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The combination of Caprini risk assessment scale and thrombotic biomarkers to evaluate the risk of venous thromboembolism in critically ill patients

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Abstract

To evaluate the correlation between the Caprini risk assessment scale and plasma thrombosis biomarkers and estimate the validity of this method in identifying critically ill patients at high risk of venous thromboembolism (VTE).

Patients with VTE who were admitted to the intensive care unit (ICU) department of West China Hospital SiChuan University from October 2016 to October 2017 were enrolled in this case–control study. We retrieved relative clinical data and laboratory test results included in the Caprini risk assessment scale to calculate the Caprini score and compared thrombosis biomarkers between various risk stratifications (low, moderate, high, and highest).

A total of 151 critically ill patients were enrolled in our research, including 47 VTE and 94 non-VTE patients. The differences in Caprini score and levels of thrombosis biomarkers between the VTE and control group were significant. Thrombomodulin (TM) was positively correlated with Caprini score (*R*-value was .451, $P < .05$). Based on the receiver operating characteristic analysis, TM, tissue plasminogen activator-inhibitor complexes, D-dimer, and fibrinogen degradation products had a certain diagnostic efficiency in distinguishing VTE from others ($P < .05$). Using the logistic regression model, we identified that 5 risk factors, namely drinking history, major surgery (>3 hours), swollen legs (current), TM, and D-dimer, were independent factors for the occurrence of VTE in critically ill patients admitted in the ICU.

Thrombosis markers were positively correlated with Caprini risk stratification. The combination of plasma markers and Caprini risk assessment scale can further increase the predictive value in critically ill patients with VTE.

Abbreviations: BMI = body mass index, CTPA = computed tomography pulmonary angiogram, DD = D-dimer, FDP = fibrinogen degradation products, MPRA = magnetic resonance pulmonary angiography, PIC = α_2-plasmin inhibitor-plasmin complexes, PTE = pulmonary thromboembolism, ROC = receiver operating characteristic curve, TAT = thrombin–antithrombin complexes, TM = thrombomodulin, t-PAIC = tissue plasminogen activator-inhibitor complexes, VTE = venous thromboembolism.

Keywords: Caprini risk assessment scale, critically ill patients, risk assessment, thrombosis biomarkers, venous thromboembolism

1. Introduction

Venous thromboembolism (VTE) is the third most common vascular disease following acute coronary syndromes and stroke.[1] As it lacks specific clinical manifestations, the rate of misdiagnosis and omission diagnosis of VTE was high. How to take effective measures to reduce the morbidity and mortality of VTE, especially in high-risk patients, is very important.[2]

The VTE prevention guidelines formulated by the American college of chest physicians (ACCP) in 2012 clearly indicated that all critically ill patients required VTE risk assessment, and preventive treatment should be undertaken for high-risk patients. In the recent years, Caprini risk assessment model has been extensively verified in VTE risk identification and individualized prevention of different patients and has made some achievement.[3–6] At the same time, the determination of various thrombosis biomarkers in plasma has been increasingly emphasized in clinical and research fields.[7–9] Markers of coagulation (thrombomodulin [TM]); markers of thrombin generation (thrombin–antithrombin complex [TAT]); markers of fibrinolysis (α2-plasmin inhibitor-plasmin complexes [PIC]), and tissue plasminogen activator-inhibitor complexes (t-PAIC)) could effectively represent all the stages in the clotting pathway.[10,11]

However, in clinical applications, we found that some patients had low Caprini scores because of hidden early symptoms upon admission, but with increased plasma thrombosis biomarker levels, which could sensitively reflect the abnormality of coagulation system. Moreover, some patients in the high and highest risk groups of the Caprini model had normal levels of thrombosis biomarkers, for example, a young patient could have plaster immobilization, history of inflammatory bowel disease, or laparoscopy test, but normal levels of thrombosis biomarkers. Even if their risk scores according to the Caprini model can be over 5 points indicating highest risk, an overtreatment with prophylactic therapy is suspected. Therefore, we conducted this research to evaluate the correlation between Caprini model and thrombosis biomarkers to better identify the VTE. We retrospectively analyzed the plasma thrombosis risk markers and the Caprini risk model in VTE patients to evaluate the correlation between the Caprini risk assessment scale and plasma

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thrombosis biomarkers and estimate the validity of this method in identifying critically ill patients at high risk of VTE.

2. Methods

The study protocol was approved by West China Hospital's ethical review board, and informed consent was obtained from the patients or their families. We confirmed that all methods were performed in accordance with relevant guidelines and regulations.

2.1. Patients

Data of VTE patients who were admitted to the ICU department of West China Hospital SiChuan University from October 2016 to 2017 were retrospectively analyzed in this study. The inclusion criteria of VTE patients were aged >18 years; deep venous thrombosis (DVT) diagnosed using upper and lower limb duplex ultrasonography or venography, pulmonary thromboembolism (PTE) diagnosis confirmed using computed tomography pulmonary angiogram (CTPA), radionuclide pulmonary ventilation, perfusion scanning, magnetic resonance pulmonary angiography (MPRA), and pulmonary angiography; and complete and full clinical data. The exclusion criteria of VTE group were patients with superficial vein thrombosis and patients who refused to be evaluated by the assessment or dropped out. We recorded data regarding patients' age, sex, BMI, cancer history, smoking history, drinking history, hematology test, biochemical indicator, and inflammatory biomarkers for baseline analysis. Moreover, we retrieved the relative clinical data and laboratory test results included in the Caprini risk assessment scale of eligible patients in calculating the Caprini score. All patients were evaluated using the Caprini risk assessment model revised in 2009 for risk scoring and stratification.[12] This risk assessment model included 40 risk factors, which covers many risk factors for VTE in hospitalized patients. Each risk factor was assigned a 1 to 5 score according to the corresponding risk levels. We calculated the total score and divided patients into 4 grades: low risk (0–1 point), moderate risk (2 points), high risk (3–4 points), and highest risk (≥5 points). In addition, we compared the thrombosis biomarkers between different risk stratifications (low, moderate, high, and highest).

2.2. Biomarker testing

All biomarker tests were performed using automatic analyzers and recommended reagents, under strict quality control following the manufacturer's instructions. Levels of TM, TAT, PIC, and t-PAIC were measured using an automatic chemiluminescence analyzer (HISCL-5000; Sysmex, Japan). Levels of fibrinogen degradation products (FDP) and D-dimer were measured using an automatic immunonephelometric analyzer (CS5100; Sysmex, Japan).

2.3. Statistical analysis

All data were analyzed using the SPSS software (version 19.0; SPSS Inc., Chicago, IL). Differences in the patients' demographic characteristics and biomarker levels were analyzed using the *t*-test or Mann–Whitney *U* test.[13] All tests were two-tailed, and *P*-values of $< .05$ were considered statistically significant. The risk grading comparison was evaluated using the chi-square test. The correlation between the thrombosis markers and Caprini score in patients was evaluated using the Spearman correlation analysis. Receiver operating characteristics (ROCs) were used to determine the values for sensitivity, specificity, areas under the receiver operating characteristic curves (AUROC), and cutoff values. VTE in ICU patients was taken as a dependent variable (VTE: $Y=1$, non-VTE: $Y=0$). We evaluated 40 risk factors in the Caprini assessment model and thrombosis biomarkers using the uni- and multivariate logistic regression analyses as independent risk factors to predict the occurrence of VTE in critically ill patients. Risk factors in the Caprini model were assessed as binary variables, and thrombosis biomarkers were assessed as continuous variables, assuming the linear relationships between biomarker levels and log odds of VTE, conditioning on other variables. The multivariable results were expressed by odds ratios (OR) with 95% confidence intervals (CI) and the ORs were adjusted by age, sex, and history of alcohol consumption. Variable screening method in multivariate logistic regression analysis: backward selection based on likelihood ratio.[14]

3. Results

3.1. The baseline data of clinical and laboratory characteristics

A total of 151 critically ill patients were enrolled in our research, including 47 VTE and 94 non-VTE patients during the same period in the ICU department. When we compared the groups with and without VTE, a significant difference was observed in drinking history. However, we did not detect any significant differences in their demographic characteristics, BMI, tumor history, smoking history, time of invasive ventilation, time of mechanical ventilation, hematology test, biochemical indicator, coagulation time, and inflammatory biomarkers (Table 1).

3.2. Comparison of the Caprini score and risk stratification between the VTE and control groups

The Caprini score of VTE group was higher than that of non-VTE group, and the difference was statistically significant ($P < .001$). In the VTE group, 95.7% of patients were categorized in the highest- or high-risk group. However, among the non-VTE patients, although their Caprini scores were on average lower than those of the VTE patients, 88.3% of non-VTE patients were categorized as having a high or highest risk of having VTE, suggesting that using the Caprini score overestimated the risk of VTE in these patients. The details are shown in Table 2.

3.3. Comparison of the plasma biomarkers between the VTE and control groups

Thrombosis biomarkers reflected the dysfunction of coagulation, anticoagulation, and fibrinolytic system. We measured 6 thrombosis biomarkers in 151 critically ill patients and the results indicated that the VTE group had significantly higher levels of TM, PIC, FDP, and D-D, compared to the control group (all $P < .05$). No significant differences were observed in TAT and t-PAIC levels between the 2 groups (Table 3).

3.4. Comparison of thrombosis biomarkers in different risk stratification of Caprini assessment model

We further confirmed the changes in the level of thrombosis indicators between different risk grading groups. Table 4 shows a significant difference in TM and t-PAIC among different Caprini risk stratification groups (low, moderate, high, and highest). The level of TM in the highest-risk group was obviously higher than

Table 1

Baseline of clinical parameter in venous thrombosis and control group.

	VTE group (n = 47)	Control group (n = 94)	P
Age	55.85 (66–48)	53.85 (68–44.75)	.354
Sexy (M/F)	38/9	62/32	.066
BMI	22.6 (20.2–24.2)	22.0 (19.7–24.9)	.906
Cancer (yes/no)	5/42	15/79	.393
Smoking (yes/no)	18/29	31/63	.532
Drinking (yes/no)	23/24	29/65	.036*
Department (internal/surgery)	44/50	14/33	.053
Time of invasive ventilation (h)	49.55	39.85	.233
Time of mechanical ventilation (h)	49.55	39.85	.233
Hematology test			
RBC, $\times 10^{12}$/L	3.21 (2.65–4.31)	3.40 (2.88–4.56)	.084
Hb, g/L	98 (77–130)	114 (89–133)	.102
PLT, $\times 10^{9}$/L	156 (100–216)	179 (107–243)	.320
WBC, $\times 10^{9}$/L	10.62 (7.72–15.21)	10.28 (7.13–14.8)	.610
Biochemical indicator			
TB, μmol/L	13.6 (9.3–22.3)	13.2 (9.3–22.7)	.812
DB, μmol/L	6.9 (4.3–12.0)	6.6 (3.8–11.9)	.675
TP, g/L	59.9 (52.2–66.6)	60.6 (54.1–69.8)	.252
ALB, g/L	32.5 (27.4–38.8)	35.6 (29.4–41.7)	.169
ALT, IU/L	26 (12–56)	24 (15–49)	.888
AST, IU/L	29 (22.8–92)	36 (22.0–69)	.620
ALP, IU/L	79 (66–139)	85 (65–124)	.988
GGT, IU/L	31 (15–110)	38 (20–77)	.791
UREA, mmol/L	6.83 (4.3–11.0)	6.3 (4.05–10.0)	.424
CREA, μmol/L	73 (51–125)	68 (48–94)	.300
CYS-C, mg/L	1.03 (0.86–1.39)	1.04 (0.82–1.42)	.623
UA, μmol/L	281 (170–423)	275 (147–403)	.454
TG, mmol/L	1.33 (0.98–2.11)	1.58 (0.9–2.45)	.592
TC, mmol/L	2.55 (1.93–3.49)	2.88 (1.97–3.78)	.411
HDL-C, mmol/L	0.39 (0.28–0.59)	0.52 (0.28–0.76)	.151
LDL-C, mmol/L	1.16 (0.71–1.84)	1.33 (0.6–1.91)	.839
Coagulation time			
PT, seconds	13.7 (12.0–15.2)	13.1 (11.5–15.2)	.640
APTT, seconds	36.3 (30.1–46.5)	32.3 (28.4–42.2)	.109
TT, seconds	18.0 (17.3–19.0)	18.4 (17.1–19.6)	.598
FIB, g/L	2.39 (1.77–4.28)	2.89 (2.10–4.45)	.209
ATIII (%)	63.0 (47.5–82.4)	70.5 (55.3–85.9)	.237
Inflammatory biomarkers			
IL-6, pg/mL	74.8 (32.4–166.9)	65.3 (25.7–187.7)	.668
CRP, mg/L	104 (59.4–139)	74.9 (13.8–143)	.050

The data were described as median with interquartile range.

ALB = albumin, ALP = alkaline phosphatase, ALT = alanine transaminase, APTT = activated partial thromboplastin time, AST = aspartic transaminase, ATIII = antithrombinIII, CREA = creatinine, CRP = C reactive protein, CYS-C = cystatin C , DB = direct bilirubin, FIB = fibrinogen, GGT = gamma-glutamyl transpeptidase, HDL = high-density lipoprotein, IL-6 = interleukin-6, LDL = low-density lipoprotein, PT = prothrombin time, TB = total bilirubin, TC = total cholesterol, TG = triglyceride, TP = total protein, TT = thrombin time, UA = uric acid.

Table 2

The frequency of different risk rating in VTE and control group.

	VTE group (n = 47)	Control group (n = 94)	P
Caprini score	10 (7–12)	6 (3–10)	.000*
Risk rating, n (%)			.012*
Low (0–1)	1 (2.13%)	9 (9.57%)	
Moderate (2)	1 (2.13%)	12 (2.12%)	
High (3–4)	9 (19.14%)	16 (17.02%)	
Highest (⩾5)	36 (76.60%)	57 (71.29%)	

The data were described as median with interquartile range or n (%).

Table 3

The comparison of thrombosis biomarkers in venous thrombosis and control group.

	VTE group (n = 47)	Control group (n = 94)	P
TM, TU/mL	15.97 (11.57–27.17)	11.55 (8.99–15.22)	.000*
TAT, ng/mL	8.70 (5.03–20.04)	8.24 (3.59–18.64)	.213
PIC, μg/mL	1.48 (0.99–2.09)	0.97 (0.60–1.70)	.003*
t-PAIC, ng/mL	5.53 (4.30–11.39)	7.61 (4.55–12.90)	.234
DD, mg/L	7.56 (4.35–13.41)	4.36 (1.87–9.55)	.011*
FDP, mg/L	17.3 (11.1–31.7)	10.1 (4.5–21.5)	.008*

The data were described as median with interquartile range.

DD = D-dimer, FDP = fibrinogen degradation products, PIC = α_2-plasmin inhibitor-plasmin complexes, TAT = thrombin–antithrombin complexes, TM = thrombomodulin, t-PAIC = tissue plasminogen activator-inhibitor complexes.

that of low-risk group, a significant P (TM_{low} vs $TM_{highest}$) was obtained through a pairwise comparison ($P = .001$). A significant higher level of TM was observed in the highest-risk group than that of moderate-risk group through a pairwise comparison ($P = .005$). The other thrombosis biomarkers showed no significant difference among various risk grades.

Based on Spearman correlation analysis, Caprini score was positively correlated with TM ($R = .451$, $P = .001$), and both reflected a similar variation tendency of the risk of VTE.

3.5. ROC analysis on thrombosis markers in discriminating Caprini different risk stratification groups and VTE/non-VTE

We conducted ROC curve analysis to evaluate the ability of biomarkers to discriminate among patients who had highest and high risk developed VTE. Based on the ROC results, TM, t-PAIC, D-D, and FDP had a certain diagnostic efficiency in discriminating the highest group and highest + high group from others. Comparatively speaking, TM was the best. The AUROC was .775 for TM (95% CI: .655-.894) in discriminating the highest +high group from others (Table 5 and Fig. 1).

We further conducted ROC analysis for diagnostic power of thrombosis biomarkers in distinguishing VTE from non-VTE (Table 6 and Fig. 2). Based on the statistical results, these biomarkers were suggested to have a certain diagnostic efficiency in thrombosis status, which reconfirmed the value of thrombosis biomarkers in the diagnosis of VTE.

3.6. Logistic regression analysis of the Caprini assessment scale and thrombosis biomarkers for VTE

We used 40 risk factors in Caprini risk assessment scale and thrombosis markers as independent variables to perform logistic regression analysis. Using the uni- and multivariate logistic regression, we identified that 5 risk factors as the independent predictors of VTE in critically ill patients: drinking, OR 2.523 (95% CI [1.071–5.943]); major surgery (>3 hours), OR 5.506 (95% CI [1.407–21.537]); swollen legs (current), OR 5.933 (95% CI [1.825–19.287]); TM, OR 1.089 (95% CI [1.033–1.147]); D-dimer, OR 1.076 (95% CI [1.022–1.133]), $P < .05$ (Table 7 and Fig. 3).

4. Discussion

ICU patients are susceptible to VTE because of long-term immobilization, various surgical treatments, trauma, and

Table 4

The comparison of thrombosis biomarkers in different level of Caprini assessment model.

	Low (n = 10)	Moderate (n = 13)	High (n = 25)	Highest (n = 93)	*P*
TM, TU/mL	8.17 (6.42–10.82)[#]	10.30 (8.64–11.44)[*]	13.33 (8.76–14.72)	14.28 (10.37–21.65)	.000
TAT, ng/mL	6.14 (4.58–17.23)	7.38 (3.82–31.47)	4.50 (2.65–21.52)	8.59 (4.95–19.63)	.490
PIC, μg/mL	1.19 (0.95–1.60)	1.04 (0.67–2.74)	0.85 (0.58–2.01)	1.18 (0.65–1.84)	.956
t-PAIC, ng/mL	4.42 (2.45–6.08)	8.02 (6.93–9.55)	5.50 (4.18–8.48)	7.40 (4.87–12.70)	.024

The data were described as median with interquartile range, #:*P* (TM_{low} vs $TM_{highest}$): 0.001, *:*P* ($TM_{moderate}$ vs $TM_{highest}$): 0.005.
PIC = α_2-plasmin inhibitor-plasmin complexes, TAT = thrombin–antithrombin complexes, TM = thrombomodulin, t-PAIC = tissue plasminogen activator-inhibitor complexes.

hypercoagulable state. The clinical symptoms and physical signs in patients with VTE greatly varied; however, these may be ignored by clinicians, leading to a low clinical detection rate and high rate of VTE misdiagnosis.[15] Therefore, risk assessment of VTE, including the Caprini score, is recommended for critically ill patients, and the ACCP's effective preventive measures for the prevention and treatment guidelines of VTE should be followed.[16] In cases when Caprini score is inconsistent with the levels of thrombosis biomarkers, which would lead to confusion on thrombosis diagnosis, the relationship between the 2 methods of prevention and treatment of VTE should be determined immediately.

Our results demonstrated that the Caprini score in VTE patients was obviously higher than that in non-VTE patients, with the proportion of highest and high stratification of VTE reaching up to 95.74%. However, although the Caprini scores in non-VTE patients were lower than those in VTE patients, 88.3% of them were categorized as having a high or highest risk of having VTE, suggesting that using the Caprini score over-estimated the risk of VTE. Therefore, laboratory thrombosis biomarkers should be fully integrated to improve the thrombosis prevention strategy for clinical comprehensive consideration.

Further analysis showed that with the increasing of Caprini risk score, the levels of thrombosis biomarkers also presented the corresponding trend, which strengthens the coagulation factor activity and inhibits the anticoagulant and fibrinolytic system. The status suggested that the more risk factors developed, the more serious is the dysfunction of the coagulation and anticoagulation system.[17] Based on the Spearman correlation analysis, Caprini score was positively correlated with TM ($R = .451$, $P = .001$), and both reflected similar variation tendency on the risk of VTE.[18]

ROC analysis showed that TM, t-PAIC, D-D, and FDP had a certain diagnostic efficiency for hypercoagulation and thrombosis status. In fact, the diagnostic power of all indicators including TM for Caprini highest and highest+high stratification were not ideal (all AUROCs $< .8$), except that TM and D-dimer were slightly better than other markers. Another ROC analysis in diagnosing VTE/non-VTE, we also found that these biomarkers can efficiently diagnose thrombosis; however, all indicators including TM were not satisfactory. This is because TM reflected coagulation activity, TAT reflected anticoagulation function, and t-PAIC and PIC reflected fibrinolytic function; however, none of them can reflect the general appearance and final effect of coagulation-anticoagulant system as a whole, which led to the deficiency in diagnosing the risk of VTE.[17,19,20] This finding could be a basis for improving existing VTE risk identification methods, which suggested that the diagnosis of VTE should not only depend on the level of thrombus markers.

Our research further analyzed the uni- and multivariate logistic regression on risk factors of Caprini model and thrombosis markers to identify risk factors of VTE. We found that 5 risk

Table 5

ROC analysis of thrombosis markers in discriminating Caprini highest and highest+high stratification groups from others.

	Sen	Spe	Cutoff value	AUC	95%CI	*P*
TM, TU/mL						
Highest	0.767	0.474	10.15	0.645	(0.545–0.745)	.008[*]
High+highest	0.758	0.769	10.05	0.775	(0.655–0.894)	.001[*]
TAT, ng/mL						
Highest	0.777	0.395	4.51	0.561	(0.447–0.674)	.271
high+highest	0.563	0.538	7.53	0.496	(0.346–0.646)	.960
PIC, μg/mL						
Highest	0.505	0.526	1.16	0.485	(0.38–0.591)	.054
high+highest	0.492	0.462	1.16	0.41	(0.277–0.544)	.288
t-PAIC, ng/mL						
Highest	0.757	0.553	4.97	0.664	(0.564–0.764)	.003[*]
high+highest	0.711	0.692	4.97	0.707	(0.558–0.857)	.014[*]
FDP, mg/L						
Highest	0.592	0.684	12.55	0.628	(0.526–0.731)	.020[*]
high+highest	0.547	0.769	12.55	0.605	(0.461–0.749)	.212
DD, mg/L						
Highest	0.563	0.684	5.57	0.6	(0.492–0.708)	.069
high+highest	0.531	0.769	5.5	0.601	(0.453–0.749)	.233

[*] $P < 0.05$, compared with AUC of reference line in ROC analysis.
DD = D-dimer, FDP = fibrinogen degradation products, PIC = α_2-plasmin inhibitor-plasmin complexes, TAT = thrombin–antithrombin complexes, TM = thrombomodulin, t-PAIC = tissue plasminogen activator-inhibitor complexes.

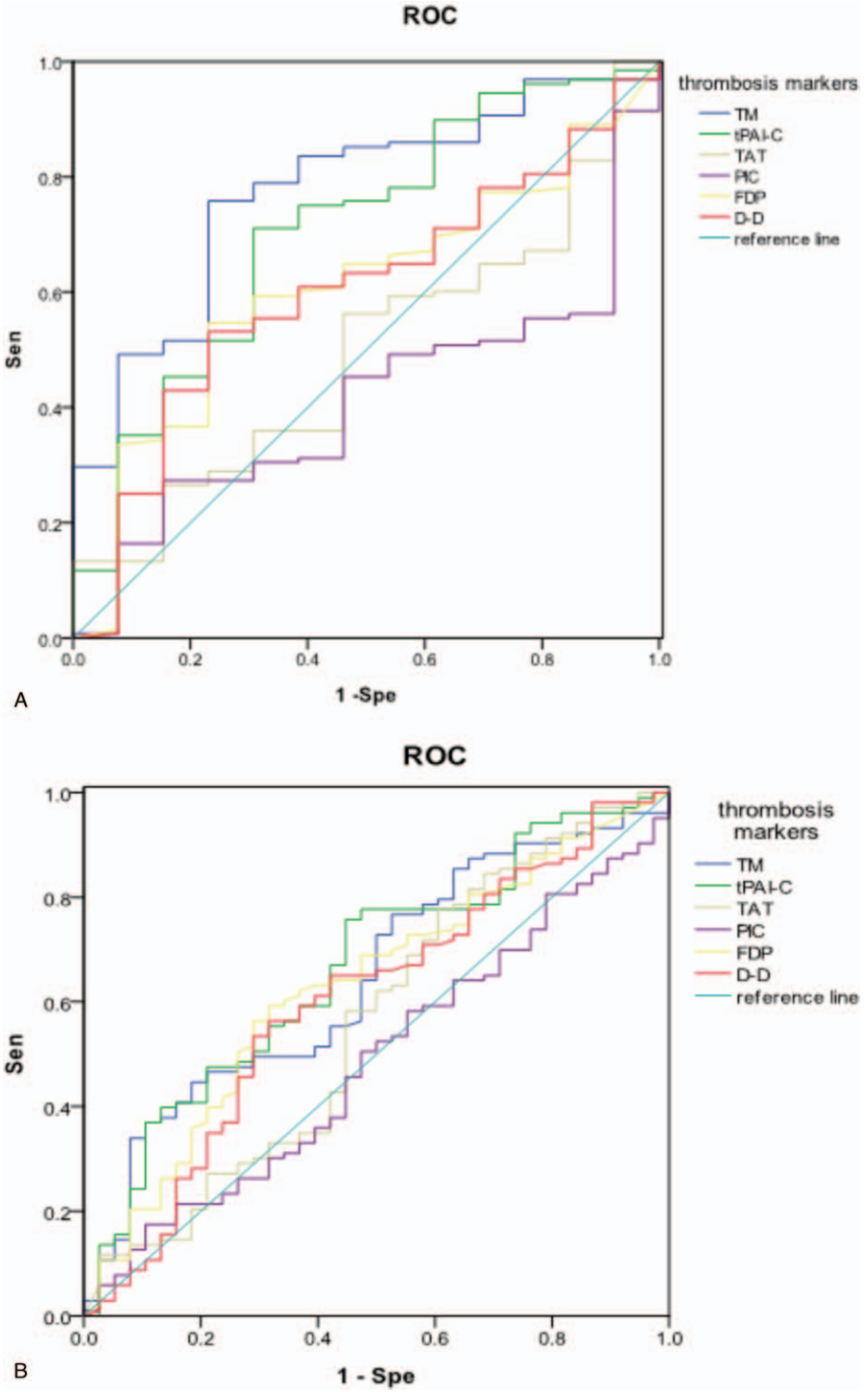

Figure 1. (A) ROC analysis to evaluate the ability of biomarkers to discriminate among patients who had highest and high risk developed VTE. The AUROC of TM (blue line) was 0.775 (95% confidence interval [CI]: 0.655–0.894), which was better than other markers. (B) ROC analysis to evaluate the ability of biomarkers to discriminate among patients who had highest risk developed VTE. AUROC = areas under the receiver operating characteristic curves, ROC = receiver operating characteristic curve, VTE = venous thromboembolism.

factors, that is, drinking history, major surgery (>3 hours), swollen legs (current), TM, and D-D, were independent for the occurrence of VTE in critically ill ICU patients. ICU clinicians were suggested to pay more attention to these risk factors during the prevention and treatment of VTE.[21–23]

We also found a phenomenon in this study that some patients may get a lower Caprini score on ICU admission because of hidden symptoms, but thrombosis biomarkers sensitively reflected coagulation and anticoagulation system abnormalities. Therefore, the preventive treatment in

Table 6

ROC analysis of thrombosis markers in discriminating VTE and non-VTE.

	Sen	Spe	Cut-off value	AUC	95%CI	*P*
TM, TU/mL	0.660	0.606	12.86	0.696	(0.600–0.793)	.000*
TAT, ng/mL	0.574	0.468	7.70	0.565	(0.467–0.662)	.213
PIC, μg/mL	0.660	0.628	1.19	0.652	(0.559–0.746)	.003*
t-PAIC, ng/mL	0.511	0.351	5.51	0.438	(0.341–0.536)	.234
FDP, mg/L	0.681	0.585	12.90	0.637	(0.541–0.732)	.008*
DD, mg/L	0.617	0.574	5.61	0.631	(0.537–0.726)	.011*

* $P < 0.05$, compared with AUC of reference line in ROC analysis.

DD = D-dimer, FDP = fibrinogen degradation products, PIC = α_2-plasmin inhibitor-plasmin complexes, TAT = thrombin–antithrombin complexes, TM = thrombomodulin, t-PAIC = tissue plasminogen activator-inhibitor complexes.

hypercoagulable patients with low Caprini score may be missed. On the contrary, in the highest and high stratification groups, the levels of thrombotic biomarkers in some patients were lower than those in low and moderate stratification groups, indicating that the coagulation system could not be significantly activated despite the evident high risk factors for VTE. Therefore, to establish an individualized thrombosis risk assessment model, the laboratory index should be fully integrated to improve the efficiency of thrombus prevention strategy.[24]

The current study opens the door to a new way of stratifying patient risk for thrombotic disease in critically ill patients. Further investigations based on larger groups are required to help optimize patient management to reduce the occurrence of VTE in the ICU.

In conclusion, thrombosis markers are strongly positively correlated with Caprini risk stratification. Caprini assessment model can help clinicians perform an effective risk identification for VTE and the plasma thrombosis markers could reflect the potential coagulation disorder, whose changes are closely related to the hypercoagulable state. Hence, the combined use of Caprini model and thrombosis biomarkers can complement each other depending on the clinical situation. This finding could serve as a foundation to improve the existing VTE risk identification methods and will be used as a guide for the preventive anticoagulation therapy in the clinical setting.

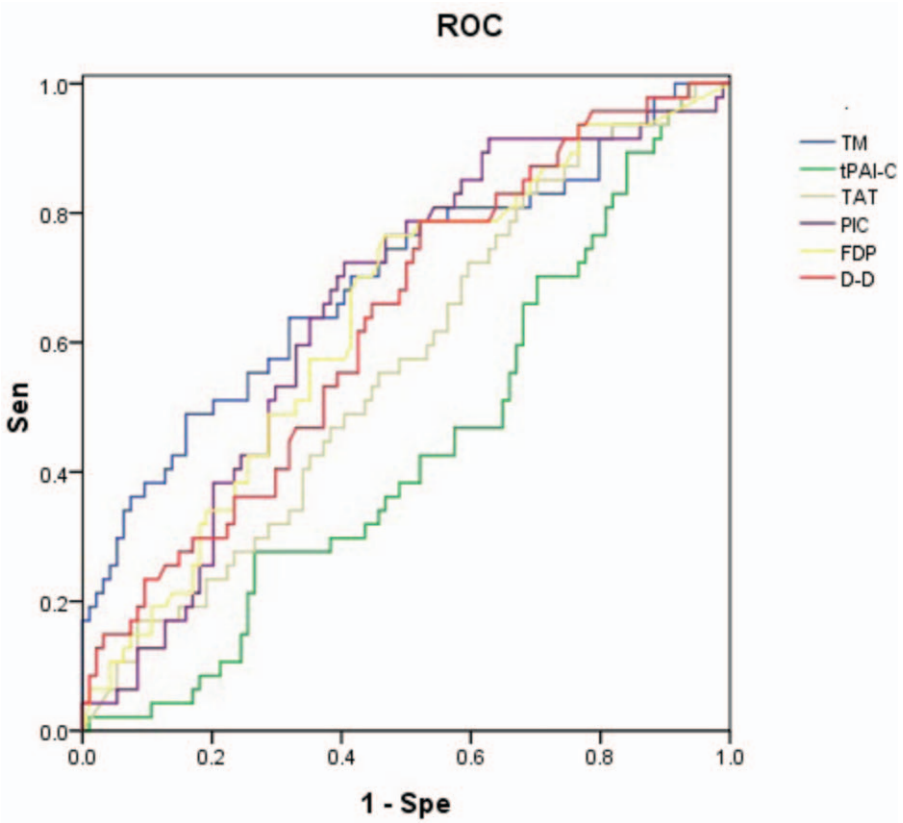

Figure 2. ROC analysis to evaluate the ability of biomarkers to discriminate patients with /without VTE. ROC = receiver operating characteristic curve, VTE = venous thromboembolism.

Table 7

Univariable/multivariable Logistic regression analysis of the risk factor in VTE.

Risk factor	Univariable logistic regression		Multivariable logistic regression	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Drinking	2.148 (1.045–4.414)	.036	2.523 (1.071–5.943)	.034
Pulmonary disease	3.122 (1.500–6.495)	.002		
Major surgery (>3 hours)	3.937 (1.091–14.214)	.036	5.506 (1.407–21.537)	.014
Multiple trauma (<1 month)	2.613 (1.083–6.303)	.033		
Swollen legs (current)	5.608 (1.972–15.948)	.001	5.933 (1.825–19.287)	.003
Sepsis (<1 month)	4.074 (1.144–14.509)	.030		
TM, TU/mL	1.110 (1.056–1.167)	.000	1.089 (1.033–1.147)	.002
DD, mg/L	1.058 (1.012–1.105)	.012	1.076 (1.022–1.133)	.005
FDP, mg/L	1.022 (1.002–1.043)	.028		

Pulmonary disease means serious lung disease including pneumonia (<1 month).
The multivariable results were expressed by odds ratios (OR) with 95% confident intervals and the ORs were adjusted by age, gender, and history of alcohol consumption.
DD = D-dimer, FDP = fibrinogen degradation products, TM = thrombomodulin

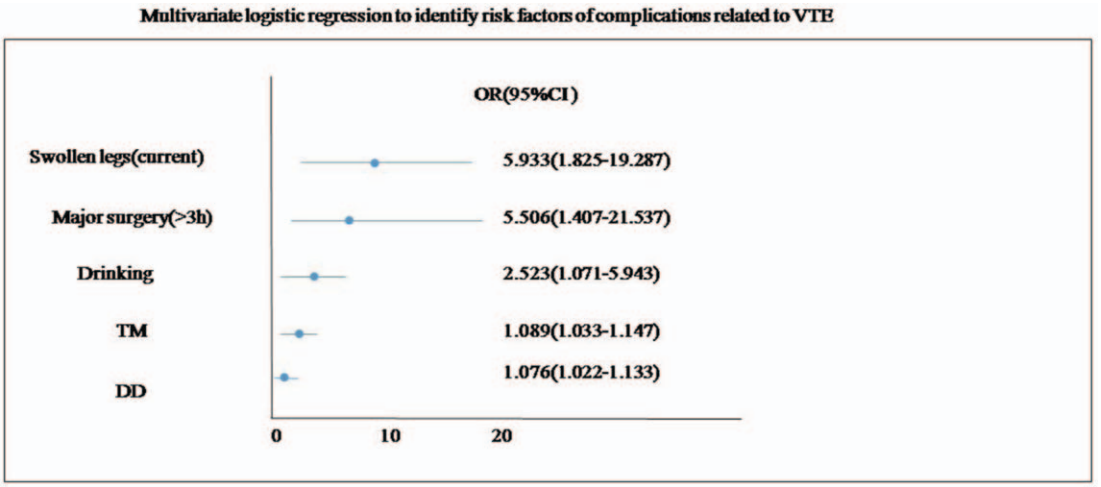

Figure 3. Multivariate logistic regression to identify risk factors related to VTE: drinking, OR 2.523[95% CI (1.071–5.943)]; major surgery (>3 hours), OR 5.506 [95% CI (1.407–21.537)]; swollen legs (current), OR 5.933 [95% CI (1.825–19.287)]; TM, OR 1.089 [95% CI (1.033–1.147)]; D-D, OR 1.076 [95% CI (1.022–1.133)]. VTE = venous thromboembolism.

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