

ORIGINAL ARTICLE

The Application Value of the D-Dimer Critical Value in Diagnosing Deep Vein Thrombosis in Patients with Bone Trauma

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SUMMARY

Background: D-dimer is used as a clinical indicator to predict venous thromboembolism, and some hospitals have included it in the critical value project. We aimed to evaluate whether the setting of a D-dimer critical value is helpful in the diagnosis of deep vein thrombosis in patients with bone trauma and to explore the rationality of setting a D-dimer critical value limit.

Methods: The clinical data of 4,897 bone trauma patients, hospitalized from April 1, 2022, to March 31, 2023, were retrospectively analyzed. Our hospital set the critical value limit for when the D-dimer value was greater than 15.0 mg/L, and Bayesian model was used to evaluate the relationship between deep vein thrombosis and the D-dimer limit.

Results: During this period, 199 times the D-dimer detection value was greater than 15.0 mg/L, and the critical value was reported and accounted for 4.06%. The predicted probability of lower limb venous thrombosis in patients who triggered the critical value of D-dimer was 40.21%, and the actual incidence was 34.67%. There were 376 patients with lower limb venous thrombosis during hospitalization, and 81.38% of the D-dimer value did not reach the critical value limit.

Conclusions: The role of D-dimer as a critical value item in predicting DVT in patients with orthopedic trauma is small. Whether to list D-dimer as a critical value item can be comprehensively considered according to the own situation of medical institutions and the recommendations of clinicians. The same can be applied for the setting of critical value boundaries.

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KEYWORDS

D-dimer, critical value, bone trauma, deep vein thrombosis, lower limb vein thrombosis

INTRODUCTION

The lower limb blood stasis, caused by vascular intima injury, blood hypercoagulability and braking in patients with bone trauma, is easy to cause lower limb vein thrombosis (DVT) and pulmonary embolism (PTE) [1-2]. The high sensitivity and the high negative predictive value of D-dimer make it suitable for risk assessment and screening of DVT after bone trauma. At present, the Caprini risk assessment combined with age adjusted D-dimer is commonly used in clinical practice to predict

the occurrence of DVT, and then color Doppler vascular ultrasound results are used as diagnostic criteria for the formation of DVT. If the formation of DVT is not detected and treated in time, it may cause fatal pulmonary embolisms or post-thrombotic syndrome, that seriously affects the prognosis. Therefore, some hospitals set D-dimer as a critical value item. Through the critical value reporting system, clinicians know the detected critical value and can, therefore, deal with patients in a timely manner. However, there is no uniform standard or procedure for the determination of the critical value limit, at present. Generally, the selection of D-dimer critical value items is determined after demonstration by clinical departments, laboratory departments, hospital administrative departments, and other personnel. Therefore, there is no data demonstration or reference support for setting a D-dimer critical value limit or for the evaluation of the use effect [3-4].

This study intends to evaluate the efficiency of D-dimer critical value in predicting the occurrence of DVT by analyzing the clinical data of perioperative bone trauma patients and to explore the optimal D-dimer critical value limit [5].

MATERIALS AND METHODS

General information

Clinical data of orthopedic trauma patients, hospitalized between April 1, 2022, and March 31, 2023, were retrospectively analyzed, and a total of 4,897 patients were included in the study. Inclusion criteria: patients with perioperative bone trauma. Exclusion criteria: patients younger than 10 years of age, patients with infection, pregnancy, or cancer, and patients who were previously taking anticoagulant or antiplatelet drugs.

Whether the patient developed DVT during hospitalization was confirmed by ultrasonography of deep veins of both lower limbs. Depending on the severity of the patient's condition, D-dimer may be tested one or more times. If a patient did not develop DVT, the highest value of multiple measurements was used as the D-dimer test value for inclusion in the study. If a patient developed DVT, D-dimer measurements on the day of diagnosis were included in the study.

Critical value setting

D-dimer has been listed as a critical value item of clinical departments in our hospital, which was determined by the medical affairs department, clinical departments, and clinical laboratory departments through consultation. When the D-dimer value is greater than 15 mg/L (reported once per patient), a critical value alert is triggered, and the laboratory staff should report the critical value to the clinical department within 5 minutes.

Instruments and reagents

Instrument: ACL-TOP700 automatic coagulation analyzer of American Beckman Kurt Company.

Reagent: original reagent matched with the instrument. Methodology: D-dimer is detected by immune turbidimetry.

Reference interval: 0 - 0.5 mg/L.

Statistical methods

D-dimer values and Caprini risk assessment are plotted with receiver operating characteristic (ROC) curves, and the area under the curve (AUC) was calculated.

The DVT probability of each laboratory test value was calculated according to Bayes theorem to reflect the curve relationship between laboratory value and DVT probability prediction ability [6].

STATA/MP 17.0 was adopted for statistical analysis.

RESULTS

Among 4,897 patients included in the study, 376 patients had DVT, and the incidence of thrombosis was 7.68%. As seen in Table 1 for baseline characteristics of patients, our hospital sets the critical value limit for when the D-dimer value is greater than 15.0 mg/L, which needs to be reported to the clinic, according to the critical value process. During hospitalization, the same patient is reported as critical only once.

During this period, 199 D-dimer detection values > 15.0 mg/L were reported, and the critical value accounted for 4.06%. The probability of DVT in patients who triggered the critical value of D-dimer was 34.67%. There were 376 patients with DVT, and 81.38% D-dimer value did not reach the critical value limit. The risk of DVT was assessed by Caprin score, and the proportion of high-risk patients with DVT reached 45.21%. In addition, the risk of DVT cannot be completely excluded for low-risk patients.

D-dimer test is the only blood test that can help diagnose DVT, and usually has a high negative predictive value and sensitivity, but the specificity is low. The possibility of DVT can be judged clinically by combining D-dimer test and Caprini score. The AUC of Caprini score is 0.8204, and the AUC of D-dimer is 0.8274 (Figure 1).

The optimal limit of D-dimer was calculated according to Bayes theorem. By analyzing Table 2, it can be seen that when the critical value threshold of D-dimer is 15.0 mg/L, the highest probability of DVT is 40.21%. From Figure 2, the probability, that the highest incidence of DVT predicted by D-dimer value does not exceed 50%, is obtained.

DISCUSSION

Critical value reporting is the primary post-test phase activity of the laboratory, and it is an area in which the laboratory plays an active role in the clinical chain of care by alerting clinical colleagues to avoid adverse results. Inappropriate critical value thresholds can lead to

Table 1. Baseline characteristics of the patients.

Factor	Total number of patients (4,897)	DVT group (376 (7.68%))	Non-DVT group (4,521 (92.32%))
Age (years)			
10 - 17	74 (1.51%)	0 (0.00%)	74 (1.64%)
18 - 49	1,265 (25.83%)	14 (3.72%)	1,354 (29.95%)
50 - 64	1,866 (38.10%)	68 (18.09%)	1,798 (39.77%)
65 - 79	1,466 (29.94%)	119 (31.65%)	1,347 (29.79%)
≥ 80	299 (6.11%)	61 (16.22%)	238 (5.26%)
Gender			
Male	2,523 (51.52%)	118 (31.38%)	2,405 (53.20%)
Female	2,374 (48.48%)	258 (68.62%)	2,116 (46.80%)
D-dimer (mg/L)			
< 0.5	2,276 (46.48%)	2 (0.53%)	2,273 (50.28%)
0.5 - 15.0	2,422 (49.46%)	292 (77.66%)	2,130 (47.11%)
> 15.0	199 (4.06%)	80 (21.28%)	119 (2.63%)
Caprin Score			
0 - 2	3,292 (67.22%)	57 (15.16%)	3,235 (71.55%)
3 - 4	658 (13.44%)	39 (10.37%)	619 (13.69%)
≥ 5	947 (19.34)	170 (45.21%)	880 (19.46%)

Remarks: 0 - 2 points (low-risk); 3 - 4 points (medium-risk); ≥ 5 points (high-risk).

Table 2. Prediction probability of DVT occurrence with different D-dimer thresholds and reporting proportion of critical value.

D-dimer (mg/L)	> 5.0	> 10.0	> 15.0	> 20.0	> 25.0	> 30.0
DVT probability (%)	28.05	34.4	40.21	37.2	38.38	31.38
Proportion of critical value (%)	11.58	6.48	4.06	2.47	1.76	1.04

over- or under notification. The former can lead to alarm fatigue, while the latter risks delaying the timely treatment of critically ill patients. There is currently a limited basis for defining critical outcome thresholds, and to some extent, this is a challenge in designing outcome threshold studies in different laboratories [7-9]. Although the concept of critical value is widely used, the selection conditions and parameter limits of critical value are still controversial. In 2016, the China clinical laboratory center investigated the hematology critical value items of 862 laboratories nationwide [10], and only 120 (13.92%) laboratories listed D-dimer as a critical value item. Because the critical value limits of D-dimer set by different laboratories are very different, no consensus can be reached [6,8]. The American Society of Hematology's 2018 Guidelines for the management of venous thromboembolism has clear recommendations on the diagnosis of DVT in the lower extremities. For

low-risk patients, the standard D-dimer threshold (< 0.5 mg/L) is used to exclude DVT strategy, and then ultrasonic examination of the lower extremities is conducted for the patients who need additional examination [11-13]. In patients with medium- and high-risk, it is recommended to perform lower limb ultrasound examination directly, because the efficacy of D-dimer is low, especially in patients with suspected recurrence [14]. In 2021, China issued the first VTE guideline for orthopedic trauma; guidelines for the prevention of perioperative venous thromboembolism in Chinese orthopedic trauma patients (2021), recommending patients with a positive D-dimer examination before surgery to perform a Doppler ultrasound examination of both lower limbs. The data of this study shows that the probability of excluding DVT is 99.91% for patients with D-dimer < 0.5 mg/L, which indicates that D-dimer is an indicator with high negative predictive value. Our hospital sets the D-

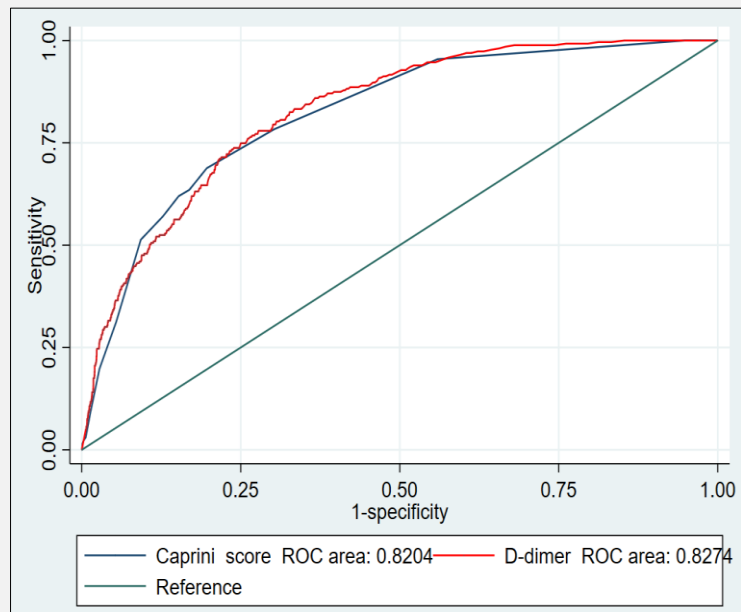


Figure 1. Caprini score of DVT and ROC curve of D-dimer.

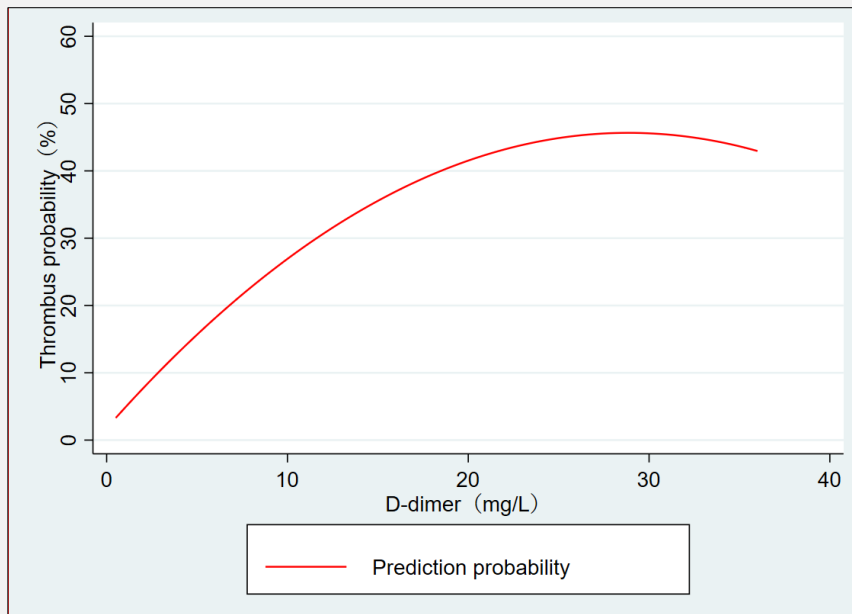


Figure 2. Prediction probability of DVT according to the D-dimer value.

dimer critical value limit as 15.0 mg/L, and the critical value needs to be reported if it exceeds this limit. The reporting rate of D-dimer critical value is about 4.06%, and the reporting intensity of critical value is not high. However, the probability of DVT in patients who trigger the D-dimer critical value is 34.67%, while when 376 patients have DVT, only 18.62% of D-dimer critical value alerts. These facts indicate that the D-dimer critical value limit is 15.0 mg/L, which has a limited effect on an auxiliary diagnosis of DVT, and whether the D-dimer critical value limit is increased or decreased, it is not high enough for predicting the incidence of DVT. In addition, if the critical value limit is lowered, the critical value notification rate will increase, which will increase the workload of medical staff and affect the work efficiency. Therefore, it is questionable whether D-dimer should be listed as a critical value item in the department of orthopedics and traumatology.

In general, the role of D-dimer as a critical value in predicting DVT in patients with orthopedic trauma is small, because not every patient with D-dimer critical value will develop DVT, and many patients with DVT fail to reach the critical value limit. However, in clinical practice, some suddenly increased high D-dimer values can still provide help for a clinical auxiliary diagnosis of DVT, and clinicians also need to exclude the occurrence of DVT in patients in time through the early warning of critical D-dimer values. Due to the differences in the specific conditions of various medical institutions and due to the fact that the characteristics of the distribution of patients are not the same, whether to list D-dimer as a critical value item can be comprehensively considered according to the own situation of medical institutions and the recommendations of clinicians, and the same can be applied for the setting of the critical value limit.

Declaration of Interest:

All authors declare that they have no competing interests.

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