Article

The Value of Coagulation-Related Indicators Combined with Vascular Ultrasound Parameters in the Risk Assessment of Deep Vein Thrombosis after Secondary Traumatic Fracture Surgery

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Objective: The incidence of deep vein thrombosis (DVT) after traumatic fracture is high, and DVT causes serious adverse effects on the postoperative recovery of patients. The purpose of this study was to explore the effect of coagulation-related indicators combined with vascular ultrasound measurements for the risk assessment of DVT after secondary traumatic fracture, and to provide a new method for predicting the occurrence of DVT.
Methods: The clinical data of patients with secondary traumatic fracture surgery in our hospital from January 2019 to January 2022 were retrospectively analyzed. The patients were divided into a non-DVT group and a DVT group according to whether DVT was indicated in the medical record system. The coagulation-related indices and vascular ultrasound measurements of the two groups were compared, and the risk factors for postoperative DVT were analyzed by bivariate correlation and multivariate logistic regression.
Results: According to the medical record system, 55 patients (47.41%) had DVT, and 61 patients (52.59%) did not have DVT. There was no significant difference in prothrombin time (PT) or activated partial thromboplastin time (APTT) between the two groups ($p >$ 0.05). The thrombin time (TT) in the DVT group was lower than that in the non-DVT group. The levels of fibrinogen (FIB) and D-dimer (D-D) in the DVT group were higher than those in the non-DVT group (t = 2.766, 3.242, 2.649, p = 0.007, 0.002, 0.009). Spearman correlation analysis showed that peak systolic velocity (Vs), end-diastolic velocity (Vd), pulsatility index (PI), resistance index (RI), FIB, and D-D were positively correlated with the risk of DVT after secondary traumatic fracture surgery (r = 0.264, 0.656, 0.293, 0.276, 0.287, 0.251, $p < 0.05$). TT was negatively correlated with DVT risk after secondary traumatic fracture surgery (r = –0.249, $p < 0.05$). The measurements of peak systolic velocity (Vs), end diastolic velocity (Vd), pulsatility index (PI) and resistance index (RI) in the DVT group were higher than those in the non-DVT group (t = 2.663, 2.998, 3.135, 2.953, p = 0.009, 0.003, 0.002, 0.004). FIB, D-D, Vs, Vd, PI, and RI were independent risk factors for DVT after secondary traumatic fracture surgery (Odds Ratio (OR) = 1.483, 2.026, 2.208, 1.893, 1.820, 1.644, $p < 0.05$). TT index was an independent protective factor for DVT after secondary traumatic fracture surgery (OR = 0.868, $p < 0.05$). The sensitivity and specificity for prediction of DVT based on combined coagulation-related indicators and vascular ultrasound imaging measurements were higher than those of individual measurements ($p < 0.05$).
Conclusions: Coagulation-related indicators and vascular ultrasound parameters can effectively predict the formation of DVT. Through the analysis of factors related to DVT formation, screening of high-risk patients for effective intervention may help to reduce the risk of DVT. Further verification in additional, large-scale clinical trials is advocated.

Keywords: coagulation-related indicators; vascular ultrasound parameters; secondary traumatic fracture surgery; deep VEIN embolism

Introduction

Secondary traumatic fracture refers to a fracture at a previous fracture site. Most of these fractures occur in patients that did not heal completely after the primary fracture. Thus, external force application can result in refracture of the bone. Secondary fractures usually occur in older people due to serious loss of calcium in the bone, or in patients with osteoporosis, etc. In these patients, the healing ability of the fracture site will be affected, resulting in a higher probability of secondary traumatic fracture [1,2,3].

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After secondary traumatic fracture surgery, patients require prolonged bed rest with limited mobility. A variety of factors, such as aggravation of an inflammatory reaction, can easily cause sudden thrombosis of the deep venous system of the lower limbs of patients; the deep vein thrombosis (DVT) can block the deep veins and cause serious venous return disorders [4,5,6,7]. Epidemiological studies have shown that the incidence of postoperative DVT in 19 orthopedic centers in seven Asian countries, among patients not administered drugs to prevent thrombosis, is as high as 41% [8]. Studies have shown [9,10,11] that thrombin time (TT), fibrinogen (FIB), and D-dimer (D-D) are coagulation-related indicators. When DVT forms, prothrombin time (PT) and activated partial thromboplastin time (APTT) decrease, resulting in an increase in coagulation-related indicators. Doppler ultrasound can detect the velocity and di-

Table 1. Comparison of general data of patients.

Group		DVT group (n = 55)	Non-DVT group (n = 61)	χ^2/t/F	p
Gender (n, %)	Male	27 (49.09)	32 (52.46)	0.131	0.717
	Female	28 (50.91)	29 (47.54)		
Body mass index (kg/m^2)		22.13 ± 2.25	22.18 ± 2.32	0.116	0.908
Time from injury to operation (d)		6.52 ± 0.67	6.32 ± 0.65	1.603	0.112
Mean age (years)		51.37 ± 5.14	51.58 ± 5.18	0.215	0.830
Fracture site (n, %)	Upper limbs	20 (36.37)	24 (39.34)	0.315	0.854
	Lower limbs	18 (32.73)	21 (34.43)		
	Pelvis bone	17 (30.91)	16 (26.23)		
Underlying disease (n, %)	Hypertension	21 (38.18)	25 (40.98)	0.338	0.844
	Diabetes	15 (27.28)	18 (29.51)		
	Other	19 (34.55)	18 (29.51)		

DVT, deep vein thrombosis.

Table 2. Comparison of coagulation parameters ($\bar{x} \pm s$).

Group	n	TT (s)	PT (s)	APTT (s)	FIB (g/L)	D-D (μg/L)
The DVT Group	55	17.55 ± 1.78	12.45 ± 1.25	21.89 ± 2.21	4.26 ± 0.45	895.85 ± 90.74
The Non-DVT Group	61	18.49 ± 1.87	12.36 ± 1.38	21.47 ± 2.28	4.01 ± 0.41	853.05 ± 83.25
t	-	2.766	0.362	0.990	3.242	2.649
p	-	0.007	0.718	0.324	0.002	0.009

Note: TT, thrombin time; PT, prothrombin time; APTT, activated partial thromboplastin time; FIB, fibrinogen; D-D, D-dimer.

rection of blood flow in the blood vessels of patients. The vascular ultrasound measurements provided by it can effectively evaluate the intravascular situation of patients, and can evaluate the elasticity and thickness of the blood vessel wall [12,13,14,15,16]. Since the formation of DVT after secondary traumatic fracture surgery has a serious impact on the physical health and psychology of patients, it is necessary to evaluate the possible risk factors for effective prevention.

At present, there is a lack of clinical research on coagulation-related indicators and vascular ultrasound measurements to evaluate the risk of DVT formation after secondary traumatic fracture surgery. Therefore, this study collected patient data and used Spearman correlation analysis and logistic regression analysis to evaluate the risk of DVT formation after secondary traumatic fracture surgery to fill the clinical gap. In this study, we sought to improve screening of high-risk groups for postoperative DVT formation. The results can provide effective guidance for clinical practice, and potentially reduce the incidence of DVT.

Materials and Methods

General Information

The clinical data of patients who underwent secondary traumatic fracture surgery in our hospital from January 2019 to January 2022 were retrospectively analyzed. Inclusion criteria were: (1) patients diagnosed with secondary traumatic fracture through clinical X-ray and CT examination; (2) all fracture sites met the requirements of surgical diagnosis and treatment; (3) age >18 years old; (4) clinical data integrity; (5) the diagnosis of DVT met the diagnostic criteria of the American Society of Hematology 2020 guidelines for the management of venous thromboembolism [17], and the vascular ultrasound imaging detected by the chief vascular surgeon met the clinical diagnostic criteria of venous thickening, cavity filled with low solid echo, and no blood flow signal; (6) the patient did not have any other related diseases. Exclusion criteria were: (1) patients with comorbidities including heart, liver, and kidney disorders; (2) patients with malignant tumors; (3) patients with systemic infections and immune diseases; (4) patients with psychiatric disorders or cognitive impairment; (5) coagulopathy; (6) patients that had received long-term anticoagulation therapy before participating in the study. The study was approved by the ethics committee of Jingmen Central Hospital (202402007). The clinical data were obtained from the hospital case system, signed consent forms were obtained from all patients and their families. The study adhered to the principles outlined in the Helsinki Declaration.

Methods

Coagulation-related indicators were measured and vascular ultrasound was performed in the two groups. The specific operations were as follows: (1) Vascular ultrasound: ultrasound diagnostic instrument (model: PHILIPS 5500, specification: L12-5) After imaging, the obtained Doppler information was coded, marked by red and blue colors and brightness to distinguish the direction and speed of the patient's blood flow, and superimposed on the B ultrasound

Table 3. Comparison of vascular ultrasound imaging measurements and strain values ($\bar{x} \pm s$).

Group	n	Vs (cm/s)	Vd (cm/s)	PI	RI
The DVT Group	55	39.01 ± 3.91	9.36 ± 0.95	3.51 ± 0.27	3.18 ± 0.32
The Non-DVT Group	61	37.12 ± 3.73	7.87 ± 0.79	3.33 ± 0.34	3.01 ± 0.30
t	-	2.663	2.998	3.135	2.953
p	-	0.009	0.003	0.002	0.004

Notes: Vs, peak systolic velocity; Vd, end-diastolic velocity; PI, pulsatility index; RI, resistance index.

image to observe the blood flow velocity, distribution, direction, etc. The diagnostic criteria of DVT were as follows: ① The patient's vein was thickened, the cavity was filled with low solid echo, and there was no blood flow signal, indicating the formation of DVT. ② The thrombus echo was enhanced, showing strong and low solid echo, and there was punctate blood flow or blood flow column in the blocked lumen indicating DVT delay. ③ Mixed hyperechoic and hypoechoic thrombi, intermittent blood flow signals, valve insufficiency, obvious thickening of the lumen, disappearance of bamboo joints, and blood regurgitation. (2) Detection of coagulation-related indicators: ① One day before surgery, a 5 mL sample of fasting peripheral venous blood was collected from the patient. Samples were centrifuged (TL80, Jiang Yan Tian Li Medical Instrument Co., Ltd., Taizhou, China) at 3500 r/min for 10 min, and stored at –80 °C for later use. ② PT was detected using a kit (GN999367, Shanghai Jing Kang Biological Engineering Co., Ltd., Shanghai, China), APTT was detected using a coagulation kit (9002-04-4, Beijing Ita Biotechnology Co., Ltd., Beijing, China), and D-D was detected using a fluorescence immunochromatography kit (20152400528, Guangzhou Fei Kang Biotechnology Co., Ltd., Guangzhou, China). ③ Samples were also analyzed using an automatic biochemical analyzer (AU5800, Beckman Coulter Co., Ltd., Pasadena, CA, USA), a fluorescence method kit (K349-100, Emeijie Technology Co., Ltd., Wuhan, China), and an o-phthalaldehyde colorimetric method kit (R23238, Shanghai Yuan ye Biotechnology Co., Ltd., Shanghai, China).

Observation Indicators

(1) TT, PT, APTT, FIB and D-dimer (D-D) coagulation-related indices were detected and compared between the two groups. The normal range was TT: 14–21s; PT: 9–13 s; APTT: 20–40 s; FIB: 2–4 g/L; D-D: 0–0.55 mg/L [18].

(2) The vascular ultrasound imaging measurements included peak systolic velocity (Vs), end diastolic velocity (Vd), pulsatility index (PI) and the resistance index (RI). These indices were compared between the two groups. Normal range Vs: 25–40 cm/s; Vd: <40 cm/s; PI: 2.5–4.5; RI: 0.5–0.75 [19].

(3) The efficacy of vascular ultrasound imaging measurements TT, FIB, and D-D for prediction of DVT after secondary traumatic fracture was analyzed.

Table 4. Correlation between each indicator and DVT.

Indicators	DVT		95% CI
	r	*p*	
Vs	0.264	0.004	0.0801∼0.4300
Vd	0.656	<0.001	0.5430∼0.7510
PI	0.293	0.001	0.1120∼0.4559
RI	0.276	0.003	0.0931∼0.4407
TT	–0.249	0.007	–0.4169∼–0.0642
FIB	0.287	0.002	0.1054∼0.4506
D-D	0.251	0.007	0.0670∼0.4192

(4) Multivariate logistic regression analysis was conducted for predictors of DVT after secondary traumatic fracture.

Statistical Analysis

SPSS 21.0 (IBM Corp., Armonk, NY, USA) statistical software was used for data analysis. The count data were expressed as [n (%)] and compared using the χ^2 test. Measurement data were expressed as ($\bar{x} \pm s$), and *t* tests were used for comparisons between the two groups. Spearman correlation analysis was used to analyze correlations between coagulation-related indicators, vascular ultrasound parameters, and DVT risk, and p values < 0.05 were considered statistically significant.

Results

Comparison of General Data of Patients

There were 61 patients in the DVT group and 55 patients in the DVT group. There were no significant differences in gender, body mass index, time from injury to operation, age, fracture site, and underlying diseases between the two groups ($p > 0.05$), as shown in Table 1.

Comparison of Coagulation Function Parameters

The PT and APTT indices of the two groups were not significantly different ($p > 0.05$). The TT of the DVT group was lower than that of the non-DVT group, and the FIB and D-D indices were higher than those of the non-DVT group (t = 2.766, 3.242, 2.649, p = 0.007, 0.002, 0.009), as shown in Table 2.

Table 5. Multivariate logistic regression analysis for predictors of DVT after secondary traumatic fracture.

Project	β	S.E.	Wald X^2	p	OR	95% CI
TT	–0.142	0.058	5.994	0.007	0.868	0.774～0.973
FIB	0.394	0.090	19.165	0.002	1.483	1.244～1.768
D-D	0.706	0.117	36.411	0.009	2.026	1.610～2.549
Vs	1.737	0.354	21.628	0.009	2.208	3.284～8.717
Vd	1.793	0.368	23.774	0.003	1.893	3.921～9.128
PI	1.761	0.335	27.642	0.002	1.820	3.284～10.314
RI	1.894	0.374	25.638	0.004	1.644	3.921～11.258

OR, Odds Ratio.

Table 6. Efficacy of coagulation-related indicators and vascular ultrasound imaging parameters for prediction of deep vein thrombosis (DVT) after secondary traumatic fracture surgery.

Indicators	S.E.	p	95% CI	The best cut-off value	Sensitivity	Specificity	Youden index
Vs	0.044	0.009	0.732～0.815	37.66 cm/s	0.709	0.623	0.332
Vd	0.027	0.003	0.764～0.868	8.63 cm/s	0.818	0.852	0.671
PI	0.028	0.002	0.665～0.786	3.27	0.855	0.475	0.330
RI	0.374	0.004	0.791～0.883	3.02	0.782	0.492	0.274
TT	0.050	0.007	0.630～0.826	18.64 s	0.525	0.727	0.252
FIB	0.045	0.002	0.693～0.870	4.24 g/L	0.691	0.639	0.330
D-D	0.041	0.009	0.736～0.897	853.49 ug/L	0.709	0.590	0.299
Combined testing	0.033	0.002	0.850～0.979	-	0.927	0.879	0.805

Comparison of Vascular Ultrasound Imaging Measurements

The Vs, Vd, PI, and RI measurements of patients in the DVT group were higher than those in the non-DVT group (t = 2.663, 2.998, 3.135, 2.953, p = 0.009, 0.003, 0.002, 0.004), as shown in Table 3.

Correlation between Each Index and DVT

Spearman correlation analysis showed that Vs, Vd, PI, RI, FIB, and D-D were positively correlated with the risk of DVT after secondary traumatic fracture surgery (r = 0.264, 0.656, 0.293, 0.276, 0.287, 0.251, $p < 0.05$). TT was significantly negatively correlated with the risk of DVT after secondary traumatic fracture surgery (r = –0.249, $p < 0.05$), refer to Table 4.

Multivariate Logistic Regression Analysis for Predictors of DVT after Secondary Traumatic Fracture

FIB, D-D, Vs, Vd, PI and RI were independent risk factors for DVT after secondary traumatic fracture surgery (Odds Ratio (OR) = 1.483, 2.026, 2.208, 1.893, 1.820, 1.644, $p < 0.05$). TT index was an independent protective factor for DVT after secondary traumatic fracture surgery (OR = 0.868, $p < 0.05$), as shown in Table 5.

Efficacy Analysis of Coagulation-Related Indices and Vascular Ultrasound Imaging Parameters on the Occurrence of DVT after Secondary Traumatic Fracture

The sensitivity and specificity for DVT prediction based on combined coagulation-related indicators and vascular ultrasound imaging parameters were higher than those of individual measurements ($p < 0.05$), as shown in Table 6.

Discussion

The incidence of DVT after secondary traumatic fracture surgery is high, and this condition contributes to unexpected mortality in the hospital. DVT is one of the most common complications after fracture surgery, and can not only cause disability in patients, but can also lead to the occurrence of pulmonary thromboembolism. Moreover, due to the atypical symptoms, pulmonary embolism in patients is usually difficult to detect, and 70% of pulmonary embolism is detected after the death of patients. Data show that the mortality rate of DVT is 20% at 2 years and as high as 31% at 8 years [20]. DVT after secondary traumatic fracture surgery is characterized by a high disability rate and high mortality. These effects on the physical health and psychology of patients, and the high cost of diagnosis and treatment, can aggravate the burden for patients and their families. Therefore, it is very important to identify factors that contribute to DVT formation and carry out prevention or diagnosis and treatment as soon as possible [21].

This study showed that Vs, Vd, PI, RI, FIB, and D-D indices in the DVT group were higher than those in the non-DVT group, and TT in the DVT group was lower than that in the non-DVT group. Vs, Vd, PI, RI, FIB, and D-D were positively correlated with the formation of DVT, and were significant risk factors for DVT in multiple regression analysis (OR >1). TT was negatively correlated with the formation of DVT, and was a significant protective factor against DVT (OR <1). The sensitivity and specificity for DVT prediction based on combined coagulation-related indicators and vascular ultrasound imaging measurements were higher than those of individual measurements. Xu Q *et al*. [22] reported that Doppler ultrasound detection can effectively predict the occurrence of DVT in patients. In addition, Langella V *et al*. [23] reported that coagulation function parameters were correlated with DVT formation and poor prognosis of patients. The above results are consistent with the results of the present study, and further support its conclusions. (1) D-D formation begins with conversion of fibrinogen into fibrin monomers by thrombin, and these monomers polymerize to form fibrin. D-D is a product of cross-linked fibrin degradation, and fibrin is one of the main components of thrombosis, so the production of D-D can indirectly reflect the formation and dissolution of thrombi. Previous studies have shown that the increase in the D-D index level indicates a hypercoagulable state of blood and secondary hyperfibrinolysis, which is an important independent predictive risk factor for the occurrence of DVT. Thus, D-D plays an important role in the diagnosis and treatment of thrombotic diseases in patients [24]. In addition, Cheng J *et al*. [25] showed that the early monitoring of patients' FIB and other indicators was an important predictor of postoperative DVT through the study of DVT formation in patients with traumatic lower limb fracture surgery. The reason is that FIB is the most abundant of all coagulation factors; its content is far higher than that of other coagulation factors. FIB binds to the platelet receptor and promotes platelet aggregation. When its level rises, coagulation in patients is promoted, which is an important factor for thrombosis. Previous studies have pointed out that TT reflects the blood coagulation time after the addition of standardized thrombin in plasma. When its index is too low, it indicates that the body's blood is in a hypercoagulable state, increasing the likelihood of DVT in patients. Thus, TT can predict the formation of DVT and is an important influencing factor [26]. (2) Vs, Vd, PI, and RI are important measurements of ultrasound detection, during which waves reflect back through the interface generated by different tissues to form images. This imaging technique can effectively evaluate the intravascular situation of patients, allowing one to assess the elasticity and thickness of the blood vessel wall and to observe blood flow dynamics in the vessels. When the index measurements increase, it means that the peripheral blood vessel contraction and blood flow velocity have increased due to the body's hypercoagulable state and blood vessel blockage. Previous studies have shown that the compression ultrasound technique for multiple sites, using a probe to diagnose patients, can effectively assess patient thrombosis. Therefore, vascular ultrasound imaging measurements and coagulation indices have a clear relationship to the formation of DVT [27]. Previous studies have found that coagulation indicators in patients after total hip replacement have diagnostic value for the formation of DVT. Measurements collected using vascular ultrasound can effectively evaluate the risk of DVT formation before and after an operation. Moreover, the predictive value of combined coagulation-related indicators and vascular ultrasound imaging measurements is higher than that of individual measurements [28,29,30].

There are some limitations in this study. Firstly, our sample size is relatively small. Second, the study had a single-center design and was conducted in a specific health care setting, and the special characteristics of that setting may limit the generalizability of the findings to other health care settings with different backgrounds and care practices. Finally, this study was a retrospective study, with the potential for bias caused by confounding factors. Moreover, since the study was correlational in nature, causation could not be established. Despite the limitations of this study, it still provides substantial support for the ability of coagulation-related indicators and vascular ultrasound imaging parameters to predict postoperative DVT formation. In the future, further multi-center and large-sample studies are needed to verify our results to make up for these limitations and establish a more accurate prediction model to provide reference for clinical practice.

Conclusions

In conclusion, the combination of coagulation-related indicators and vascular ultrasound imaging parameters can predict the formation of postoperative DVT, and the combined detection has high sensitivity and specificity. It can effectively screen high-risk groups and carry out effective intervention in time to reduce the risk of DVT.

Availability of Data and Materials

The datasets used or analysed during the current study were available from the corresponding author on reasonable request.

Author Contributions

YD and XL: designed the study; XL and XX: collected and analyzed the data; YD and XX: participated in drafting the manuscript. All authors conducted the study and contributed to critical revision of the manuscript for important intellectual content. All authors gave final approval of the version to be published. All authors participated fully in the work, took public responsibility for appropriate potions of the content, and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or completeness of any part of the work were appropriately investigated and resolved.

Ethics Approval and Consent to Participate

The study was approved by the ethics committee of Jingmen Central Hospital (202402007). Since the clinical data were obtained from the hospital case system, signed consent forms were obtained from all patients and their families. The study adhered to the principles outlined in the Helsinki Declaration.

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Conflict of Interest

The authors declare no conflict of interest.

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