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Risk factors and a nomogram model for deep vein thrombosis in critically ill patients with sepsis: a retrospective analysis

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Sepsis is one of the risk factors for deep vein thrombosis (DVT). However, studies on risk factors for DVT in critically ill patients with sepsis are limited, and no specific assessment tool is available for evaluating the risk of DVT in this population. We aimed to determine the risk factors of DVT and develop a simple nomogram for this vulnerable population. In this retrospective observational study, patients with sepsis using Sepsis-3 criteria, who were admitted to the intensive care unit (ICU) of West China Hospital of Sichuan University from January 2015 to May 2022, were enrolled. Patients with a diagnosis of DVT before admitting to ICU, cancer, trauma, pregnancy, surgery more than 45 min, or long-term use of glucocorticoids were excluded. Patients were assigned to the DVT group or non-DVT group based on the results of ultrasonography. We generated receiver operating characteristic curves (ROC) to calculate the cut-off of the continuous variables. A forest plot and a nomogram were developed by multivariable logistic regression. A total of 1057 patients were finally included. The multivariable logistic regression analysis showed that age (≥ 48 years old, odds ratio (OR) = 2.99, 95% confidence interval (CI): 2.19–4.12, $P < 0.001$), the use of vasoactive drugs (≥ 336 h, OR = 5.66, 95%CI 4.05–7.99, $P < 0.001$), PaO2/FiO2 (≤ 275, OR = 1.68, 95%CI 1.24–2.27, $P < 0.001$), respiratory infection (OR = 1.44, 95%CI 1.02–2.06, $P < 0.05$), D-dimer level (≥ 3.6, OR = 1.59, 95%CI 1.12–2.26, $P < 0.05$), fibrinogen level (≤ 3.9, OR = 1.45, 95%CI 1.09–1.95, $P < 0.05$), physical prophylaxis (OR = 0.51, 95%CI 0.37–0.71, $P < 0.001$) were independently associated with DVT. There were no significant differences in the insertion of the central venous catheter (CVC) or peripherally inserted central catheter (PICC), Sequential Organ Failure Assessment (SOFA) score, duration of mechanical ventilation, stay in ICU, and length of hospitalization between the two groups, while the DVT group had a higher proportion of use of pharmacologic thromboprophylaxis (61.8% vs. 47.2%, $P < 0.001$). In critically ill patients with sepsis, physical prophylaxis was found as an independent protective factor for DVT. Advanced age, long-term use of vasoactive drugs, elevated D-dimer levels, decreased fibrinogen levels, low oxygenation index, and respiratory infection were independent risk factors for DVT.

Abbreviations

ALB	Albumin
ALT	Alanine transaminase
APTT	Activated partial thromboplastin time
AST	Aspartate transaminase
AT-III	Antithrombin III
BMI	Body mass index
CI	Confidence interval
COPD	Chronic obstructive pulmonary disease
CRP	C-reactive protein
CVC	Central venous catheter
DVT	Deep vein thrombosis

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FDP	Fibrinogen degradation product
GNB	Gram-negative bacteria
GPB	Gram-positive bacteria
HDL	High density lipoprotein
INR	International normalized ratio
ICU	Intensive care unit
IQR	Interquartile ranges
NE	Neutrophilic granulocyte
OR	Odds ratio
PICC	Peripherally inserted central catheter
PLT	Platelet
PT	Prothrombin time
ROC	Receiver operating characteristic curves
SOFA	Sequential organ failure assessment
TBIL	Total bilirubin
TT	Thrombin time
VTE	Venous thromboembolism
WBC	White blood cell

Previous studies have established sepsis as a significant risk factor for the development of deep vein thrombosis (DVT)[1–3]. Evidence suggests DVT is associated with prolonged mechanical ventilation, extended intensive care unit (ICU) and hospital stays[4–6], and exacerbation of sepsis-related pathophysiological disorders. A large cohort study further identified DVT as both a cause and consequence of sepsis, contributing to acute and chronic vascular complications[7].

A multicenter prospective study by Kaplan et al. suggested that sepsis patients exhibit elevated venous thromboembolism (VTE) incidence despite guideline-adherent thromboprophylaxis[5]. The nonspecific clinical manifestations of deep vein thrombosis (DVT) in this population frequently lead to underdiagnosis, potentially resulting in severe complications including hypotension, hypoxia, and sudden death[8]. Therefore, early identification of patients at high risk of DVT and timely intervention are crucial. However, there is a lack of study and risk-scoring scale specifically for critically ill patients with sepsis. The Caprini scale is primarily used for surgical patients, whereas the Wells score is mainly used for outpatients. They both lack some of the high-risk factors seen in sepsis, such as systemic inflammatory response, multiple organ dysfunction, and invasive mechanical support.

This retrospective study aims to investigate the risk factors of DVT in patients with sepsis and serve as a foundation for the subsequent development of diagnostic criteria and risk stratification tools, thereby guiding clinical prevention and management.

Method
Study design
We conducted an observational study to analyze the clinical data of patients who met the diagnostic criteria of sepsis during their hospitalization in the ICU of West China Hospital of Sichuan University from January 2015 to May 2022. We followed the reporting standards set by Reporting of studies Conducted using Observational Routinely collected health Data in this study[9]. The study was approved by the ethics committee of West China Hospital of Sichuan University (Chengdu, China; approval number WCH 2023–2333). Informed consent was waived due to the retrospective and observational nature of the study. This study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient population
The inclusion criteria were as follows: (1) diagnosed with sepsis; (2) adult patients aged ≥ 18 years old; (3) ICU stay > 72 h. We excluded patients who met any of the following criteria: (1) incomplete information on ultrasound; (2) pre-existing DVT prior to ICU admission; (3) incorporation of malignant tumors (such as leukemia and liver cancer); (4) long-term treatment with glucocorticoids; (5) trauma patients; (6) surgery ≥ 45 min; (7) pregnancy.

Diagnosis criteria
According to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)[10], sepsis was diagnosed by infection with Sequential Organ Failure Assessment (SOFA) score ≥ 2.

Based on the definition of the prevalence and incidence of DVT in ICU as defined in the existing literature[4], patients with DVT diagnosed by venous ultrasonography within 72 h of admission to ICU were excluded. DVT was diagnosed if ultrasonography reported thrombosis in any vein listed in Supplementary Table S1[11].

Data collection
Clinical data were collected by reviewing the electronic medical record database of the Department of Critical Care Medicine of West China Hospital, Sichuan University.

From each patient, we thoroughly collected the following information: demographic characteristics (age, sex, body mass index (BMI), and ethnicity), medical data (SOFA score, Caprini score, vital signs on admission to ICU, medication use, rehabilitation, thromboprophylaxis, mechanical ventilation, and intravenous catheterization), diagnosis (etiology of sepsis, complications and comorbidities), laboratory tests (biochemistry, inflammatory index, hematology, coagulation, blood gas analysis, site of infection and microbiology), past medical history,

and family history. The multiple imputation of chained equations (MICE) technology in R language was used to process missing data. The missing data situation is shown in Supplementary Table S2.

Statistical analysis

Demographic characteristics and other baseline values were described using descriptive statistics. Continuous variables were tested for normality by the Shapiro-Wilk test and Histogram. Data of normal distribution was described by means and standard deviations. Data of skewed distribution was reported as medians and interquartile ranges (IQR). Categorical variables were reported as percentages.

The χ^2 test or Fisher's exact probability method was used for the comparison of categorical variables, Wilcoxon rank sum test or t test for the comparison of continuous variables. Variables showing an univariable relationship with DVT ($p < 0.1$) were entered into a multivariable logistic regression model to calculate the odds ratio (OR) and 95% confidence interval (CI). We generated receiver operating characteristic curves (ROC) to calculate the cut-off of the continuous variables which were subsequently converted into binary data. A forest plot and nomogram based on the result of the multivariable logistic regression model were generated.

All statistical analyses were performed using packages implemented in R software, V.4.2.3, and the statistical significance of the two-sided tests performed was set at 0.05.

Results

Characteristics of the study population

A total of 3143 patients diagnosed with sepsis using Sepsis-3 criteria were enrolled. 1057 patients were finally included in the analysis, of which 458 cases developed DVT and 599 cases without DVT (Fig. 1). The median age in the DVT group was 58 years (IQR 48–71) versus 51 years (IQR 37–67) in the non-DVT group. 68.7% of patients included were men and 30.6% had shock upon admission and required vasoactive drugs to maintain circulation. The most common comorbidities were hypertension (29.7%), diabetes (18.7%), and chronic obstructive pulmonary disease (6.1%) (Table 1).
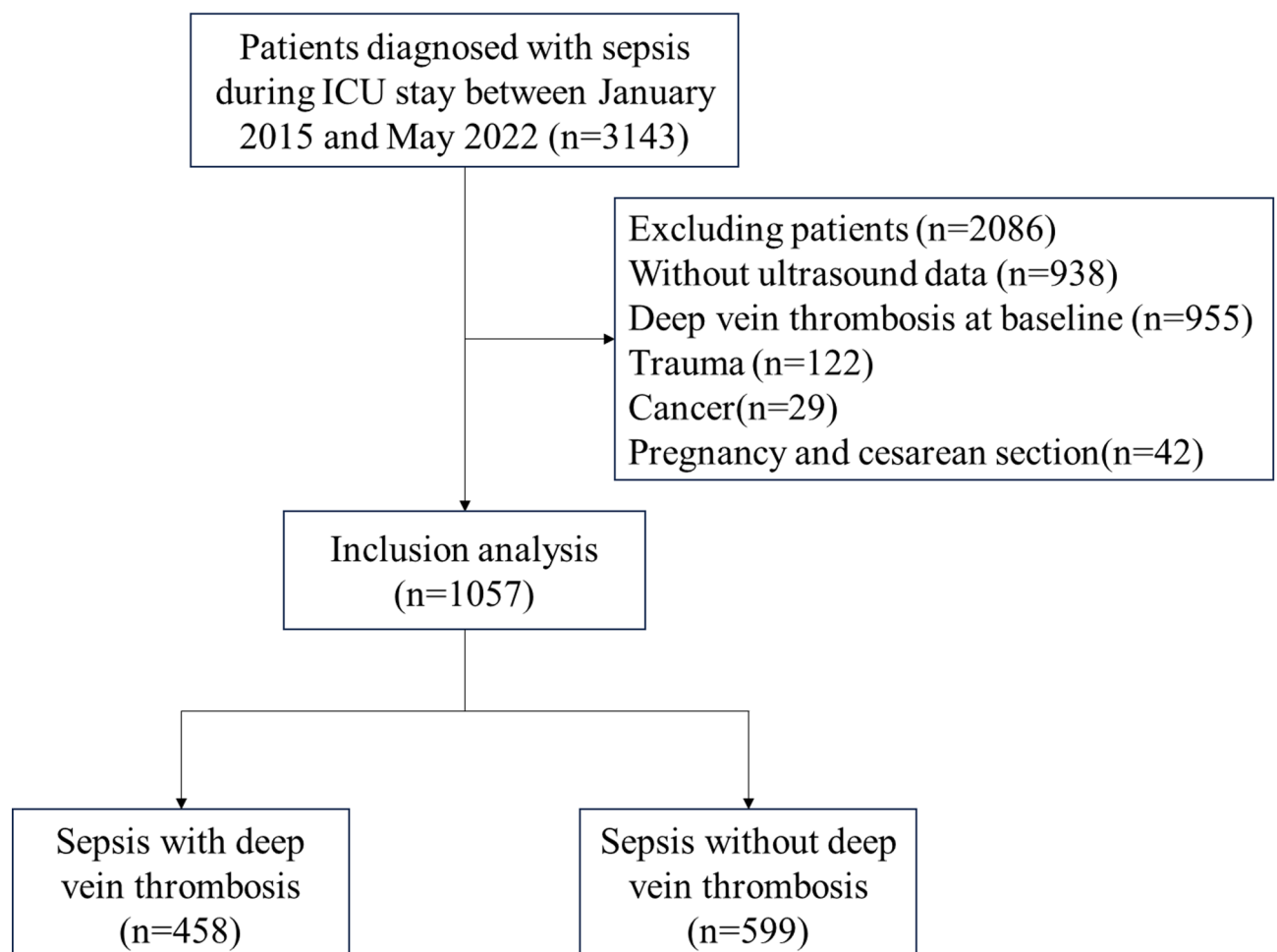
Fig. 1. Study flow chart.

Characteristic	Sepsis with deep vein thrombosis (N = 458)	Sepsis without deep vein thrombosis (N = 599)
Age(yr)	58 (48,71)	51 (37,67)
Female sex	140 (30.6)	191(31.9)
Body mass index, kg/m^2	23.4 (21.2,25.3)	23.6 (21.0,25.8)
SOFA score	7 (5,9)	7 (5,9)
Caprini DVT score	7 (5,9)	7 (5,8)
PaO2/FiO2	232.5 (183.3,296.5)	253.3 (192.4,332.1)
Shock requiring vasopressors	137 (29.9)	186 (31.1)
CVC/PICC	86 (18.8)	104 (17.4)
Vital signs admission to ICU		
Temperature, °C	37.0 (36.5,37.1)	37.0 (36.5,37.0)
Heart rate, beats/min	99 (85,114)	101 (85,116)
Respiratory rate, breaths/min	16 (20,23)	19 (16,20)
Systolic blood pressure, mmHg	130 (116,146)	130 (114,145)
Diastolic blood pressure, mmHg	75 (65,86)	75 (65,85)
Comorbidity		
Hypertension	152 (33.2)	162 (27.0)
COPD	31 (6.8)	34 (5.7)
Diabetes	86 (18.8)	112 (18.7)
Chronic liver disease	27 (5.9)	34 (5.7)
Chronic kidney disease	1 (0.2)	9 (1.5)

Table 1. Demographic and clinical characteristics of the study population at baseline. Data are presented as No. (%) or median (interquartile range) unless otherwise indicated; SOFA, sequential organ failure assessment; CVC, central venous catheter; PICC, peripherally inserted central catheter; COPD, chronic obstructive pulmonary disease.

Risk factors of DVT in sepsis patients

There were no significant differences between the patients with DVT and those without DVT in terms of BMI, SOFA score, Caprini score, platelet count, prothrombin time (PT), and activated partial thromboplastin time (APTT) at admission ($p > 0.05$). Compared with patients without DVT, patients with DVT had a longer median duration of mechanical ventilation (393.6 vs. 225.2 h; $p < 0.001$), vasoactive drugs (390.6 vs. 223.6 h; $p < 0.001$), ICU stay (19.8 vs. 11.8 d; $p < 0.001$), and hospitalization (28 vs. 20 d; $p < 0.001$) (Table 2).

The proportion of sex, insertion of central venous catheter (CVC) or peripherally inserted central catheter (PICC), bedridden status before admission, emergency surgery, recent fracture history, cases of shock requiring vasopressors, utilization of antiplatelet, drugs to improve circulation, and glucocorticoid were similar between the two groups ($p > 0.05$). Significant differences in intermittent pneumatic compression and anticoagulation were found between DVT and non-DVT patients ($p < 0.001$) (Supplementary Table S3).

Multivariable logistic regression showed that independent risk factors for DVT were older age, prolonged use of vasoactive drugs, elevated D-dimer, absence of intermittent pneumatic compression, decreased fibrinogen, low oxygenation index, and respiratory infection (Table 3). Whereas anticoagulation treatment did not reach statistical significance. Based on the final multivariable model, a forest plot (Fig. 2) and a nomogram were generated (Fig. 3).

Subgroup analysis of patients with chemoprophylaxis

There was no significant difference in the duration and dosage of anticoagulation between the patients with and without DVT (Supplementary Table S4). The prevalence of comorbidities did not differ significantly among patients on anticoagulant or antiplatelet regimens (Supplementary Table S5 and S6).

Discussion

Patients in the ICU exhibit a higher risk of DVT compared to general hospital populations. Studies on DVT in critically ill patients have been conducted since the 1980s, but explorations specifically for sepsis are still inadequate[12,13]. Current risk stratification tools demonstrate limited clinical utility in sepsis due to non-specific risk categorization and inadequate weighting of critical sepsis-related factors[14,15]. Both the Caprini and the Wells scores are initially developed for the evaluation of DVT in the general population, which may not be reliable in septic patients. For instance, the latest update of the Caprini scale assigns only one point to serious infection[16]. Septic patients often present with altered mental status or are sedated, posing challenges in accurately evaluating certain clinical signs and symptoms included in the Wells score. Consequently, the risk of DVT in patients with sepsis may be underestimated by existing scales. Besides, international guidelines lack recommendations on DVT risk assessment models for critically ill patients[17]. Therefore, no applicable scale exists for evaluating DVT in critically ill patients with sepsis. To address these limitations, the development of a specific assessment tool that incorporates the unique risk factors and pathophysiological markers associated with sepsis is needed.

Variables	Sepsis with deep vein thrombosis (N = 458)	Sepsis without deep vein thrombosis (N = 599)	z-value	P Value
Age	58 (48,71)	51 (37,67)	-5.54	<0.001
Body mass index, kg/m2	23.4 (21.2,25.3)	23.6 (21.0,25.8)	0.73	0.46
SOFA score	7 (5,9)	7 (5,9)	-1.23	0.22
Caprini score	7 (5,9)	7 (5,8)	-0.28	0.78
Length of mechanical ventilation/hours	393.6 (189.0, 730.6)	225.2 (96.0, 417.1)	-8.25	<0.001
Length of use of vasoactive drugs/hours	390.6 (169.3,536.0)	223.6 (96.1,323.8)	-8.76	<0.001
ICU length of stay/d	19.8 (11.6,30.9)	11.8 (6.7,21.0)	-8.37	<0.001
Hospital length of stay/d	28.0 (19.0,46.0)	20.0 (11.0,33.0)	-8.24	<0.001
Lactate	1.7 (1.3,2.3)	1.6 (1.3,2.4)	0.75	0.45
PaO2/FiO2	232.5 (183.3,296.5)	253.3 (192.4,332.1)	3.36	<0.001
PLT count/10^9	155 (84,232)	145 (85,216)	-1.18	0.24
PT	13.4 (12.2,15.2)	13.3 (12.0,15.3)	-0.59	0.56
APTT	32.2 (28.3,38.9)	32.2 (28.5,39.0)	0.08	0.94
TT	17.4 (16.1,18.7)	17.2 (16.1,18.9)	-0.42	0.67
AT III	66.3 (50.8,79.9)	66.1 (50.0,81.8)	-0.06	0.96
INR	1.2 (1.1,1.3)	1.2 (1.1,1.4)	0.30	0.76
D-dimer	6.7 (3.3,11.7)	5.0 (2.3,9.8)	-3.51	<0.001
Fibrinogen	3.6 (2.3,5.0)	3.9 (2.5,5.2)	1.95	<0.1
FDP	16.2 (9.2,27.6)	13.1 (7.2,21.9)	-3.9	<0.001
Hemoglobin	94.0 (79.0,114.0)	99.0 (79.0,120.0)	1.67	<0.1
TBIL	14.4 (9.1,24.0)	13.8 (8.6,26.4)	-0.27	0.79
ALT	31.0 (17.0,63.0)	28.0 (16.0,59.0)	-1.21	0.23
AST	39.5 (24.0,76.0)	38.0 (21.0,74.0)	-0.89	0.37
Triglyceride	1.4 (1.0,2.1)	1.4 (0.9,2.2)	0.45	0.65
HDL	0.6 (0.4,0.9)	0.7 (0.4,1.0)	2.17	<0.05
ALB	31.4 (27.7,34.9)	31.3 (27.6,35.6)	-0.05	0.96
CRP	107.0 (47.5,145.3)	112.0 (51.5,150.0)	1.35	0.18
WBC count/10^9	10.8 (7.5,14.9)	10.9 (7.2,14.8)	-0.16	0.87
NE%	85.9 (80.5,90.4)	85.8 (79.7,90.2)	-0.82	0.41

Table 2. Mann–Whitney U test of potential risk factors for DVT in sepsis. ALB, albumin; ALT, alanine transaminase; APTT, activated partial thromboplastin time; AST, aspartate transaminase; AT-III, antithrombin III; CRP, C-reactive protein; FDP, fibrinogen degradation product; HDL, high density lipoprotein; INR, international normalized ratio; NE, neutrophilic granulocyte; PLT, platelet; PT, prothrombin time; TBIL, total bilirubin; TT, thrombin time; SOFA , sequential organ failure assessment; WBC, white blood cell.

To our knowledge, this is one of few studies evaluating DVT risk factors specifically in classical sepsis patients after rigorous exclusion of major confounders including trauma, cancer, and pregnancy. In this study, we analyzed data from 1057 patients with sepsis and developed a nomogram for the prediction of DVT. The result showed that the use of intermittent pneumatic compression was a protective factor for DVT. Consistent with our findings, a prospective cohort study conducted in the adult medical-surgical ICU showed that pneumatic compression was associated with a lower risk of VTE, irrespective of concurrent administration of pharmacologic thromboprophylaxis[18]. However, mechanical thromboprophylaxis in critically ill patients is still debated[19]. A multicenter randomized controlled trial demonstrated that adding pneumatic compression to pharmacologic thromboprophylaxis did not result in a significantly lower incidence of DVT[20]. Another study by Charlisa D. Gibson also found that there was no added benefit of dual chemical and mechanical prophylaxis compared to chemoprophylaxis alone[21]. A meta-analysis demonstrated that in critically ill adults, low-molecular-weight heparin significantly reduces DVT incidence compared to controls, including a composite of no prophylaxis, placebo, or compression stockings only, while unfractionated heparin and mechanical compression demonstrated potential benefit[22]. However, despite the appropriate use of pharmacologic thromboprophylaxis, critically ill patients still demonstrated high rates of DVT, which vary from 7.8–37.5%[5,20,21,23–25]. In our study, the proportion of patients receiving pharmacologic thromboprophylaxis in the DVT group was greater than that in the group without DVT, while the subgroup analysis showed no statistical difference in anticoagulant duration or dose between the two groups. Critical knowledge gaps persist regarding the optimal dosing frequency of thromboprophylaxis and therapeutic drug monitoring timing in ICU patients[26]. We speculated that currently recommended DVT prophylaxis strategies may not be as effective in critically ill populations compared with patients in the general ward, and the current level of anticoagulation for sepsis may be insufficient. However, clinical characteristics vary, and the balance of thrombotic and bleeding risk can change daily among critically ill patients, making it difficult to initiate and determine the dosage of anticoagulation for individual patients.

Variables	Group	B value	Standard error of B value	OR (95%CI)	Wald value	P value
Age	≥48	1.10	0.16	2.99 (2.19,4.12)	46.05	<0.001
	<48*					
Length of mechanical ventilation/hours	≥372	0.02	0.19	1.02 (0.69,1.48)	0.01	0.94
	<372*					
Length of use of vasoactive drugs/hours	≥336	1.73	0.17	5.66 (4.05,7.99)	100.42	<0.001
	<336*					
ICU length of stay/d	≥14	0.34	0.19	1.41 (0.96,2.06)	3.05	0.08
	<14*					
Hospital length of stay/d	≥18	0.34	0.20	1.40 (0.94,2.07)	2.80	0.09
	<18*					
PaO_2/FiO_2	≤275	0.52	0.15	1.68 (1.24,2.27)	11.39	<0.001
	>275*					
D-dimer	≥3.6	0.46	0.18	1.59 (1.12,2.26)	6.61	<0.05
	<3.6*					
FDP	≥20	0.21	0.17	1.23 (0.88,1.74)	1.46	0.23
	<20*					
Fibrinogen	≤3.9	0.37	0.15	1.45 (1.09,1.95)	6.29	<0.05
	>3.9*					
Hemoglobin	≤118	0.02	0.19	1.02 (0.71,1.47)	0.01	0.93
	>118*					
HDL	≤0.7	0.21	0.16	1.23 (0.90,1.69)	1.72	0.19
	>0.7*					
Intermittent pneumatic compression	Yes	-0.67	0.17	0.51 (0.37,0.71)	16.02	<0.001
	No*					
Anticoagulation	Yes	0.07	0.16	1.08 (0.79,1.46)	0.22	0.64
	No*					
Respiratory infection	Yes	0.37	0.18	1.44 (1.02,2.06)	4.17	<0.05
	No*					
Urinary infection	Yes	0.12	0.25	1.13 (0.69,1.83)	0.23	0.63
	No*					
Mixed infection With GPB and GNB	Yes	0.12	0.25	1.13 (0.70,1.84)	0.25	0.62
	No*					

Table 3. Multivariate analysis of independent risk factors for deep vein thrombosis. *Represents control group; FDP, Fibrinogen Degradation Product; HDL, High Density Lipoprotein; GPB, Gram-positive bacteria; GNB, Gram-negative bacteria.

It should be highlighted that the high incidence of DVT was more than a failure to provide thromboprophylaxis. Rather, this means patients with sepsis frequently develop DVT and clinicians should maintain a high clinical suspicion for DVT in these patients even when appropriate prophylaxis has been used[5]. Flow stasis, endothelial damage, and hypercoagulability often occur contemporarily in critically ill patients with sepsis, so they are more likely to meet Virchow's triad[4]. Moreover, the dysregulated hemostasis and coagulation in severe sepsis differ from that of non-infectious critical illnesses. Although exact mechanisms remain incompletely understood, sepsis-induced endotheliopathy and associated molecular dysfunction have been well documented. Coagulopathy has been proposed to play a key role through the crosstalk between inflammation and coagulation pathways as a result of the destructive endothelial response of the host[27]. Inflammation, immunity, and coagulation participate in the systemic endothelial injury altogether, leading to hypercoagulability and impaired fibrinolysis[28,29]. This imbalance between procoagulant and anticoagulant pathways not only exacerbates the inflammatory response but also potentiates thrombosis, thereby establishing a self-perpetuating cycle of thrombo-inflammation[30,31].

Our findings revealed that the prolonged use of vasoactive drugs was a significantly independent risk factor for DVT in patients with sepsis. Cook et al. also identified vasopressor use as a risk factor for acquired DVT in the ICU[32]. Prolonged use of vasoactive drugs often indicates microcirculatory disturbance and endothelial dysfunction, which again suggests the positive associations between endothelium and thrombosis. Besides, we found that the decreased oxygenation index and respiratory infection were associated with DVT. Previous studies have found that hypoxia is associated with the incidence of thrombosis[33,34]. A real-world study revealed that patients with respiratory infections were more likely to have pulmonary embolism as initial VTE presentation than other types of infection[35]. A letter published in *Thrombosis Journal* refers to hypoxia as a possible cause as well as a consequence of thrombosis in sepsis patients[36]. Thus, a better understanding of the pathways between endothelial dysfunction and hypoxia in thrombus formation could aid in the development of novel prophylactic
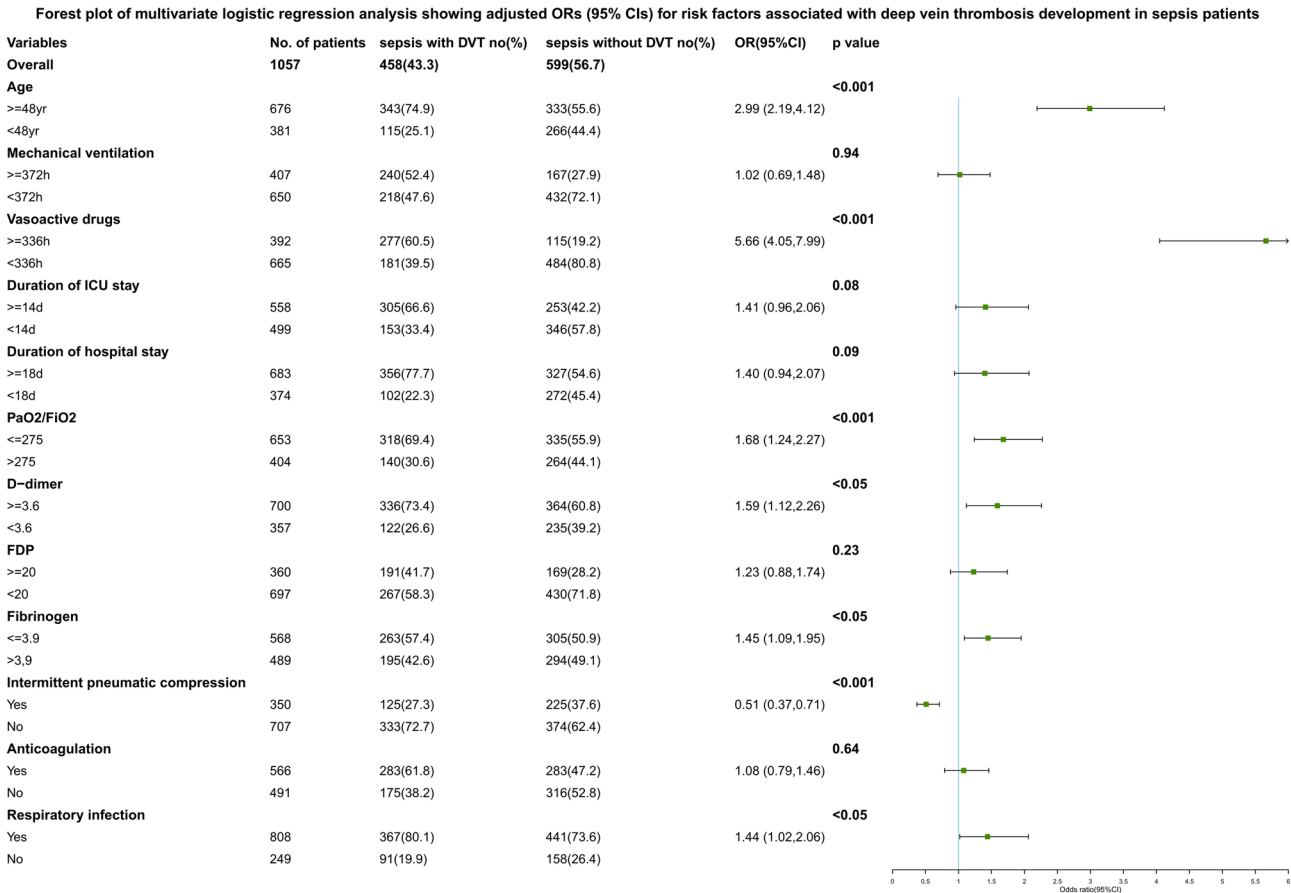
Forest plot of multivariate logistic regression analysis showing adjusted ORs (95% CIs) for risk factors associated with deep vein thrombosis development in sepsis patients

Variables	No. of patients	sepsis with DVT no(%)	sepsis without DVT no(%)	OR(95%CI)	p value
Overall	1057	458(43.3)	599(56.7)		
Age					<0.001
>=48yr	676	343(74.9)	333(55.6)	2.99 (2.19,4.12)	
<48yr	381	115(25.1)	266(44.4)		
Mechanical ventilation					0.94
>=372h	407	240(52.4)	167(27.9)	1.02 (0.69,1.48)	
<372h	650	218(47.6)	432(72.1)		
Vasoactive drugs					<0.001
>=336h	392	277(60.5)	115(19.2)	5.66 (4.05,7.99)	
<336h	665	181(39.5)	484(80.8)		
Duration of ICU stay					0.08
>=14d	558	305(66.6)	253(42.2)	1.41 (0.96,2.06)	
<14d	499	153(33.4)	346(57.8)		
Duration of hospital stay					0.09
>=18d	683	356(77.7)	327(54.6)	1.40 (0.94,2.07)	
<18d	374	102(22.3)	272(45.4)		
PaO2/FiO2					<0.001
<=275	653	318(69.4)	335(55.9)	1.68 (1.24,2.27)	
>275	404	140(30.6)	264(44.1)		
D−dimer					<0.05
>=3.6	700	336(73.4)	364(60.8)	1.59 (1.12,2.26)	
<3.6	357	122(26.6)	235(39.2)		
FDP					0.23
>=20	360	191(41.7)	169(28.2)	1.23 (0.88,1.74)	
<20	697	267(58.3)	430(71.8)		
Fibrinogen					<0.05
<=3.9	568	263(57.4)	305(50.9)	1.45 (1.09,1.95)	
>3,9	489	195(42.6)	294(49.1)		
Intermittent pneumatic compression					<0.001
Yes	350	125(27.3)	225(37.6)	0.51 (0.37,0.71)	
No	707	333(72.7)	374(62.4)		
Anticoagulation					0.64
Yes	566	283(61.8)	283(47.2)	1.08 (0.79,1.46)	
No	491	175(38.2)	316(52.8)		
Respiratory infection					<0.05
Yes	808	367(80.1)	441(73.6)	1.44 (1.02,2.06)	
No	249	91(19.9)	158(26.4)		

Odds ratio(95%CI)

Fig. 2. Forest plot showing multivariate logistic regression analyses of risk factors for DVT in sepsis patients.
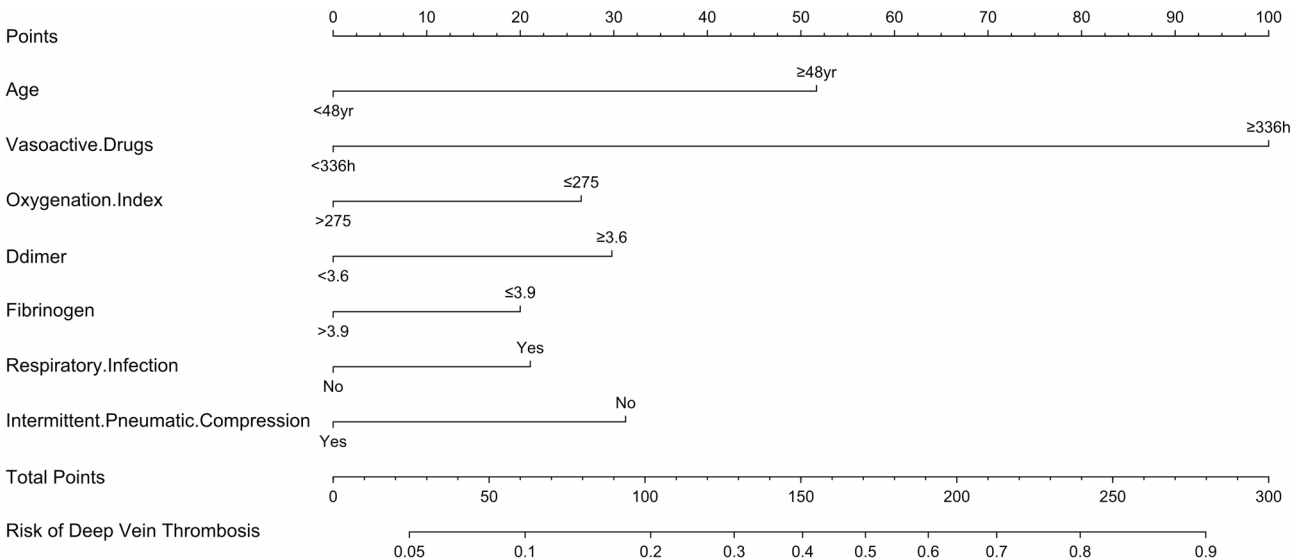

Fig. 3. Nomogram for predicting the probability of DVT in patients with sepsis. Each variable is individually plotted on the nomogram axis and assigned a partial score from the upper point scale. The sum of all partial scores yields a total score, which is then projected onto the lower total point scale to determine the corresponding predicted probability of DVT.

therapies against thrombosis. Further, the key to preventing DVT may lie in controlling the pathophysiologic disorders of sepsis.

In addition, age, D-dimer levels, and fibrinogen levels were independently associated with DVT in patients with sepsis. There were no significant differences in the insertion of CVC or PICC, SOFA score, duration of mechanical ventilation, ICU stay, and hospitalization between the two groups, which is similar to previous studies[15,21,37].

The risk assessment tool for DVT and optimal anticoagulation management has not been established in critically ill patients with sepsis. Large, well-designed, randomized control trials specifically studying thromboprophylaxis in patients with severe sepsis and septic shock are necessary to improve the prevention of DVT and advance our understanding and care of these vulnerable patients.

Our study has several strengths. We specifically focused on critically ill patients with sepsis. The potential interference of common risk factors of DVT such as trauma, cancer, and pregnancy were excluded in the selection of the study population. Nevertheless, our study has some limitations. First, the single-center/facility nature and small sample size of our study hinder the generalizability of our findings. Although our study of 1,057 patients surpasses the sample sizes of most sepsis-associated DVT studies conducted in Chinese populations[38,39], this sample size may still be insufficient for robust subgroup analyses, particularly in smaller strata such as antiplatelet therapy recipients. Second, our study did not differentiate between proximal and distal thromboses, which exhibit distinct clinical implications regarding both progression risk and therapeutic management. Furthermore, our nomogram requires external validation in independent cohorts and comparative evaluation against established risk assessment tools. Since the present study was retrospective, patients in ICU were not regularly screened for DVT. The exclusion of patients without venous ultrasound records may have disproportionately removed lower-risk DVT candidates from our study, potentially introducing selection bias. We cannot completely exclude the possibility of DVT that occurred before ICU admission, although we attempted to mitigate this possibility by excluding patients with the presence of DVT or without ultrasound data at baseline. Nevertheless, our study is still important for further understanding of the risk factors for DVT in critically ill patients with sepsis, as well as clinical practice.

Prospective clinical studies across diverse healthcare settings with protocolized ultrasound screening intervals and medication adherence timelines are necessary to clarify baseline thrombosis prevalence and to differentiate proximal or distal DVT outcomes. Multicenter validation of the nomogram against established scores in diverse populations is also needed. While heparin remains the primary treatment of DVT, its efficacy is limited, and superior alternatives are still lacking. Recent research reveals the interplay between immunity and coagulation. Understanding these mechanisms could improve thrombotic risk assessment and anti-inflammatory anticoagulant therapies[40].

Conclusions

In summary, in critically ill patients with sepsis, physical prophylaxis was found as an independent protective factor for DVT. In contrast, age, use of vasoactive drugs, D-dimer level, fibrinogen level, oxygenation index, and respiratory infection were noted as independent risk factors for DVT. Patients with sepsis in ICU are more likely to develop DVT, thromboprophylaxis should be implemented in this population unless contraindicated. Further studies are needed to explore risk stratification strategies and innovative approaches for DVT prevention, perhaps beyond the existing traditional methods.

Data availability

The data used in this study can be obtained by the corresponding author upon request.

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Author contributions

J.S. and X.T. contributed equally to this article. W.H.Y., J.S., T.J.Z., and R.Z. contributed to study conception and design. J.S. and X.T. takes responsibility for drafting the manuscript. W.H.Y., T.J.Z. and R.Z. provided critical consultancy on the study implementation. JS analyzed the data. W.H.Y., J.S., X.T., R.Z., T.J.Z. interpreted the data. L.Y., M.L.H., X.C., and X.L. contributed to data acquisition. W.H.Y. are responsible for revision of the manuscript. All authors read and approved the final manuscript.

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Declarations

Competing interests
The authors declare no competing interests.

Ethical approval and consent to participate
The study was approved by the ethics committee of West China Hospital of Sichuan University (Chengdu, China; approval number WCH 2023–2333). Informed consent was waived due to the retrospective and observational nature of the study.

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