Study on the Risk Factors of Deep Vein Thrombosis (DVT) in Patients With Lower Extremity Fracture

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Research article

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Abstract

Background: The objective of this work is to discuss and analyze the related factors of lower extremity fracture complicated by deep vein thrombosis (DVT), and to help surgeons aptly prevent it.

Methods: A retrospective analysis was conducted on the orthopedic inpatient records of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine from July 2014 to November 2018, and 11,891 patients with closed fractures of lower extremities were selected. By analyzing each patient's gender, age, presence or absence of diabetes and hypertension, preoperative plasma D-dimer level, and color Doppler ultrasound of the lower extremity vein, the pertinent factors of the patients with lower extremity fractures complicated by DVT were analyzed.

Results: A total of 11,891 patients were selected, including 4462 with cases of peri-hip fractures, 754 with cases of femoral shaft fractures, 1776 with cases of peri-knee fractures, 1961 with cases of tibiofibular fractures, and 2938 with cases of ankle fractures. Of these patients, 643 with DVT were detected, displaying a total incidence of 5.4%. All patients were categorized into either the DVT group or non-DVT group. The results demonstrate that there were statistically significant differences between the two groups in age, the presence of diabetes and hypertension, the fracture site, and the preoperative plasma D-dimer level ($p < 0.05$), but there was no statistically significant difference in sex ($p > 0.05$). Logistic multivariate analysis revealed that age, the presence of diabetes, and the preoperative plasma D-dimer level of patients were independent risk factors for lower extremity fracture complicated by DVT.

Conclusion: Age, the presence of diabetes and hypertension, the fracture site, and the preoperative plasma D-dimer level were found to be correlated with the incidence of DVT. Moreover, age, the presence of diabetes, the preoperative fracture site, and the plasma D-dimer level were found to be independent risk factors.

Introduction

Deep vein thrombosis (DVT) is a common complication after trauma, especially after lower extremity fractures^[1]. The incidence of preoperative DVT has been reported to be as high as 32%^[2]. Underlying fatal effects, such as pulmonary embolism (PE), can be caused by DVT, and research has shown that patients treated for venous thromboembolism (VTE) have approximately twice the length of stay and the total cost of hospitalization as those not treated for VTE^[3]. Past studies have shown that DVT in fracture patients is associated with many factors, such as age, sex, the fracture site, and the D-dimer level^[4–6]. For instance, a previous study has shown that DVT is most common in middle-aged patients with lower extremity fractures, but there is no difference in its incidence between sexes^[4]. Different from the results of that study, Williams et al. suggested that older age is a risk factor for DVT^[7]. In a study involving 829 patients, the incidences of DVT in patients with hip, femur shaft, knee, lower leg, and foot or ankle fractures were found to be 16.7%, 12.2%, 9%, 3.7%, and 2.3%, respectively^[8]. In another study of 462 patients, 71.2% of patients with DVT had hip fractures, 11.9% had tibiofibular fractures, and 10.4% had

femoral shaft fractures^[9]. These findings indicate that the hip fracture group had the highest incidence of DVT. Other factors, such as the presence of diabetes and hypertension, have been found to increase the risk of DVT^[2, 10]. However, it is necessary to conduct more research to clarify the controversial conclusions of these studies and expand the sample size. Therefore, further study on the factors that affect the formation of VTE in patients with lower extremity fractures is conducive to the formulation of a more reasonable diagnosis and treatment plan, which will allow orthopedic surgeons to choose the optimal operating time.

The purpose of this study was to evaluate the risk factors associated with DVT in patients with lower extremity fractures in the Affiliated Hospital of Shandong University of Traditional Chinese Medicine. Specifically, the potential diagnostic and preventive values of sex, age, fracture sites, chronic diseases, and D-dimer levels in patients with lower extremity fractures were explored via retrospective cohort studies.

Materials And Methods

Design, sample, and criteria for participation

In this study, 11,891 patients with lower extremity fractures treated in the orthopedic department of the Affiliated Hospital of Shandong University of Traditional Chinese Medicine from July 2014 to November 2018 were retrospectively reviewed. The inclusion criteria for patients included the following: adult patients with lower extremity fractures (excluding pelvic fractures); patients with closed fractures (non-emergency surgery); fresh fracture patients (hospitalized within 1 week after injury). The following patients were excluded: patients under the age of 18; patients with open fractures of the lower extremities; patients with old lower extremity fractures; patients with a previous history of DVT.

Data Collection And Dvt Diagnosis

Data on the sex, age, previous history of hypertension or diabetes, the preoperative plasma D-dimer level, and the lower extremity fracture site of patients were collected. In this study, fractures were categorized according to the site of trauma into peri-hip fractures (including femoral neck fractures and intertrochanteric fractures, the proximal femur fractures), femoral shaft fractures, peri-knee fractures (including distal femoral fractures, femoral condyle fractures, patellar fractures, and tibial plateau fractures), tibiofibular fractures, and ankle fractures (including ankle joint fractures and foot fractures). The normal range of the preoperative D-dimer level was set at 0-0.5 µg/ml. All patients underwent the preoperative ultrasound examination of venous thrombosis in the fractured lower extremity. Regardless of the size of the thrombosis and whether all the vessels were blocked, all patients were treated according to a venous thrombosis diagnosis in the lower extremity, and the location of the thrombosis was recorded. Patients with venous thrombosis were classified as the DVT group, while the rest were classified as the non-DVT group.

Statistical analysis

SPSS 25.0 software was used for statistical analysis. Because of the large sample size of the study data, these samples were regarded to follow an approximately normal distribution. The incidence rate was expressed as a percentage, independent sample t-tests and χ^2 tests were used for statistical analysis, and $p < 0.05$ was considered to indicate a statistically significant difference. If $p < 0.05$ for a factor in the univariate analysis, relevant factors were selected for logistic multivariate regression analysis to determine the factors that affect the occurrence of lower extremity venous thrombosis.

Results

Patient characteristics

A total of 11,891 patients meeting the inclusion criteria were selected, including 578 with cases of preoperative DVT and 65 with cases of postoperative DVT. These 643 patients were classified as the DVT group, while the remaining 11,248 patients were classified as the non-DVT group. The total incidence of lower extremity venous thrombosis was 5.4%. The patient characteristics are reported in Table 1. No pulmonary embolism events or deaths were recorded in this study.

Univariate Analysis Of Dvt

There were no significant differences in sex between the two groups ($p > 0.05$). Also, the incidence of DVT in patients with diabetes or hypertension (6.2%, 7.0%) was found to be higher than that in patients without diabetes or hypertension (5.2%, 5.4%). The χ^2 test indicated that there were significant differences in the rate of DVT between patients with and without diabetes or hypertension ($p < 0.05$).

The subjects ranged in age from 18 to 93, with an average age of 61.4 ± 8.29 years. The patients were divided into three groups based on age, among which 2,024 belonged to the young adult group (18–40 years old), 3,480 belonged to the middle-aged group (41–60 years old), and 6,387 belonged to the elderly group (over 60 years old). The numbers of DVT cases in each group were 59, 160, and 424, respectively. The average ages of each group were 34.3 ± 5.06 years, 55.7 ± 3.42 years, and 79.2 ± 7.40 years, respectively, and the respective rates of DVT were 2.9%, 4.6%, and 6.6%. The χ^2 test results showed that there were significant differences between the rates of DVT in patients of different age groups ($p < 0.05$), which indicates that age is a factor that influences DVT.

Of the 11,891 patients, 4,462 had peri-hip fractures, 754 had femoral shaft fractures, 1,776 had peri-knee fractures, 1,961 had tibiofibular fractures, and 2,938 had ankle fractures, and the respective numbers of DVT cases were 312, 50, 174, 48, and 59; thus, the prevalences of DVT were respectively 7.0%, 6.6%, 9.7%, 2.4%, and 2.0%. The χ^2 test results showed that there were significant differences in the rate of DVT in patients with different fracture sites ($p < 0.05$), and patients with peri-knee fractures had the highest incidence of DVT (Fig. 1).

Among the 11,891 subjects, the plasma D-dimer data of 1,567 patients were excluded due to various reasons, and therefore the number of effective cases was 10,324, among which the number of effective cases in the DVT group was 410. The plasma D-dimer levels of the patients were divided into five groups: 0-0.5 µg/ml (8880 cases in the normal group), the 0.5-1 µg/ml group (451 cases), the 1–2 µg/ml group (257 cases), the 2–5 µg/ml group (397 cases), and the greater than 5 µg/ml group (339 cases). The numbers of patients with DVT in each group were 15, 33, 85, 155, and 122, respectively, and the rates of DVT were 0.17%, 7.3%, 33%, 39%, and 36%, respectively. According to the χ^2 test, $p < 0.05$, which indicates that there were significant differences between the rates of DVT in patients with different plasma D-dimer levels.

Multivariate Analysis Of Risk Factors

Multivariate logistic regression analysis further demonstrated the correlations between DVT and age, diabetes, hypertension, the fracture site, and the plasma D-dimer level. Table 2 reveals that age, diabetes, the plasma D-dimer level, and the fracture site were independent risk factors for DVT after lower extremity fractures.

Table 1 Risk factors for DVT.

Factors	Patients	DVT Patients%	χ^2	P
Sex			1.489	0.222
Male	5330	282 (5.3%)		
Female	6561	381 (5.6%)		
Age			47.965	0.000*
18-40	2024	59 (2.9%)		
41-60	3480	160 (4.6%)		
≥60	6387	424 (6.6%)		
Diabetes			4.484	0.034*
Yes	2667	166 (6.2%)		
No	9224	477 (5.2%)		
Hypertension			23.734	0.000*
Yes	3568	248 (7.0%)		
No	8323	395 (5.4%)		
Fracture sites			190.985	0.000*
Peri-hip	4462	312 (7.0%)		
Femoral shaft	754	50 (6.6%)		
Peri-knee	1776	174 (9.7%)		
Tibiofibular	1961	48 (2.4%)		
Ankle	2938	59 (2.0%)		
D-dimer			3112.332	0.000*
0-0.5	8880	15 (0.17%)		
0.5-1	451	33 (7.3%)		
1-2	257	85 (33%)		
2-5	397	155 (39%)		
≥5	339	122 (36%)		

* $P < 0.05$.

Table 2 Multivariate logistic regression analysis results.

Factors	B value	Standard error	Wald value	P
Age	-0.084	0.018	21.031	0.000*
Diabetes	1.482	0.548	7.315	0.007*
Hypertension	0.713	1.007	0.501	0.479
D-dimer	-1.343	0.149	27.213	0.000*
Fracture sites	2.079	1.294	30.769	0.000*

* $p < 0.05$.

Discussion

Virchow's triad describes the three main causes of DVT, namely stasis, hypercoagulability, and endothelial changes^[11, 12]. Patients with lower extremity fractures must stay in bed and rest after injury. However, long-term bed rest leads to reduced muscle pumping, severe local blood flow stagnation, and serious vascular endothelial injury. Moreover, the accumulation of coagulation factors leads to the overactivation of the coagulation system, thereby leading to accelerated thrombosis^[9, 13–15]. However, once the venous thrombosis of lower extremities is formed, due to changes in the body position or local massage factors, the thrombosis tends to fall off and form fatal PE; it has been reported that 10% of patients with DVT develop fatal PE^[16]. It is therefore necessary to solve the problem of DVT in lower extremity fractures before operation.

In the present study, patients with lower extremity fractures at the age of > 60 years were found to have the highest incidence of DVT (6.6%), and this was similar to the findings of Williams et al^[7]. In the opinion of the present authors, there are more internal diseases in elderly patients, which results in a longer preparation time for surgery and longer preoperative resting time. Moreover, elderly patients often have vascular sclerosis, high blood viscosity, and poor venous valve function, which lead to a high incidence of lower extremity DVT^[17]. Moreover, similar to the findings of the present study, Li et al. found that femoral neck fractures and intertrochanteric fractures are more common in older patients, and that many patients with these fractures choose arthroplasty surgery, which also increases the risk of DVT^[8].

Previous studies have shown that diabetes, a metabolic disease, affects the occurrence of DVT, and that the clinical effect is relatively obvious. Chung et al. found that the risk of VTE in diabetic patients is 1.44 times higher than that in non-diabetic patients^[18]. The findings of Fu et al.^[2] and Kang et al.^[19] also

indicated that diabetes increases the risk of DVT. The results of the present study revealed that the prevalence of DVT was significantly higher in the diabetic group than in the non-diabetic group (6.2%:5.2%). After fracture, the body is in a state of stress, so the blood glucose in the diabetic patients had a large range of changes, thereby leading to the release of a large number of cytokines and further activating the coagulation system in the body, which can also lead to increased platelet activation and damage to the fibrinolytic system^[18, 20]. In addition, it is believed that diabetic patients must regulate their blood glucose before surgery, which increases the preoperative preparation time and the postoperative wound healing time of diabetic patients as compared to that of normal patients^[21]. These factors lead to patients spending more time in bed, thereby delaying postoperative functional exercise and further increasing the risk of DVT.

The results of the χ^2 tests conducted in the present study indicate that there were significant differences between the rate of DVT among patients with or without hypertension, but logistic multivariate analysis showed that hypertension was not an independent risk factor in the formation of DVT in patients with lower extremity fractures. It is speculated that this result occurred because older patients accounted for a larger proportion of the subjects, and studies have shown that the prevalence of hypertension increases with age^[22].

Furthermore, in the cohort study, the fracture site was found to be an independent risk factor for DVT in lower extremities after fracture, and the incidence of DVT in patients with peri-hip fractures was 7.0%. Peri-hip fractures are more common in older patients, and many patients with these fractures choose arthroplasty surgery; this is one of the reasons for the high incidence of DVT following peri-hip fractures^[8]. Some researchers have also confirmed that hip fracture is an important risk factor for, and is significantly associated with, the occurrence of DVT^[9]. However, in the present study, patients with peri-knee fractures had the highest prevalence at 9.7%. In the authors' opinion, peri-knee fractures contain many complicated comminuted fractures caused by violence, which can cause relatively serious vascular endothelial injury in addition to bone injury. Moreover, the fixation of the affected extremity after the injury can impair venous function, and these lesions can lead to a hypercoagulable state^[6]. Thus, patients with peri-knee fractures exhibit the three risk factors associated with Virchow's triad, which is one reason for the high incidence of DVT found in the present study.

When fibrin filaments are degraded by fibrinolytic enzymes during coagulation, plasma D-dimer is produced. Therefore, an increased D-dimer content in plasma indicates the occurrence of thrombosis and dissolution in vivo, and can therefore be used as an indicator of non-invasive thrombosis^[23]. The results of the present study demonstrated that the plasma D-dimer level is an independent factor that affects the formation of DVT, which is similar to the results of Zhang et al^[9]. However, the D-dimer level increases with age and elderly patients are more prone to false-positive test results, which reduces the specificity of detection in these patients; therefore, studies have demonstrated the need to set the best cut-off value according to age to increase the specificity of detection^[24]. In addition, any increased fibrin or decomposition process, such as pregnancy, cancer, trauma, inflammation, infection, etc., will increase the

D-dimer level; therefore, an increase in the D-dimer level cannot be used for the specific detection of VTE^[25]. The D-dimer level alone is often unreliable for the diagnosis of DVT; however, as a low-cost and readily available biomarker, an elevated D-dimer level is useful for clinicians to identify or exclude VTE in patients based on symptoms and imaging findings^[26].

Conclusion

In summary, age, the presence of diabetes, the fracture site, and increased D-dimer levels were found to be potential risk factors and indicators for DVT in patients with lower extremity fractures. In addition, the preoperative plasma D-dimer level has certain guiding significance for the prediction of venous thrombosis after lower extremity fracture, which is conducive to the early prediction and diagnosis of DVT. Therefore, it is suggested that orthopedic surgeons analyze whether these risk factors are present in patients with lower extremity fractures to effectively prevent the formation of lower extremity venous thrombosis.

Abbreviations

DVT: Deep Vein Thrombosis; PE:Pulmonary Embolism; VTE:Venous Thromboembolism

Declarations

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Authors' contributions

This study was developed by ZYK and XWP. The first draft of the manuscript, data collection and data analysis of this study were completed by CWJ and WB.LQWalso participated in the collation of clinical data.All authors have approved the final manuscript before submission.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

The Ethics Committee of Affiliated Hospital of Shandong University of Traditional Chinese Medicine concluded that no approval is necessary for study based on its retrospective design. All patients agreed to the use of data in the study by oral consent. The oral consent approval was documented in the patients' files, which was approved by the Ethics Committee of Affiliated Hospital of Shandong University of Traditional Chinese Medicine. All clinical investigations were conducted in accordance with the guidelines of the Declaration of Helsinki.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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Figures

Figure 1

The distribution of DVT in different fracture sites.