

Original Article

Factors affecting the formation of deep vein thrombosis in the lower extremities after orthopedic surgery

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Abstract: Deep vein thrombosis (DVT) is one of the most common complications after orthopedic surgery. This complication could be fatal if pulmonary embolisms occur. Aiming to analyze factors affecting the formation of deep vein thrombosis (DVT) in the lower extremities after orthopedic surgery and to develop an effective diagnosis tool, 282 patients undergoing orthopedic surgery due to lower extremity fractures, from November 2015 to November 2018, in the Central Hospital of Weihai, were enrolled in the study. Clinical data, including age, gender, fracture site, operation times, mechanical ventilation, hypertension, coronary heart disease, diabetes, and D-dimer levels, were collected and analyzed for factors related to DVT. Of the patients studied, 99 developed DVT and the overall DVT incidence was 35%. Age, chronic diseases, mechanical ventilation, and severity of disease were found to be main factors leading to DVT ($P < 0.05$). Sensitivity and specificity rates of D-dimer levels in the diagnosis of DVT were 95.2% and 85.9%. In addition, operation times, chronic diseases, pulmonary infections, and post-operative bedding times influenced the formation of DVT. Analysis showed age, gender, surgery duration, post-operative bedtimes, complications of chronic disease, use of ventilators, and fracture sites to be independent risk factors for DVT. D-dimer levels can also be used to predict the formation of DVT.

Keywords: Orthopedic surgery, deep venous thrombosis, risk factor, intervention strategy, D-dimer

Introduction

Deep vein thrombosis (DVT) is one of the most common complications after orthopedic surgery, leading to abnormal blood coagulation in deep veins and reflux disorder [1]. Clinical manifestations of DVT include swelling and limb pain. DVT often occurs after major orthopedic surgery in the lower extremities. It may form in proximal and distal fractures, despite the use of many prophylactic methods, including low-dose heparin, aspirin, and intermittent pneumatic calf compression [2]. Proximal DVT may lead to pulmonary embolisms, leading to high mortality rates [3]. It has been estimated that 200,000 people die from pulmonary embolisms each year [4]. The formation of DVT not only hampers patient recovery but also impacts prognosis, even risking patient lives [5]. Therefore, early and effective assessment of factors affecting DVT formation is important for

the implementation of prophylaxis and intervention strategies, aiming to decrease morbidity rates [6].

In previous studies, incidence rates of DVT have been investigated regarding fracture types, age, and chronic diseases. For example, Magetsari et al. found that hip fractures generate the highest incidence of DVT, at 17-58% of patients [7]. Incidence rates were shown to be 25% in distal femur fractures [8] and only 2.1% in foot and ankle surgeries [4]. Williams et al. showed that older age is a risk factor for DVT. However, body mass index and gender are not risk factors [8]. In another study of 901 consecutive patients, Park et al. suggested that older age, cardiovascular disease, and chronic lung disease are independent risk factors [9]. In addition, predicting the formation of DVT has been a clinical challenge. Moreover, the development of an easy, reliable, and non-invasive tool is of great clinical significance [10].

Aiming to better understand factors affecting DVT formation, particularly in Asian populations, and to develop diagnostic markers for DVT formation, the current study retrospectively analyzed data obtained from patients after orthopedic surgeries. Present findings may help develop and implement effective intervention and prophylaxis strategies, reducing DVT formation.

Subjects and methods

Subjects

Two hundred and eighty-two patients undergoing orthopedic surgery, from November 2015 to November 2018, in the Weihai Central Hospital, Shandong, China, were retrospectively reviewed. Clinical data, including age, gender, fracture site, operation times, use of tourniquets and ventilation, hypertension, coronary heart disease, diabetes, and bedding times were collected. Patients were divided into control (non-DVT, $n = 173$) and DVT ($n = 109$) groups. In the control group, there were 56 males and 117 females. They were aged 19-79 years, with an average age of 51.7 ± 22.7 years. Sixty-eight had lower extremity fractures, 47 had pelvic fractures, 23 had acetabular fractures, and 42 had multiple and complex fractures. Of these patients, 32 had chronic diseases. In the DVT group, there were 55 males and 54 females, aged 26 to 75 years, with an average age of 53.6 ± 8.4 years. Forty-two had lower extremity fractures, 32 had pelvic fractures, 15 had acetabular fractures, and 14 had multiple and complex fractures. Of these patients, 66 had chronic diseases (30 diabetes mellitus and 26 cardiovascular diseases).

Inclusion criteria: 1) Diagnosed with fractures of the lower extremities; 2) Treated surgically; and 3) Confirmed to have DVT, according to venography and Doppler ultrasonography. Clinical manifestations included swelling on one or both affected limbs, elevated local skin temperature, pain, color change, and superficial vein eminence. Diabetes mellitus was diagnosed according to 1999 WHO criteria [11]. Cardiovascular disease included primary hypertension and coronary heart disease. Exclusion criteria: 1) Younger than 18 years or older than 80 years; and 2) History of thrombosis, myocardial infarction, cerebral embolisms, cerebral infarction, coagulation dysfunction, and severe liver and kidney dysfunction. The two groups

showed no differences in general conditions, operation methods, nursing measures, and rehabilitation treatments ($P > 0.05$). The current study was approved by the Ethics Committee of the hospital.

Methods

This was a retrospective case study. All patients underwent surgical treatment and were treated, cared for, and observed similarly. Clinical data, including age, gender, duration of surgery, intraoperative use of tourniquets, complications of chronic disease, fracture site, and post-operative management were retrieved from electronic clinical database systems. Data was reviewed, scored, and analyzed for potential risk factors. For D-dimer assays, fasting blood samples were taken the next day after admission. Serum was separated from the blood by centrifugation at 3,000 rpm for 10 minutes. D-dimer levels were measured with INNOVANCE® D-Dimer (Siemens Healthcare Diagnostics Products GmbH, Marburg, Germany) immunoturbidimetric assays, as previously described [12]. Monoclonal antibody against 8D3 was used to quantify cross-linked D-dimer fragments. Samples were considered positive if levels were higher than 500 $\mu\text{g/L}$.

Doppler ultrasonography was used to diagnose DVT, according to the Robinov Group's criteria [13]. The patients were examined before and after the operation in both lower limbs 1 day before the planned surgery, as well as days 3-5 after the operation. A positive diagnosis of DVT required the demonstration of filling defect signs in contrast-filled veins or cutoff signs of one or several deep veins (indirect signs of DVT) [14].

In addition, computed tomographic venography (CTV) procedures were performed, diagnosing DVT with a dual-source CT scanner (Somatom Definition, Siemens Medical Solutions). Non-contrast CT scans of the lower extremities were performed. Next, 50 mL of iopromide (Ultravist; 300 mg I/mL, Bayer Schering Pharma, Berlin, Germany) was injected at a rate of 3 mL/s via an 18-gauge catheter. It was typically positioned in the instep vein. Images were acquired with a 25-second and 60-second delay from the start of intravenous contrast injections. They were reconstructed with a slice thickness of 1.25 mm at an interval of 0.625 mm for analysis. All radiographic images were interpreted

DVT and fractures

Table 1. Comparison of deep vein thrombosis formation in orthopedic surgery patients suffering lower extremity fractures

Factors	No. case	No. DVT case	Over-all DVT incidence (%)	P value
Gender				0.085
Male	111	55	19.50	
Female	171	44	15.61	
Age (year)				0.011
> 65	72	65	23.01	
≤65	210	34	12.12	
Complication of chronic disease				0.001
Yes	77	66	23.41	
No	205	33	11.72	
Use of tourniquet				0.066
Yes	124	52	18.42	
No	158	47	16.71	
Post-operative bedtime (d)				0.011
≥5	138	77	27.31	
<5	144	22	7.82	
Pulmonary infection				0.031
Yes	64	61	24.13	
No	218	38	10.11	
Site of fracture				
low extremity	126	42	14.91 ^a	
pelvic	80	31	11.02	
acetabular	34	15	5.31	
multiple and complex	42	11	3.91	

^aFigures labeled with same superscript are not different significantly by X^2 -test ($P > 0.05$).

by an independent radiologist blinded to the study.

Statistical analysis

Enumeration data are expressed as numbers and percentages, tested using X^2 -tests. Measurement data are expressed as mean \pm standard deviation (sd), tested using Student's t-tests. Logistic regression analysis was performed, aiming to identify factors related to the formation of DVT. $P < 0.05$ or < 0.01 indicates statistically significant or highly significant. Receiver operating curves were plotted, evaluating the diagnostic value of D-dimer. Statistical analysis was conducted with SPSS 21.0 (SPSS Inc., Chicago, IL, USA).

Results

DVT in different patient groups

In this study, the age of patients varied from 19 to 75 years, with an average age of 51.7 ± 22.7

years. Moreover, 19.9% of the patients were older than 65 years, 44% of them used tourniquets during the operation for bleeding control, 27.3% had complications of chronic disease, 22.7% had pulmonary infections, and 44.7% and 28% had lower limb fractures and pelvis fractures, respectively. Multiple and complex fracture accounted for 14.9% of the patients. Overall DVT incidence was 35.1% in the 282 patients. Additionally, X^2 tests showed that gender and use of tourniquets did not impact the formation of DVT. In contrast, age, chronic diseases, pulmonary infections, and site of fractures significantly affected the formation of DVT ($P < 0.05$, **Table 1**). There were significant differences in rates of DVT among patients with different fracture sites ($P < 0.05$). The low extremity fracture group presented the highest overall rate of DVT (**Table 1**). Specific DVT rates were similar between the site groups (33.3%, 38.8%, 44.1, and

26.2% in low extremity, pelvic, acetabular, and multiple and complex fractures).

Logistic analysis of risk factors associated with DVT

Using multivariate logistic regression analysis, risk factors associated with DVT were assessed. Independent variables included gender, age, use of a ventilator and tourniquet, post-operative bedtimes, complications of chronic diseases, and fracture sites. Formation of DVT was a dependent variable. Results showed that age, gender, surgery duration, post-operative bedtimes, complications of chronic diseases, use of ventilators, and fracture sites were associated with DVT positively ($P < 0.05$, **Table 2**).

Diagnostic value of D-dimer levels for DVT

Average levels of D-dimer in patients with DVT were significantly higher than those without DVT (738 vs 456 $\mu\text{g/L}$, $P < 0.01$). ROC curve

Table 2. Logistic analysis of factors affecting deep vein thrombosis formation in lower extremities

Independent variables	B	Wald	P	OR
Gender	1.16	1.14	0.332	1.12
Age	1.25	1.79	0.035	1.51
Chronic disease	1.55	1.37	0.018	1.68
Operation time	1.91	1.66	0.031	1.39
Ventilation time	1.77	1.57	0.021	1.66
Use of tourniquet	2.19	1.88	0.112	1.90
Post-operative bedtime	2.13	1.47	0.012	1.63
Site of fracture	1.99	1.76	0.031	1.52

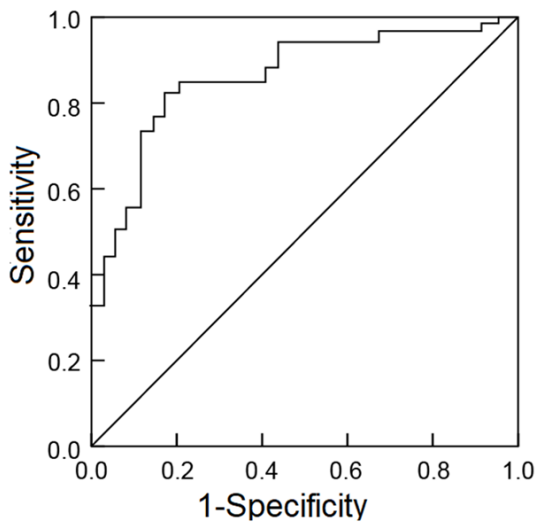


Figure 1. Receiver operating curve of D-dimer for diagnosis of deep vein thrombosis in patients after orthopedic surgery.

analysis showed that sensitivity and specificity rates to diagnosis of DVT by D-dimer were 95.2% and 85.9%, respectively. AUC was 0.91, indicating that D-dimer is a reliable biomarker predicting DVT formation (**Figure 1**).

Discussion

Age and surgery times

Results of the current study suggest that age is positively associated with DVT formation, particularly in those aged 65 years or older with chronic diseases, such as diabetes mellitus and cardiovascular disease. Age is an independent risk for lower extremity DVT. This is consistent with previous conclusions [15]. Surgery times and use of ventilators during the operation were found to be associated with DVT for-

mation. Since immune function in elderly patients is generally low, if surgical exposure is long and invasive diagnosis and treatments are excessive, the respiratory system may generate defensive stress. This leads to increased secretion of inflammation cells and the formation of DVT.

Bedding and fracture sites

After orthopedic surgery, particularly major surgery, patients often need to lie in the bed for a long time. This may result in slow blood flow, facilitating the formation of DVT. Other clinical measures that may lead to decreased blood flow are the use of tourniquets and anesthesia, as well as reduced water intake before the operation [16]. The current study suggests that bedtimes are related to the formation of DVT. For severely traumatized patients, such as patients with multiple fractures, the use of tourniquets and mechanical ventilation may lead to more serious injuries of vascular intima. After the operation, their activity may be restricted due to pain and passive recumbent positions. These factors may result in slowed blood flow and formation of DVT, particularly in patients with lower extremity trauma [17]. Differing from previous studies [17], present results did not show significant differences in DVT formation according to specific fracture types, although overall DVT rates were lower in patients suffering acetabular multiple and complex fractures, due to a fewer number of cases.

Tourniquets

Previous studies have shown that the use of pneumatic tourniquets increase the risk of distal DVT [16]. They have also suggested that it is beneficial to relax the tourniquet immediately after implantation of the components, aiming to reduce incidence of DVT after primary total knee arthroplasty procedures [18]. However, in the present study, the use of tourniquets during the operation did not impact the formation of DVT. It is likely that the effects of tourniquet use during the operation are not only to block bleeding, but also related to patient tolerance and conditions, as well as the habits of the operating surgeon.

Pulmonary infections

Current results suggest that pulmonary infections increase DVT formation, suggesting that

pulmonary infections provide synergistic effects on patient prognosis after the operation. Therefore, it is important to diagnose infections as early as possible, treating them effectively. This will lower the risk of DVT and improve prognosis.

Chronic complications

Patients with chronic complications, such as diabetes mellitus, are more likely to have DVT. Diabetes patients often have increased blood glucose and lipids, along with reduced immunity. Therefore, they are prone to DVT formation [19]. It is especially important to provide reasonable and effective intervention for diabetes patients, aiming to prevent DVT formation.

Cardiovascular diseases

Hypertension and coronary heart disease are common complications in fracture patients. Present analysis suggests that cardiovascular disease is positively related to DVT formation. This is consistent with previous studies [20]. In patients with hypertension or coronary heart disease, vascular endothelial cells may have been injured. This retards blood flow and the blood vessels are hardened and less flexible, with poor contraction capacity. This leads to adhesion and aggregation of platelets, promoting coagulation and DVT formation.

D-dimer

D-dimer is a fibrin degradation product, a small protein fragment that can be detectable in the blood. D-dimer assays are fast, accurate, and readily available [21]. Present data shows that D-dimer has significant diagnostic value for DVT, with an AUC of > 0.9. Since it is a relatively high-throughput and low-cost assay, it will facilitate the diagnosis of DVT for better treatment.

In summary, the current study found that occurrence of DVT after orthopedic surgery is mainly associated with age, operation duration, lung infections, bedtimes, chronic diseases, and fracture sites. Due to pain, postoperative bedding, passive recumbent positions, and anesthetics, orthopedic surgery patients are prone to DVT. Thus, they should be cared for with great attention given to risk factors, aiming to effectively prevent DVT formation. In addition, D-dimer can be used to predict the formation of DVT.

Disclosure of conflict of interest

None.

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