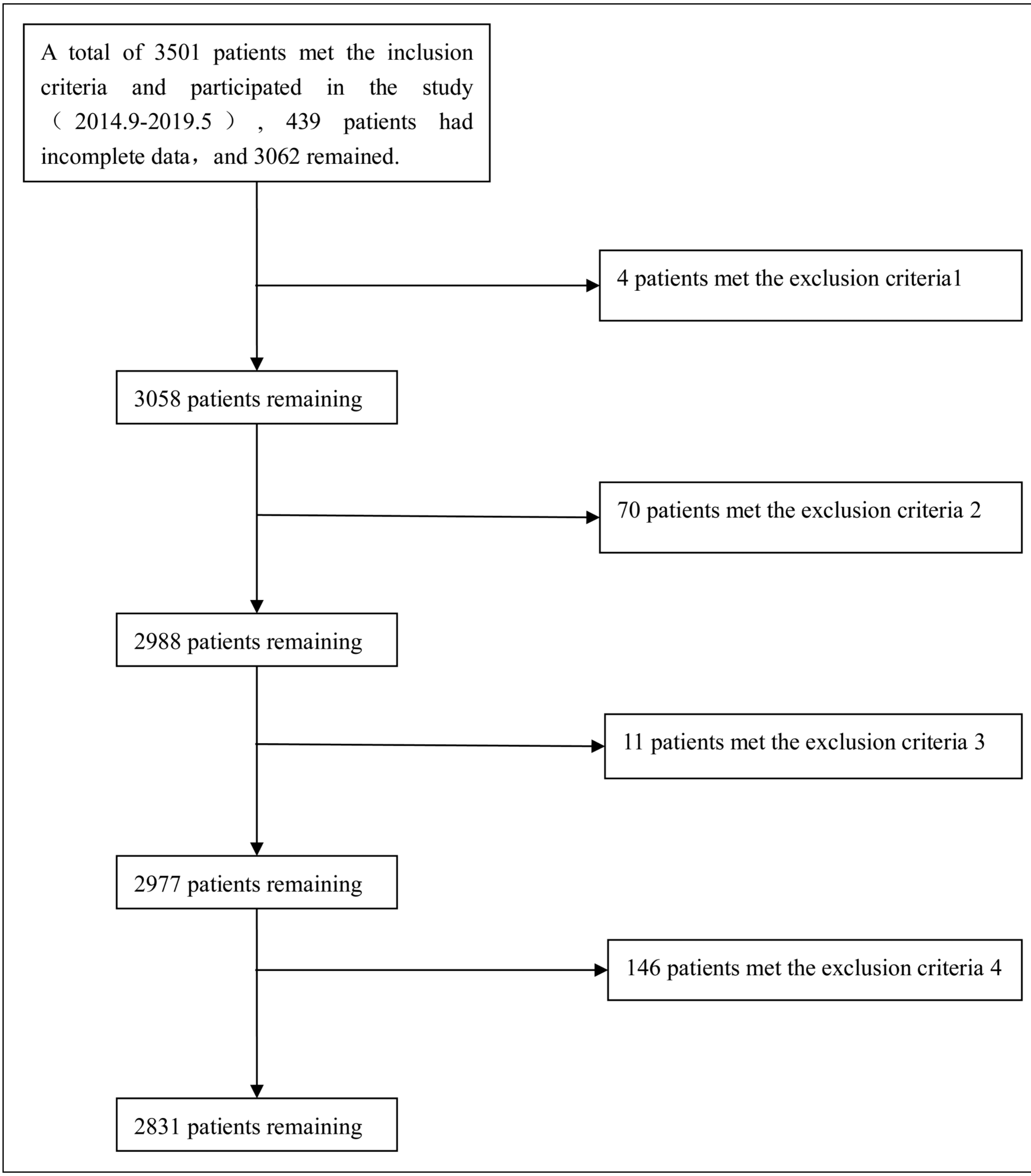

Figure 1. Derivation of the patient cohort.

study. Derivation of the study cohort was shown in Figure 1. General information of the patients was shown in Table 1. 1395 cases were male and 1436 cases were female with a mean（+/-SD）age of 59.43 ± 19.31 (16-102 years). There were 1740 hip fractures, 717 knee fractures, and 374 ankle and foot fractures. There were 1401 left lower extremity fractures, 1280 right lower extremity fractures, 44 bilateral lower extremity fractures, and 106 pelvic fractures (not counting the side of the fracture). 295 cases were associated with other fractures. Combined medical diseases: 581 cases of coronary heart disease, 622 cases of primary hypertension, 240 cases of diabetes mellitus, 137 cases of stroke. 61 cases had preoperative inferior vena cava filters. No pulmonary embolism occurred preoperatively.

Table 1. Patient Characteristics According to TFITS

	0-2d	3-4d	5-7d	>7d	P
Number	332	835	909	755	
Age	57.25 ± 19.08	61.34 ± 18.93	59.82 ± 19.47	57.80 ± 19.44	0.000
Gender					
Male	152	397	450	396	
Female	180	438	459	359	0.128
Medical morbidity(%)					
Coronary heart disease	48(8.3)	187(32.2)	189(32.5)	157(27.0)	0.025
Hypertension	62(10.0)	188(30.2)	203(32.6)	169(27.2)	0.495
Diabetes)	18(7.5)	66(27.5)	88(36.7)	68(28.3)	0.075
Stroke	11(8.0)	41(29.9)	41(29.9)	44(32.1)	0.320
Lung injury	2 (2.5)	11 (13.8)	30 (37.5)	37 (46.3)	0.000
Associate fracture	15(5.1)	59(20.0)	88 (29.8)	133 (45.1)	0.000
Fracture Site(%)					
Hip	181 (10.4)	534 (30.7)	575 (33.0)	450 (25.9)	
Knee	118 (16.5)	215 (30.0)	195 (27.2)	189 (26.4)	
Ankle and foot	33 (8.8)	86(23.0)	139 (37.2)	116 (31.0)	0.000
Fractures side(%)					
Left	176(12.6)	442(31.5)	428(30.5)	355(25.3)	
Right	152(11.9)	375(29.3)	430(33.6)	323(25.2)	
Both	1(2.3)	9(30.2)	14(31.8)	20(45.5)	0.019
Preoperative DVT (%)	66(8.0)	195(23.8)	263(32.0)	297(36.2)	0.000
DVT type %)					
Proximal	1(6.7)	6(40.0)	2 (13.3)	6 (40.0)	
Distal	59(8.2)	174(24.2)	234 (32.5)	252 (35.0)	
Mixed	6(6.9)	15(17.2)	27 (31.0)	39 (44.8)	0.0000
DVT side(%)					
Left	31 (8.8)	87 (25.0)	109 (31.3)	121 (34.8)	
Right	24 (8.0)	77 (25.8)	98 (32.8)	100 (33.4)	
Both	10 (6.7)	29 (19.3)	47 (31.3)	64 (42.7)	0.000
TFITA(days)	0.02 ± 0.15	0.26 ± 0.55	0.88 ± 1.25	4.99 ± 4.65	0.000
Admission HGB (g/L)	126.05 ± 17.67	122.87 ± 19.20	121.81 ± 20.56	117.97 ± 20.21	0.000
Admission Hct (%)	38.23 ± 4.99	37.02 ± 5.56	36.57 ± 6.03	35.57 ± 5.84	0.000
Admission D-dimer (mg/L)	11.52 ± 15.51	11.41 ± 14.35	11.16 ± 19.89	7.86 ± 14.13	0.000

TFITA: Time from injury to admission

The mean (+/-SD) time from injury to admission (TFITA) (days) was 1.69 ± 3.22 (0 to 18 d), and the mean (+/-SD) time from injury to surgery was 6.13 ± 3.74 (0 to 21 d). The mean (+/-SD) admission HGB was 121.56 ± 19.91 (50.00 to 177.00 g/L), the mean (+/-SD) admission Hct was 36.62 ± 5.78 (13.60 to 53.60), and the mean (+/-SD) admission D-dimer was 10.39 ± 16.49 (0.13 to 274.32 mg/L). In the 0-2d group, the mean (+/-SD) admission HGB was 126.05 ± 17.67 g/L, the mean (+/-SD) admission Hct was 38.23 ± 4.99, and the mean (+/-SD) admission D-dimer was 11.52 ± 15.51 mg/L, higher than the other groups; the mean (+/-SD) age was 57.25 ± 19.08 years, which was younger than other groups. In the 5-7d group, the incidence of coronary heart disease was 32.5%, the incidence of hip fracture was 33.0%, and the incidence of ankle and foot fracture was 37.2%, which were higher than the other groups. In the >7d group, the incidence of lung injury was 46.3%, the incidence of bilateral lower extremity fracture was 45.5%, and the mean (+/-SD) time from injury to admission was 4.99 ± 4.65 d, which were higher than the other groups.

Univariate Analyses

Between the different groups, there were no statistically significant differences in gender and comorbid diseases (primary hypertension, diabetes, stroke). However, the age, combined diseases (coronary heart disease, associated fractures), fracture site, fracture side, preoperative DVT incidence, DVT type, admission hemoglobin, admission Hct, and admission D-dimer were vital contributing factors to the time from injury to surgery.

Prevalence of DVT on Preoperative Ultrasonography

Among the preoperative ultrasound findings, a total of 821 (29.0%) cases had preoperative DVT, including 15 (1.8%) proximal thrombosis, 719 (87.7%) distal thrombosis, and 87 (10.5%) mixed thrombosis. In 106 patients with pelvic fractures, DVT occurred in 24 cases. Of the remaining 2725 patients, DVT occurred in 797 (29.2%), 150 (18.8%) in both lower extremities, 550 (28.8%) in the injured ipsilateral lower extremity, and 89 (11.2%) cases in the injured contralateral

Table 2. The Correlation Between TFITS and DVT in Different Models

Variable	Crude model (OR,95%CI,P)	Minimally adjusted model (OR,95%CI,P)	Fully adjusted model (OR,95%CI,P)
TFITS	1.086(1.063,1.109)0.000	1.095(1.072,1.119)0.000	1.093(1.068,1.118)0.000
Group			
0-2d	Ref	Ref	Ref
3-4d	1.228(0.897,1.680)0.199	1.132(0.822,1.558)0.447	1.115(0.789,1.575)0.539
5-7d	1.272(1.092,1.481)0.002	1.242(1.062,1.452)0.007	1.194(1.007,1.417)0.041
＞7d	1.380(1.246,1.528)0.000	1.383(1.247,1.535)0.000	1.396(1.242,1.568)0.000

Crude model: we did not adjust other covariants.
Minimally adjusted model: we adjusted age and sex.
Fully adjusted model: we adjusted age, sex, coronary heart disease, lung injury, associated fractures, fracture site, preoperative HGB, preoperative Hct, and preoperative D-dimer.

lower extremity. Double lower extremity DVT occurred in 146 cases of single lower extremity fractures. The incidence of DVT in the uninjured side was 8.6% (235/2725), which accounted for preoperative DVT was 29.4% (235/797).

The number(incidence) of DVT was 66(8.0%) in the 0-2d group, 195(23.8%) in the 3-4d group, 263(32.0%) in the 5-7d group, and 297(36.2%) in the >7d group, with statistically significant differences ($P < 0.05$) among all the groups, and the incidence of DVT gradually increased with the prolongation of preoperative time. The differences between groups in preoperative DVT type and side were statistically significant ($P<0.05$), among which the distal DVT incidence rate 35.0%, mixed DVT incidence rate 44.8%, and bilateral lower limb DVT incidence rate 42.7% were higher in the >7d group than the other groups.

The Correlation Between TFITS and DVT

We used a logistic regression model to evaluate the correlation between TFITS and the incidence of preoperative DVT. We showed the crude and adjusted models in Table 2. In the crude model, TFITS was positively correlated with the incidence of preoperative DVT (OR: 1.086; 95% CI: 1.063-1.109; $P = 0.000$). In the minimally adjusted model (adjusted age, sex), the results were positively correlated (OR: 1.095; 95% CI: 1.072-1.119; $P = 0.000$). In the fully adjusted model (adjusted age, sex, coronary heart disease, lung injury, associated fractures, fracture site, preoperative HGB, preoperative Hct, preoperative D-dimer), the results were positively correlated (OR: 1.093; 95% CI: 1.068-1.118; $P = 0.000$).

Discussion

Our findings showed that the incidence of DVT after lower extremity fracture was 29.0%, with a progressive increase in preoperative DVT as the time from injury to surgery increased from 8.3% in the 0-2d group, to 36.1% in the >7d group. A secular trend suggested a fivefold increase of hospitalized venous thromboembolic events during the past decade in China, and 7292 patients were diagnosed with DVT after surgery per 100,000 population in 2016.[16] Delay in delivery of surgical care for patients with acute trauma is known to be one of the most important factors contributing to the high incidence of preoperative DVT.

Takaomi[9] reviewed 3123 Asian hip fracture, and prolonged time from injury to surgery was associated with a high risk of DVT. In hospitalized patients, early surgery reduced the incidence of DVT in the lower extremity and delaying surgery by 1-7 d increased the incidence of DVT in hip fractures from 14.5% to 33.3%.[17] As the incidence of DVT increases, patients were at an even higher risk of fatal pulmonary embolism. In a large cohort study of 216 trauma centers,[18] patients treated at centers where delayed fixation was most common were at significantly greater risk of pulmonary embolism（2.6% VS 1.3%, OR:2.0, 95%CI:1.2-3.2）.

In this situation, the study of the relationship between TFITS and the incidence of preoperative DVT becomes extremely important for predicting the occurrence of DVT in the clinical work. Available series performing universal screening on admission showed a DVT prevalence of 1.4–6% on patients admitted before 48–72h.[7,19] Bengoa[12] found a 17.1% incidence of DVT for hospital stays longer than 48 h. In this study, because 73.4% of patients underwent surgery within 7d, the incidence of DVT within 7d after injury was the primary focus of the study. Further, the TFITS within 7d was classified into three groups of 0-2 d, 3-4 d, and 5-7d, to further analyze the variation in the early post-injury period. Because no previous studies had been reported in the literature, the classification in this study was based on the incidence of preoperative DVT reported in the previous literature, and also on experience in clinical work.

Risk factors for post-traumatic DVT were reported, which included age, gender, fracture, surgery, length of hospital stay, history of previous DVT, varicose veins, high-energy injuries, and immobilization.[20–22] Fei[3] showed that days between the fracture and surgery were an independent risk factor of preoperative DVT. These risk factors for preoperative DVT such as patient comorbidities, site of the fracture, and type of the fracture, could not be changed, and only the TFITS could be modified by hospitalized management. Predicting the risk of preoperative DVT was clinically important. We used logistic analysis, which was set as crude model, minimally adjusted model (adjusted for age, gender), and fully adjusted model (adjusted for age, gender, coronary artery disease, lung injury, associated fracture, fracture site, preoperative HGB, preoperative Hct, preoperative D-dimer), considering that pelvic fractures were not included in the fracture side statistics, so fracture side was not included in the fully adjusted model. The risk of preoperative DVT was found to be positively correlated with the TFITS in the crude, minimally adjusted, and fully adjusted models; the correlation gradually increased with prolonged preoperative time. The OR:1.093 in the fully adjusted model could be interpreted as excluding the effect of other factors, each 1d increase in TFITS was correlated with a 9.3% increase in the risk of preoperative DVT.

Zhang[23] reported 132 patients who underwent surgery within 72 h of fracture and showed that early intervention could save 11.85% in preoperative DVT ($P = 0.016$). Despite recognition that patients with lower extremity fractures benefit from early fixation. However, in clinical work, 66% of the patients did not receive surgery within the time frame.[24] In this study, 1659 (58.6%) of the patients underwent surgery more than 4 d from injury, and the majority of patients (73.4%) underwent surgery within 7 d. However, 26.6% of the patients still exceeded 7d. From patient rights point of view, ongoing hemodynamic instability, coagulopathy, age, and greater comorbidity were often cited as reasons to postpone definitive fixation.[18,25] Age was an independent risk factor for the incidence of preoperative DVT,[26] especially in elderly patients who were often combined with coronary heart disease, hypertension, and other medical diseases, often require the amount of time for treatment before surgery to ensure the security of surgery. Patients in this study who received surgery more than 4d had a higher proportion of comorbid diseases, which included coronary heart disease (59.7%), hypertension (59.5%), diabetes mellitus (65.0%), lung injury (84.1%), and stroke (61.3%). Among peri-articular fractures, 53.6% of patients with knee fractures and 67.9% with ankle and foot fractures, received surgery more than 4d. Swelling around the knee and ankle joint also required time for amelioration to avoid postoperative wound complications.

The mean TFITA of the >7d group in this study was 4.99 days, which required consideration of transfer from other hospitals, treatment of comorbid medical conditions in elderly patients, patient financial status, and resuscitation and hemodynamic stabilization of multiple injuries. From the hospital's points of view, differences in processes of care predominantly driven by surgeons decision-making, institutional policies, or allocation of resources were also likely to influence the timing of fixation. There was potential for variability to exist between hospitals in the number of patients undergoing delayed fixation. Such variability might affect clinical outcomes and would therefore represent an important target for quality improvement.[18] These delays in surgical intervention, while necessary in some cases, may predispose patients to developing thromboembolic problems. The challenge in patients with delayed surgery was to diagnose and protect them from thromboembolism preoperatively so as to avoid undesirable and occasionally disastrous consequences intra- and postoperatively.

There were a few limitations to this study. First, we eliminated the incomplete data, the authenticity of the results need to be evaluated. Because of the limited data, not all influencing factors of DVT were included in the fully adjusted model for the study. In future studies, a larger sample size will be needed to validate the results. Second, although ultrasonography was not the gold standard for diagnosing DVT, and the operating skills of different sonographers vary, our study was conducted by senior sonographers, which minimizes the impact on outcomes. Third, we divided the patients into four time segments according to TFITS, this categories was of different time lengths, and we did not make statistical comparison between each two groups, which may lead to bias in statistical analysis. Finally, the methodology of this study was a cross-sectional study and did not allow for dynamic observation of the occurrence of DVT in individual patients. In the next step, prospective studies are needed to dynamically observe the occurrence of DVT after fracture.

Conclusion

The TFITS was an independent risk factor of preoperative DVT. The incidence of DVT: 0-2d 8.0%, 3-4d 23.8%, 5-7d 32.0%, and >7d 36.2%. Excluding the effect of other factors, each 1d increase in TFITS was correlated with a 9.3% increase in the risk of preoperative DVT. The TFITS should be decreased to reduce the risk of preoperative DVT.

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Authors' Contributions

YXC: performed the case collection, and was a major contributor in writing the manuscript; HH: performed the case collection; BFZ: performed the case collection; HLD: performed the case collection; JLL: performed literature review; CK: performed literature review; SH: performed statistical analysis; KZ: provided guidance for conception; PFW: provided guidance for conception and writing. All authors read and approved the final manuscript.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical Approval

Our institution does not require ethical approval for reporting individual cases or case series.

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Informed Consent

Verbal informed consent was obtained from a legally authorized representative(s) for anonymized patient information to be published in this article.

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