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Original Article

Combined assessment of Caprini score, D-dimer, and thromboelastography for predicting deep venous thrombosis in lung cancer patients

Jianhui Sheng[1], Xiao Han[1], Hui Zheng[2], Hongfu Ma[1]

[1]*Yantaishan Hospital, Yantai, Shandong, China;* [2]*Department of Vascular Surgery, General Surgery Clinical Center, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, Shanghai, China*

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Abstract: Objective: To evaluate the predictive value of Caprini score, D-dimer levels, and thromboelastography parameters for deep venous thrombosis (DVT) in patients with lung cancer. Methods: A retrospective analysis was conducted on 90 lung cancer patients admitted to Yantaishan Hospital between September 2020 and August 2024. The observation group comprised 50 patients with DVT, while 40 patients without DVT formed the control group. Caprini scores, D-dimer levels, and thromboelastography parameters including coagulation angle (α angle) and maximum amplitude (MA) were compared between groups. Pearson correlation assessed associations with Villalta scores. Logistic regression identified independent risk factors for DVT. Receiver operating characteristic (ROC) curves evaluated the predictive efficacy of single and combined indicators. Results: Compared to controls, the observation group showed significantly higher Caprini scores (P=0.008), D-dimer levels (P<0.001), α angle (P<0.001), and MA (P<0.001). Within severity subgroups, these parameters were elevated in the moderate group compared to the mild group (all P<0.001). Pearson analysis demonstrated positive correlations of Caprini score (P=0.024), D-dimer levels (P=0.029), α angle (P=0.037), and MA (P=0.030) with Villalta scores. Logistic regression revealed these four parameters as independent risk factors for DVT in lung cancer patients. The combined index yielded an AUC of 0.861, outperforming individual indicators (Caprini score 0.771, D-dimer 0.789, α angle 0.747, MA 0.725) in predicting DVT. Conclusions: Caprini score, D-dimer levels, α angle, and MA are independently associated with DVT occurrence and severity in lung cancer patients. Combined assessment enhances predictive accuracy, providing valuable guidance for early identification and clinical management of DVT.

Keywords: Lung cancer, Caprini score, D-dimer levels, thromboelastography parameters, deep venous thrombosis, prognosis

Introduction

Lung cancer is one of the most common malignant tumors in China, predominantly affecting middle-aged and elderly individuals. It is characterized by high malignancy and poor overall prognosis [1]. Although surgical treatment is considered optimal, the early diagnosis rate of lung cancer in China remains low. Consequently, many patients are diagnosed at middle or advanced stages and lose the opportunity for surgery, resorting instead to palliative treatments such as chemotherapy, radiotherapy, targeted therapy, or immunotherapy.

Moik et al. reported that lung cancer is among the cancer types with the highest risk for deep venous thrombosis (DVT) [2]. DVT, a common complication in cancer patients, often involves thrombosis of the lower extremity deep veins. Without timely intervention, the thrombus can extend to proximal veins or dislodge, resulting in pulmonary embolism, which is life-threatening and one of the leading causes of death in cancer patients [3]. Therefore, early risk assessment and diagnosis of DVT in malignancies remain key clinical priorities. Studies have shown that DVT increases the mortality risk in cancer patients by two- to six-fold and is a major cause of death during hospitalization [4]. Furthermore, the American Society of Clinical Oncology (ASCO), National Comprehensive Cancer Network (NCCN), and American Society

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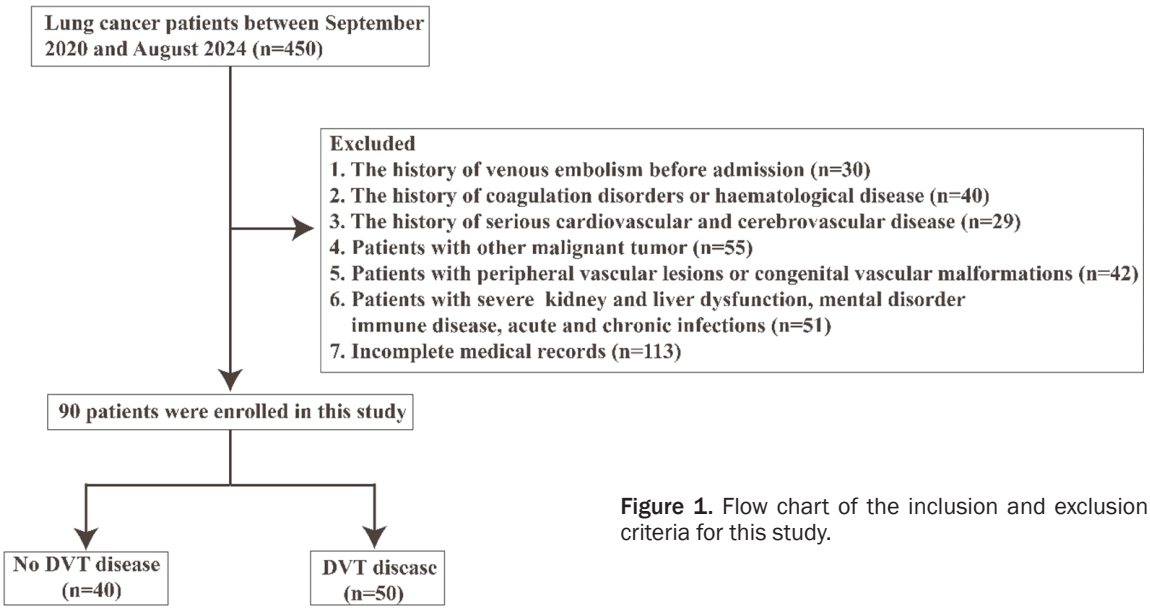

Figure 1. Flow chart of the inclusion and exclusion criteria for this study.

of Hematology (ASH) recommend thorough assessment and prevention of venous thromboembolism (VTE) in patients with malignancies [5-7]. Another study reported that accurate risk assessment and effective prophylaxis could reduce DVT incidence in cancer patients by up to 50% [8].

The Caprini Thrombosis Risk Assessment Scale, developed by Caprini and colleagues in the United States, is a widely recognized tool for thrombosis risk stratification [9]. It has been shown to effectively assess thrombosis risk in orthopedic, internal medicine, intensive care, gynecologic oncology, and postoperative abdominal surgery patients [10-12]. However, few studies in China have explored its utility in predicting thrombosis risk specifically among lung cancer patients.

D-dimer is an important marker of coagulation dysfunction. Elevated plasma D-dimer levels in lung cancer patients have been associated with tumor metastasis and advanced clinical stage [13-15], and can serve as predictors of treatment response and recurrence risk prior to surgery or chemotherapy [16]. Additionally, one study identified high D-dimer levels as an independent risk factor for pulmonary embolism in lung cancer patients [17], though in-depth analyses remain limited. Notably, the role of D-dimer in the development of DVT in lung cancer patients has not been systematically investigated.

Thromboelastography (TEG) is an effective method for evaluating coagulation function, providing dynamic and continuous assessment of the entire coagulation process. Some studies have demonstrated that TEG can predict DVT risk following lung cancer surgery [18]. However, controversy exists regarding the predictive value of Caprini scores, D-dimer, and TEG individually for DVT in cancer patients, with some studies yielding potentially biased results [19, 20]. Further analyses are warranted to clarify these associations.

To date, few reports have examined the combined predictive value of Caprini scores, D-dimer levels, and TEG parameters for DVT occurrence in lung cancer patients. Therefore, this study aimed to investigate their predictive value for DVT in this population, with the goal of providing clinical evidence to support treatment decision-making and prognosis evaluation in lung cancer patients at risk of DVT.

Materials and methods

General information

This retrospective study included lung cancer patients treated at Yantaishan Hospital between September 2020 and August 2024. As shown in **Figure 1**, a total of 450 lung cancer patients were screened. Based on the inclusion and exclusion criteria, 90 patients were enrolled. These patients were then divided into

two groups according to the presence of DVT: the observation group (50 patients with DVT) and the control group (40 patients without DVT). This study was approved by the Ethics Committee of Yantaishan Hospital (No. 2025-037).

Inclusion criteria: ① Age ≥18 years; ② Primary lung cancer confirmed by pathological biopsy, with DVT diagnosed by ultrasound [21, 22], demonstrating partial or complete vessel compression or detoured/incomplete blood flow signals; lung cancer patients without DVT were included in the control group; ③ No direct surgical indications, with disease staged as middle or advanced; ④ No history of anticoagulant therapy, long-term bedridden status, or surgery within three months prior to admission; ⑤ Voluntary participation with complete medical records.

Exclusion criteria: ① History of venous thromboembolism prior to admission; ② History of coagulation disorders or hematological disease; ③ Severe cardiovascular or cerebrovascular diseases (e.g., atrial fibrillation); ④ Presence of other malignant tumors; ⑤ Peripheral vascular lesions or congenital vascular malformations; ⑥ Severe hepatic or renal dysfunction; ⑦ Mental disorders; ⑧ Immune diseases or acute/chronic infections.

According to Villalta scores [23], patients with DVT were further categorized into a mild group (Villalta score ≤9, n=28) and a moderate-severity group (Villalta score >9, n=22). The Villalta scale assesses five symptoms (pain, cramps, heaviness, abnormal sensations, itching) and six signs (pretibial edema, skin induration, hyperpigmentation, pain on calf compression, venous ectasia, redness), each scored from 0 to 3. Total scores reflect DVT severity: ≤9 mild, 10-14 moderate, and ≥15 severe.

Data collection

Clinical data collected from medical records at admission included age, body mass index (BMI), gender, hypertension, smoking status, diabetes, alcohol consumption, family history of venous thrombosis, hyperlipidemia, histological type of neoplasm, history of chemotherapy, radiotherapy, targeted therapy, immunotherapy, and clinical stage.

Outcome measures

DVT detection: Venous ultrasonography was performed at admission by an experienced ultrasonographer. Diagnostic criteria for DVT included the presence of intraluminal echogenicity, loss of vein compressibility, and absence of venous flow [24].

Caprini scores: The Caprini Thrombosis Risk Assessment Scale (2010 version) was used to assess thrombotic risk at admission [25]. The scale includes 45 risk factors, with individual items scored according to risk level: 0-1 (low risk), 2 (moderate risk), 3-4 (high risk), and ≥5 (very high risk). Higher total scores indicate greater thrombosis risk.

D-dimer measurement: On the first morning after admission, 5 mL of fasting peripheral venous blood was collected from each patient. Samples were centrifuged at 3500 rpm for 6 minutes, and serum was analyzed using an automated coagulation analyzer (CA510, Siemens, Germany) to determine D-dimer levels, following kit instructions.

TEG assessment: TEG was performed using a TEG5000 instrument (Haemonetics, USA). Blood samples were analyzed within two hours of collection, with TEG automatically tracing the curve and recording parameters such as reaction time (R), coagulation time (K), coagulation angle (α angle), and maximum amplitude (MA). Detection was completed 30 minutes after MA determination.

Statistical analysis

All analyses were conducted using SPSS version 23.0. Continuous variables were expressed as mean ± standard deviation and compared between groups using independent t-tests. Categorical data were presented as frequencies (%) and compared using χ^2 tests. Pearson correlation analysis assessed relationships between Caprini score, D-dimer level, MA, α angle, and Villalta score.

Multiple logistic regression analysis with forward LR selection identified independent predictors of DVT occurrence, following the approach described by previous studies [26]. Predictive values including specificity and sensitivity were calculated based on established

Table 1. The comparison of general information between observation and control groups

Parameters	Control group (N=40)	Observation group (N=50)	t/χ^2	*P*
Age (years)	58.17±7.19	57.28±6.89	0.597	0.552
BMI (kg/m^2)	22.24±2.47	22.51±2.59	0.502	0.617
Gender (Male/Female)	26/14	35/15	0.254	0.614
Hypertension (%)	11 (27.50%)	20 (40.00%)	1.538	0.215
Smoking (%)	16 (40.00%)	28 (56.00%)	2.277	0.131
Diabetes (%)	9 (22.50%)	10 (20.00%)	0.083	0.773
Drinking (%)	12 (30.00%)	20 (40.00%)	0.970	0.325
Family history of venous thrombosis	2 (5.00%)	4 (8.00%)	0.321	0.571
Hyperlipaemia (%)	6 (15.00%)	10 (20.00%)	0.380	0.538
Neoplasms histologic type			0.550	0.760
Small cell cancer	5 (12.50%)	9 (18.00%)		
Squamous carcinoma	18 (45.00%)	22 (44.00%		
Adenomatous carcinoma	17 (42.50%)	19 (38.00%)		
Intervention of chemotherapy	33 (82.50%)	40 (80.00%)	0.091	0.763
Intervention of radiotherapy	24 (60.00%)	34 (68.00%)	0.621	0.431
Intervention of targeted therapy	12 (30.00%)	20 (40.00%)	0.970	0.325
Intervention of immunological therapy	13 (32.50%)	19 (38.00%)	0.293	0.588
Clinical stages			1.505	0.220
III stage	22 (55.00%)	21 (42.00%)		
IV stage	18 (45.00%)	29 (58.00%)		

Note: BMI: Body mass index.

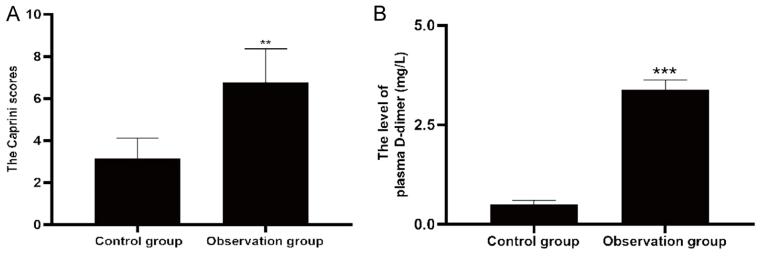

Figure 2. Comparison of Caprini scores and serum D-dimer level between two groups. A: Caprini scores; B: GFAP; ***P<0.001 vs control group. Note: IL-10: Interleukin-10; GFPA: Glial fibrillary acidic protein.

methods [27]. Receiver operating characteristic (ROC) curves evaluated predictive performance, with the DeLong test used to compare area under the curve (AUC) values [28]. A two-tailed P<0.05 was considered statistically significant.

Results

Comparison of general information

As shown in **Table 1**, there were no significant differences between the observation group and the control group in terms of age, body mass index (BMI), gender, hypertension, smoking, diabetes, alcohol consumption, family history of venous thrombosis, hyperlipidemia, neoplasm histological type, clinical stage, or history of chemotherapy, radiotherapy, targeted therapy, and immunotherapy (all P>0.05). Thus, the groups were comparable.

Comparison of Caprini scores, D-dimer level and TEG parameters

As presented in **Figure 2**, **Tables 2** and **3**, the observation group had significantly higher Caprini scores, D-dimer levels, α angle, and MA values compared to the control group (all P<0.05). Additionally, the proportion of very high-risk patients in the observation group was significantly greater than that in the control group (P<0.001). No significant differences were observed in R and K values between the two groups (both P>0.05).

Table 2. Distribution of thrombosis risk categories based on Caprini scores between two groups

Group	Classification of thrombosis risk based on Caprini scores [n (%)]			
	Low risk	Medium risk	High risk	Very high risk
Control group (n=40)	9 (22.50%)	14 (35.00%)	10 (25.00%)	7 (17.50%)
Observation group (n=50)	0 (0%)	2 (4.00%)	9 (18.00%)	39 (78.00%)
χ^2 values		39.690		
P values		<0.001		

Table 3. Comparison of thrombelastography parameters between two groups

Group	Thrombelastography parameters			
	K (min)	R (min)	MA (mm)	α angle (°)
Control group (n=40)	3.47±0.56	4.12±0.75	72.53±9.16	70.11±10.53
Observation group (n=50)	3.67±0.79	3.91±0.68	84.13±10.74	79.15±11.23
χ^2 values	1.352	1.391	5.430	3.901
P values	0.180	0.168	<0.001	<0.001

Note: K: Clotting time; R: Reaction time; MA: Maximum amplitude; α angle: Coagulation angle.

Table 4. Univariate logistic regression analysis for Caprini scores, D-dimer level, α angle and MA value for predicating venous thromboembolism in patients with lung cancer

Parameters	OR (95% CI)	P
α angle	1.981 (1.184-3.167)	0.003
MA value	2.301 (1.117-5.225)	0.029
Caprini scores	3.202 (1.571-7.095)	0.004
D-dimer level	4.023 (1.304-11.962)	0.011

Note: MA: Maximum amplitude; α angle: Coagulation angle.

Table 5. Variable assignments for multiple logistic regression analysis

Independent variable	Assignment	
	1	2
α angle	≤67.39	>67.39
MA value	≤70.62	>70.62
Caprini scores	≤4.97	>4.97
D-dimer level	≤2.14	>2.14

Note: MA: Maximum amplitude; α angle: Coagulation angle.

Multiple logistic regression analysis of predictors for VTE in lung cancer patients

Multiple logistic regression was performed using variables with P<0.05 in univariate analysis (α angle, MA value, Caprini score, and D-dimer level) (**Table 4**). Stepwise regression was conducted with VTE occurrence as the dependent variable and the above variables as independent factors (**Tables 5** and **6**). Results indicated that α angle, MA value, Caprini score, and D-dimer level were independent risk factors for VTE, with OR (95% CI) values of 2.011 (1.197-3.287), 2.291 (1.105-5.218), 3.195 (1.568-7.103), and 4.017 (1.296-11.958), respectively.

Predictive performance of Caprini scores, D-dimer level, α angle and MA value for VTE occurrence

As shown in **Table 7** and **Figure 3**, each indicator alone demonstrated moderate predictive value, with AUCs of 0.771 (Caprini score), 0.789 (D-dimer), 0.747 (α angle), and 0.725 (MA). The combined index had the highest predictive value, with an AUC of 0.861, sensitivity of 87.50%, and specificity of 91.18%. DeLong's test revealed that the combined index had significantly greater predictive power than any single indicator alone, with significant differences among the AUCs (**Table 8**).

Comparison of Caprini scores, D-dimer level, MA and α angle between mild group and moderate-severity group

As shown in **Figure 4**, the moderate-severity group had significantly higher Caprini scores, D-dimer levels, α angle, and MA values compared to the mild group (all P<0.001). Specifically, mean values in the moderate group

Table 6. Multiple logistic regression analysis for Caprini scores, D-dimer level, α angle and MA value for predicating venous thromboembolism in patients with lung cancer

Parameters	β	SE	Wald	P	OR (95% CI)
α angle	0.711	0.275	6.918	0.007	2.011 (1.197-3.287)
MA value	0.796	0.402	8.796	0.038	2.291 (1.105-5.218)
Caprini scores	1.372	0.415	9.125	0.002	3.195 (1.568-7.103)
D-dimer level	1.412	0.603	6.015	0.013	4.017 (1.296-11.958)

Note: MA: Maximum amplitude; α angle: Coagulation angle; SE: Standard error; OR: Odds Ratio; CI: Confidence interval.

Table 7. Predictive performance of Caprini scores, D-dimer level, α angle and MA value for venous thromboembolism in patients with lung cancer

Parameters	AUC	95% CI	*P* value	Cut-off value	Sensitivity (%)	Specificity (%)
α angle	0.747	0.592-0.891	0.028	67.39	81.25 (13/16)	76.47 (26/34)
MA value	0.725	0.605-0.901	0.036	70.62	75.00 (12/16)	79.41 (27/34)
Caprini scores	0.771	0.618-0.887	0.005	4.97	62.50 (10/16)	85.29 (29/34)
D-dimer level	0.789	0.637-0.925	0.017	2.14	68.75 (11/16)	82.35 (28/34)
Jointed indexes	0.861	0.756-0.943	0.008	-	87.50 (14/16)	91.18 (31/34)

Note: MA: Maximum amplitude; α angle: Coagulation angle.

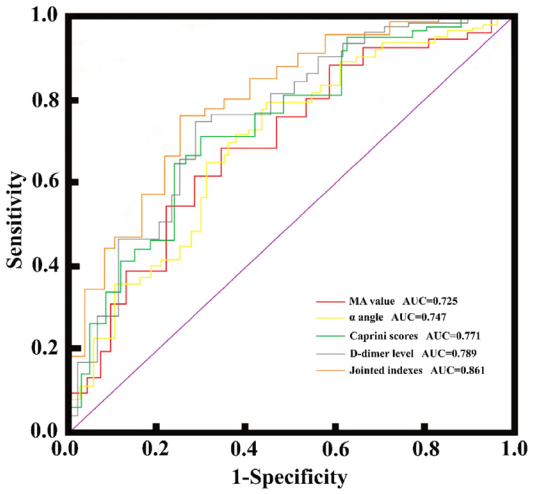

Figure 3. ROC curves for Caprini scores, D-dimer level, α angle and MA value in predicting venous thromboembolism in patients with lung cancer. Note: MA: Maximum amplitude; α angle: Coagulation angle; ROC: Relative operating characteristic.

were Caprini score: 8.47±1.23, D-dimer: 4.12±0.31 mg/L, α angle: 88.17±9.86°, and MA: 95.10±11.05 mm.

Correlations between Caprini score, D-dimer level, MA, α angle, and villalta score

Pearson correlation analysis demonstrated significant positive correlations between Caprini score, D-dimer level, MA, and α angle with Villalta scores (Caprini score: r=0.563, P=0.024; D-dimer: r=0.617, P=0.029; MA: r=0.428, P=0.030; α angle: r=0.441, P=0.037), as shown in **Table 9**.

Discussion

DVT frequently occurs during hospitalization in patients with intermediate to advanced lung cancer. It not only exacerbates patient discomfort but, if the thrombus dislodges and travels through the bloodstream, can result in pulmonary embolism, posing a direct threat to life. Clinically, tumor biology itself is believed to significantly contribute to DVT formation, as patients with lung cancer often experience coagulation abnormalities and hypercoagulability [29]. Malignant tumors have been reported to cause coagulation dysfunction and the release of procoagulant microparticles into circulation, thereby increasing thrombotic risk [30]. Moreover, the etiology of DVT is complex. Procoagulant changes and coagulation system activation have been associated with advanced lung cancer behaviors, including tumor invasion and distant metastasis [31].

Donnellan et al. [32] reported that biomarkers such as cancer site, leukocyte count, body mass index, hemoglobin, and platelet count

Table 8. Pairwise comparisons of AUCs between individual indicators and the combined model

Comparisons of variables	Difference between areas (95% CI)	Z test	*P* value
α angle vs. Jointed indexes	0.210 (0.118-0.275)	5.947	<0.001
MA value vs. Jointed indexes	0.228 (0.127-0.293)	6.381	<0.001
Caprini vs. Jointed indexes	0.196 (0.109-0.261)	4.672	<0.001
D-dimer level vs. Jointed indexes	0.184 (0.102-0.245)	3.285	0.009

Note: Caprini scores, D-dimer level, α angle and MA value were 0.771, 0.789, 0.747 and 0.725.

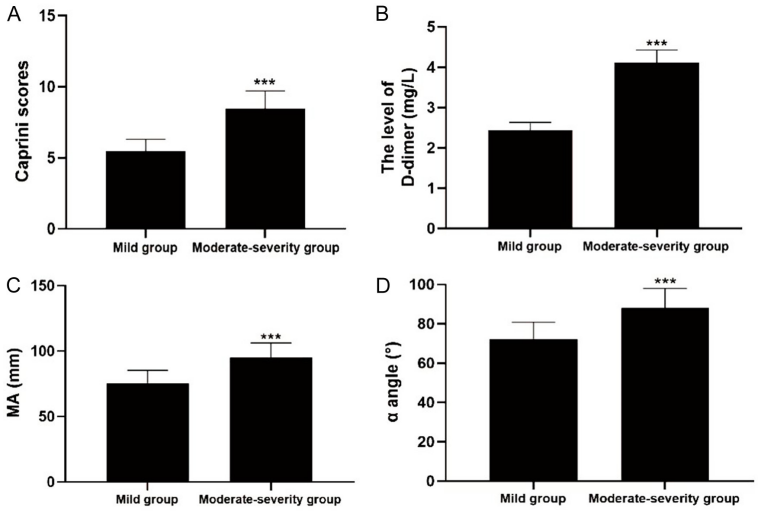

Figure 4. Comparison of Caprini scores, serum D-dimer level, MA and α angle between mild and moderate-severity groups. ***P<0.001 vs Mild group. MA: Maximum amplitude; α angle: Coagulation angle.

Table 9. Pearson analysis for the relationship of Caprini scores, serum D-dimer level, MA and α angle with Villalta scores

Parameters		Caprini scores	D-dimer (mg/L)	MA (mm)	α angle (°)
Villalta scores	r value	0.563	0.617	0.428	0.441
	P value	0.024	0.029	0.030	0.037

Note: MA: Maximum amplitude; α angle: Coagulation angle.

can help identify predictors of VTE in lung cancer patients. Additional individual risk factors including cisplatin-based chemotherapy, advanced cancer stage, immunomodulatory drugs, angiogenesis inhibitors, hospitalization, and surgical interventions have also been associated with VTE development in this population [33-36]. Therefore, early identification of these risk factors is essential to enable targeted preventive strategies. Currently, relying on a single indicator for early VTE prediction is inadequate; using thrombotic risk scoring models or combining multiple indicators is generally recommended to improve diagnostic accuracy [37].

The present study found no significant differences between the observation and control groups in general characteristics such as age, BMI, gender, hypertension, smoking status, or diabetes, consistent with findings by Jin et al. [38]. The Caprini score is widely recognized for perioperative thrombosis risk assessment. Hachey et al. [39] reported a 5.2% incidence of VTE within 60 days after lung cancer resection, with one-third occurring post-discharge, and demonstrated that the Caprini score effectively predicted postoperative VTE. They recommended enhanced anticoagulation measures for high-risk patients to prevent VTE. Similarly, Sterbling et al. [40] showed that VTE incidence was significantly reduced in high-risk lung cancer surgery patients when prophylactic interventions were implemented based on Caprini model assessments, supporting its safety and feasibility.

However, some scholars argue that the Caprini model's effectiveness in perioperative VTE risk stratification for lung cancer patients remains limited, as it does not account for tumor type or treatment-related factors, thus reducing its discriminatory ability [41]. There is still a need to explore new thrombosis risk assessment models tailored for cancer populations.

Unlike previous studies, the current study focused on patients with intermediate and advanced lung cancer who were no longer candidates for radical surgery. Results showed that Caprini scores in the observation group were

significantly higher than in the control group. Notably, no patient in the observation group was classified as low risk for VTE, with most categorized as very high risk (78.0%). In contrast, the control group mainly comprised medium-risk patients (35.0%), and the proportion of very high-risk patients was significantly lower than in the observation group. Furthermore, ROC analysis revealed an AUC of 0.771 for the Caprini score, and Pearson analysis showed a correlation coefficient of 0.563 with Villalta scores. These findings suggest that the Caprini thrombosis risk scale has valuable clinical utility in assessing VTE risk among patients with intermediate and advanced lung cancer.

D-dimer is a degradation product of cross-linked fibrin clots. Elevated D-dimer levels are mainly observed in conditions of secondary hyperfibrinolysis, including hypercoagulable states, disseminated intravascular coagulation, and thrombolytic therapy. Measurement of D-dimer is widely used for the diagnosis, treatment monitoring, and prognosis assessment of thrombotic disorders such as VTE.

Ohara et al. [42] demonstrated that preoperative fibrinogen and D-dimer levels effectively predicted recurrence-free and overall survival in patients with non-small-cell lung cancer undergoing radical surgery. Similarly, Ke et al. [43] reported that early perioperative D-dimer detection with risk-stratified cutoff values improved VTE diagnostic efficacy after lung cancer surgery.

TEG is a relatively novel clinical test assessing coagulation function. Its main parameters - R, K, α angle, and MA - are critical for diagnosing and managing thrombotic diseases, platelet disorders, coagulation factor deficiencies, and hyperfibrinolysis [44]. Qin et al. [18] found that combining TEG with clinical risk factors to construct a nomogram was a simple and effective method to predict postoperative VTE in lung cancer patients.

In this study, patients in the observation group had significantly higher serum D-dimer levels as well as higher α angle and MA values compared to the control group, with no significant differences in R and K values. The α angle reflects the rate of fibrin clot formation, while MA indicates the maximum strength of the clot, both of which are closely associated with coagulation and fibrinolytic system activity [45].

Multiple logistic regression analysis showed that serum D-dimer level, α angle, and MA were independent risk factors for VTE occurrence in patients with intermediate and advanced lung cancer. ROC curve analysis confirmed their predictive value.

Additionally, the International Society on Thrombosis and Haemostasis recommends the Villalta score as a standard tool to evaluate venous thrombosis severity and post-thrombotic syndrome due to its interrater reliability and external validity [46]. This study found that D-dimer, α angle, and MA were significantly correlated with Villalta scores, consistent with previous reports [47, 48].

Currently, single-indicator VTE assessment scales do not fully reflect the specific risk profiles of lung cancer patients. Combining multiple indicators has been shown to improve screening accuracy. Ding et al. reported that Caprini scores alone had limited validity post-lung surgery (AUC=0.751), but combining Caprini scores with hemoglobin (AUC=0.616) and D-dimer (AUC=0.763) improved predictive performance (AUC=0.822) [49]. Another study showed that combining D-dimer, fibrinogen, and TEG parameters effectively stratified and predicted VTE risk in lung cancer patients [50].

In this study, ROC analysis demonstrated that the combined use of Caprini scores, D-dimer, α angle, and MA yielded an AUC of 0.861 for predicting DVT occurrence, significantly outperforming each indicator alone. This indicates that combined assessment provides superior predictive accuracy for DVT in patients with intermediate and advanced lung cancer.

In summary, combined assessment using Caprini scores, D-dimer, α angle, and MA can effectively predict the occurrence of DVT in lung cancer patients, as these are independent risk factors. This combined approach is worth promoting in clinical practice. However, this study has limitations, including its single-center retrospective design, small sample size, lack of mechanistic exploration, and absence of long-term follow-up. Future randomized, multicenter studies with larger samples and extended follow-up are needed to validate these findings.

Disclosure of conflict of interest

None.

Address correspondence to: Hongfu Ma, Yantaishan Hospital, No. 10087, Keji Avenue, Yantai 264003, Shandong, China. Tel: +86-0535-6863159; Fax: +86-0535-6863159; E-mail: mahongfu_19@163.com; Hui Zheng, Department of Vascular Surgery, General Surgery Clinical Center, Shanghai General Hospital, Shanghai Jiao Tong University School of Medicine, No. 85, Wujin Road, Shanghai 200080, China. Tel: +86-021-63240090; Fax: +86-021-63240090; E-mail: huizheng_@hotmail.com

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