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Padua prediction score may be inappropriate for VTE risk assessment in hospitalized patients with acute respiratory conditions: A Chinese single-center cohort study☆

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ABSTRACT

Background: The Padua Prediction Score (PPS) recommended by the guidelines lacks effective external validation in a Chinese cohort. This study sought to assess the accuracy of the PPS to predict venous thromboembolism (VTE) risk in medical inpatients with acute respiratory conditions.
Methods: This consecutive cohort study included 1,574 inpatients from January to August 2019. The occurrence rate of VTE in patients classified at high-risk and low-risk groups according to PPS and Caprini risk assessment model (RAM) was compared. The discriminatory capability of the RAMs was evaluated in all the patients and the subgroup without pharmacological prophylaxis. Reclassification parameters were also used to assess the clinical utility.
Results: 170 (10.8%) patients were objectively confirmed as having VTE during hospitalization. The incidence rate of VTE in low-risk patients was 6.3% by PPS, which was significantly higher than that by Caprini RAM (2.6%, $p < 0.001$). The area under the curve (AUC) for PPS and Caprini RAM was 0.714 (95%CI, 0.672–0.756) and 0.760 (95%CI, 0.724–0.797), respectively ($p = 0.003$). The AUC of Caprini RAM was larger than PPS even in subgroups without pharmacological prophylaxis (0.774 vs 0.709, $p = 0.002$). Compared with Caprini RAM, the net reclassification index was estimated at 0.037 ($p = 0.436$), and integrated discrimination improvement was 0.015 ($p = 0.495$) by PPS.
Conclusions: According to our cohort study, PPS may not be appropriate to predict VTE risk in hospitalized patients with acute respiratory conditions. An accurate, widely applicable, validated RAM needs to be further constructed in Chinese medical inpatients.

1. Introduction

Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), continues to rank as the third most common cardiovascular disease [1]. The risk of VTE ranged from 40% to 60% in both surgical and medical inpatients when low molecular weight heparin was not available [2,3]. About 14.9% of acutely ill medical patients admitted to the hospitals experienced VTE based on screening tests [4]. However, only 10.3% to 20.2% of medical patients with VTE received standard thromboprophylaxis [2,5,6], which indicates an inadequate implementation rate. It was reported that hospitalized patients with pre-existing pulmonary diseases were associated with the highest risk of thromboembolism [7]. However, there is not enough evidence to develop an effective assessment model to detect VTE among patients with acute respiratory conditions.

The 9th edition of the American College of Chest Physicians (ACCP) guidelines recommended using the Padua Prediction Score (PPS) to evaluate the risk of VTE for internal medicine inpatients [8], while for

☆ All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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non-orthopedic surgical patients, Caprini RAM was recommended [9,10]. The PPS included 11 items that were assigned 1 to 3 points respectively [11]. Caprini RAM consisted of 39 independent VTE risk factors which were given 1 to 5 points each [12]. Based on the symptoms, laboratory results, past history and so on, physicians performed VTE risk evaluation at admission. Currently, no study has been conducted to evaluate the external validity of the PPS in assessing VTE risk among the Chinese population, particularly in the context of cohort studies. On the other hand, the Caprini RAM has been validated to be effective in hospitalized patients of internal medicine [10,13,14]. Several case-control studies found that the predictive performance of the Caprini RAM seemed to be better than the PPS in medical and surgical inpatients [15,16]. However, these domestic studies were designed as case-control studies and cannot fully represent real-world scenarios [13,15,16]. Additionally, systematic data on the prediction performance of the PPS in patients with acute pulmonary disease are rare.

Therefore, the purpose of our study is to evaluate the predictive power of PPS in identifying VTE among hospitalized patients with acute respiratory conditions in a Chinese cohort.

2. Methods

2.1. Study population

This was a single-center retrospective cohort study of patients diagnosed with acute respiratory diseases admitted to the Beijing Institute of Respiratory Medicine, Beijing Chao-Yang Hospital, Capital Medical University from January to August 2019. The pre-test probability of VTE was assessed at admission by physicians using the Wells score [17]. Patients falling into the likely group and unlikely group with elevated age-adjusted D-dimer value would complete screening tests for VTE within 48 h of admission. Screening tests include compression ultrasonography (CUS), computed tomography pulmonary angiogram (CTPA), and lung ventilation/perfusion (V/Q) scan. Patients older than 40 years old and got admitted for longer than 3 days were included in the study. Patients were excluded if they were diagnosed with VTE or received anticoagulant treatment on admission. Critically ill patients in the respiratory intensive care unit were also ruled out.

Because of the retrospective design, written informed consents were not obtained from individual patients, but permission for data analysis was approved by the Ethical Committees of Beijing Chao-Yang Hospital, Beijing Institute of Respiratory Medicine, Capital Medical University, Beijing, China.

2.2. Diagnosis of VTE

DVT was confirmed via CUS and the validated criterion for DVT was incomplete compressibility of the vein and absence or reduced flow signal [18]. If CTPA shows a segmental or more proximal filling defect or a V/Q scan yields a high probability for PTE, PTE diagnoses should be considered.

2.3. VTE risk assessment

Patient demographics including age, gender, body mass index (BMI), smoking history, and variables of the PPS and Caprini RAM were obtained from Electronic Medical Records. Other therapeutic factors and indices of laboratory tests related to VTE were also collected. The cumulative VTE risk score and associated risk level were assessed for each patient. We restricted the values of these variables to the records closest to the time of admission. Two researchers who had received in-depth training calculated scores independently.

For the PPS, the classification was consistent with the ACCP guidelines, and the score ≥ 4 was defined as a "high-risk" group. For Caprini RAM, the guidelines recommended that "low risk" if the score is between 0 and 1; "intermediate risk" if the score is 2; "high risk" if the score is between 3 and 4; "highest risk" if the score is over 5. When the risk for VTE is low or intermediate, the guidelines suggest no specific pharmacologic or mechanical prophylaxis. For patients at high or highest risk for VTE who are not at high risk for major bleeding complications, anticoagulant prophylaxis was recommended [9]. Considering the difference in preventive measures, we adopted dichotomous classification and defined that patients with a Caprini score ≥ 3 were at high risk of VTE. The primary outcome was the occurrence of VTE events.

2.4. Sample size calculation

Sample size calculation was performed using NCSS PASS 15.0, which relied on diagnostic tests for two paired samples. Previous study showed that the sensitivities of PPS and Caprini RAM in hospitalized medical patients were 0.75 and 0.40, and proportion discordant was calculated to be 0.55 [13,15,16,19]. The prospective, noninterventional, multicenter cohort study MAGNET AECOPD (MAnaGement aNd advErse ouTcomes in inpatients with acute exacerbation of chronic obstructive pulmonary disease) Registry study in China reported that the incidence of VTE in inpatients with acute exacerbation of chronic obstructive pulmonary disease is about 3.00% [20,21]. Thus, a sample size of 1567 patients corresponding with a 5% alpha error and a 10% beta error had adequate power (90%) to detect a difference of 35% in sensitivity between two tests when the proportion of discordant pairs was 55%. And we should include at least 47 VTE events based on the incidence rate.

2.5. Statistical analyses

All statistical analyses were performed with R version 3.5.1 and NCSS PASS 15.0. Mean and standard deviation or median and interquartile range were used to describe continuous variables as appropriate. The comparison of VTE rates in different categories was conducted using the Chi-squared test. Assessment of discrimination between the PPS and the Caprini RAM, irrespective of cut-offs, was evaluated by average area under the curve (AUC) using the Delong tests [22]. Then, sensitivity, specificity, and Youden index were calculated to perform diagnostic test statistics. The best cutoff value for the ROC plots, both Caprini score and PPS, was identified using the Youden's Index. The Kappa value was calculated to assess consistency. Reclassification parameters consisting of the net reclassification index (NRI) and integrated discrimination improvement (IDI) were also used to compare the PPS's clinical utility with that of the Caprini RAM. For missing variables, multiple imputation approach was used. Statistical significance was defined as a two-tailed P-value of < 0.05 for all analyses.

3. Results

3.1. Demographic and clinical characteristics

Of 3,849 screened participants, 2,275 patients were excluded and the detailed exclusion criteria were shown in Fig. 1. The main-reasons for exclusion were: 432 patients with a low clinical probability of VTE by Wells Score and negative D-dimer test results, 540 patients younger than 40 years old, 961 patients with less than 3 days of hospitalization, 186 patients diagnosed with VTE at admission, 88 patients receiving anticoagulation therapy, and 73 patients hospitalized at RICU. Finally, 1,574 hospitalized patients (954 males and 620 females) were included from January to August 2019 in our cohort study. 170 (10.8%) patients were confirmed VTE during hospitalization by CUS, CTPA and V/Q scan, of which 3 patients (1.8%) were diagnosed with DVT and PTE, 16 patients (9.4%) had PTE only, 151 patients (88.8%) had DVT only (Fig. 1). For DVT patients, 16 (9.4%) had proximal DVT and 135 (79.4%) had isolated distal DVT. Moreover, 65.9% (n = 112) had muscular calf vein thrombosis. Supplementary Table 3 showed the main reasons for admission were acute exacerbation of chronic obstructive pulmonary disease (19.1%), community-acquired pneumonia (17.3%), interstitial

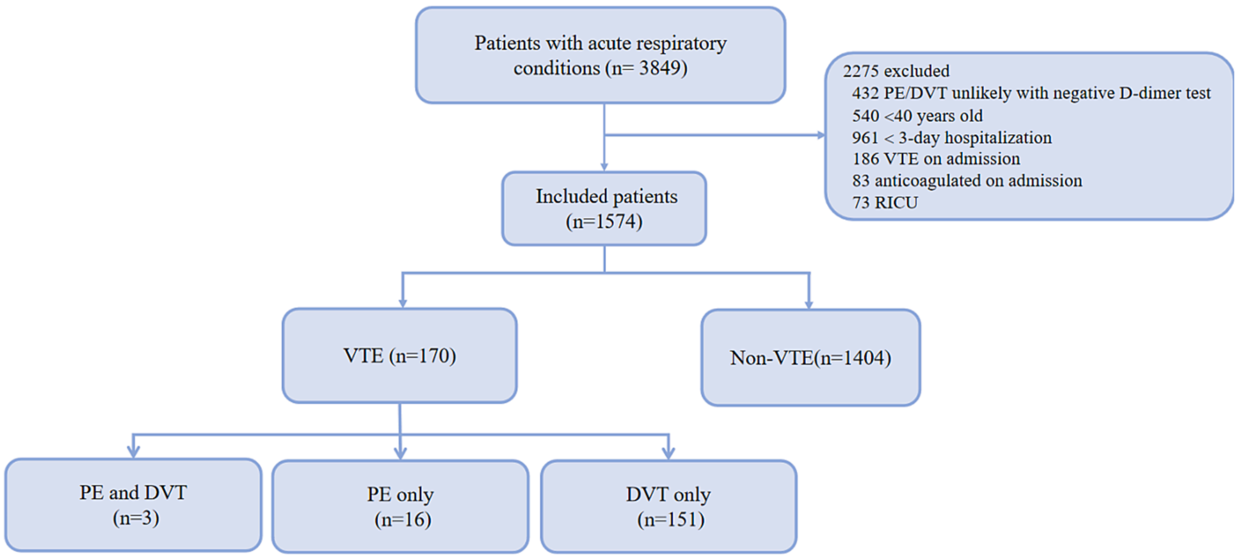

Fig. 1. Patient disposition. Abbreviation: VTE: venous thromboembolism; DVT: deep vein thrombosis; PTE: pulmonary thromboembolism.

lung disease (16.7%), and lung cancer (15.4%).

Table 1 provides the demographic and clinical characteristics of all patients on admission. The median age was 65.0 years (interquartile range [IQR], 58.0–73.0). Patients in the VTE group were older than the non-VTE group (median 72.0 vs 64.5, $p < 0.001$), and there were more men in the VTE group (69.4% vs 59.5%, $p < 0.001$). The median scores of PPS (4.5 vs 2.0, $p < 0.001$) and Caprini RAM (5.0 vs 3.0, $p < 0.001$) were higher in the VTE group.

Table 1
Demographic and clinical characteristics of the study population on admission.

	Total (n = 1574)	VTE (n = 170)	non-VTE (n = 1404)	*P* value
Age (years)	65.0 (58.0–73.0)	72.0 (63.5–80.0)	64.5 (57.0–72.0)	< 0.001
Male	954 (60.6%)	118 (69.4%)	836 (59.5%)	0.013
BMI[*] (kg·m^{-2})	24.1 ± 3.9	23.6 ± 3.7	24.2 ± 3.9	0.243
Smoking history	818 (52.0%)	93 (54.7%)	725 (51.6%)	0.450
Bedridden time (> 72 h)	268 (17.0%)	76 (44.7%)	192 (13.7%)	< 0.001
PPS (score)	2.0 (1.0, 4.0)	4.5 (2.0, 6.0)	2.0 (1.0, 3.0)	< 0.001
Caprini RAM (score)	3.0 (2.0, 5.0)	5.0 (4.0, 7.0)	3.0 (2.0, 4.0)	< 0.001
Thromboprophylaxis	283 (18.0%)	61 (35.9%)	222 (15.8%)	< 0.001
Laboratory tests on admission				
WBC (×10^{9}·L^{-1})	6.5 (5.1, 8.4)	7.1 (5.5, 9.5)	6.4 (5.1, 8.2)	0.001
Neutrophils (%)	63.5 (55.3, 72.4)	70.2 (60.5, 78.1)	62.7 (54.6, 71.1)	< 0.001
HGB (g· L^{-1})	129 (117, 141)	125 (110, 136)	130 (118, 142)	< 0.001
HCT (%)	38.0 (34.8, 41.4)	36.7 (32.4, 40.1)	38.1 (35.0, 41.5)	< 0.001
PLT (×10^{9}·L^{-1})	219 (173, 270)	205 (155, 269)	220 (175, 270)	0.027
PT[§] (s)	11.8 (11.2, 12.5)	12.0 (11.3, 13.0)	11.8 (11.2, 12.4)	0.007
APTT[§] (s)	24.9 (23.0, 27.3)	25.2 (23.0, 28.0)	24.9 (23.0, 27.0)	0.070
D-dimer[¶] (ng·ml^{-1})	553.1 (299.5, 1350.0)	1662.6 (785.0, 3881.6)	507.6 (281.7, 1115.9)	< 0.001
ESR[Ψ] (mmol·h^{-1})	16.0 (6.0, 34.0)	18.0 (8.0, 32.8)	16.0 (6.0, 34.0)	0.449
CRP[♣] (mg·dl^{-1})	0.7 (0.3, 2.4)	1.2 (0.4, 6.0)	0.6 (0.3, 2.2)	< 0.001

Data are presented as n, mean ± SD, n (%) or median (interquartile range), unless otherwise stated. VTE: venous thromboembolism; BMI: body mass index; WBC: white blood count; N%: percent of neutrophils; HGB: hemoglobin; HCT: hematocrit; PLT: platelet count; PT: prothrombin time; APTT: activated partial thromboplastin time; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

[*] Available in 1342 total,129 VTE and 1213 non-VTE. [§] Available in 1561 total,170 VTE and 1391 non-VTE. [¶] Available in 1550 total,169 VTE and 1381 non-VTE. [Ψ] Available in 1528 total,164 VTE and 1364 non-VTE. [♣] Available in 1504 total,166 VTE and 1338 non-VTE.

3.2. *VTE events assessed by PPS and Caprini RAM*

We divided all patients into two groups: VTE low-risk group and VTE high-risk group, using the Caprini RAM and the PPS respectively. Of 1,574 patients, 1,126 (71.5%) were in VTE low-risk group (<4 points) by the PPS, and 71 out of 1,126 patients (6.3%; 95% CI, 4.9%-8.0%) experienced VTE events during hospitalization, accounting for 41.8% (71/170) of all the VTE events. According to the Caprini RAM, 547 patients (34.8%) were at VTE low-risk (<3 points), and only 14 patients had VTE events (2.6%; 95% CI, 1.4%-4.3%), which was significantly less than that in the low-risk group by the PPS ($p < 0.001$, Fig. 2). 448 patients (28.5%) were identified as high-risk for VTE by PPS, and 22.1% (99 out of 448) had VTE events. While in Caprini RAM, 156 patients (15.2%) in the high-risk group developed VTE events. Thus, for patients at high risk, the incidence of VTE based on the PPS was higher than that of the Caprini RAM (22.1% vs 15.2%, $p < 0.001$, Fig. 2).

3.3. *The discriminative ability of PPS and Caprini RAM*

For all patients, the AUC of the ROC curve of Caprini RAM was 0.760 (95%CI, 0.724–0.797), which was significantly larger than that of the PPS [0.714 (95%CI, 0.672–0.756), $p = 0.003$, Fig. 3a]. The best cut-off values of the two RAMs were 4 points for PPS and 3 points for Caprini RAM. The predictive validity of the Caprini RAM and PPS was summarized in Table 2. Based on the best cut-off, the specificity of the PPS appeared higher than that of the Caprini RAM (83.69 vs 60.97, $p < 0.001$), but its sensitivity was lower (50.00 vs 80.00, $p < 0.001$). On the whole, Caprini RAM had a larger Youden index than PPS.

3.4. *Sensitivity analyses*

To assess the robustness of the findings, we plotted the ROC curve of the Caprini RAM and PPS in the subgroup of patients without pharmacological prophylaxis during their hospitalization. Therefore, 1,291 patients were included in the sensitivity analysis. The AUC of the Caprini RAM for predicting VTE was 0.774 (95% CI, 0.729–0.819), which was significantly higher than that of the PPS [0.709 (95% CI, 0.656–0.763),

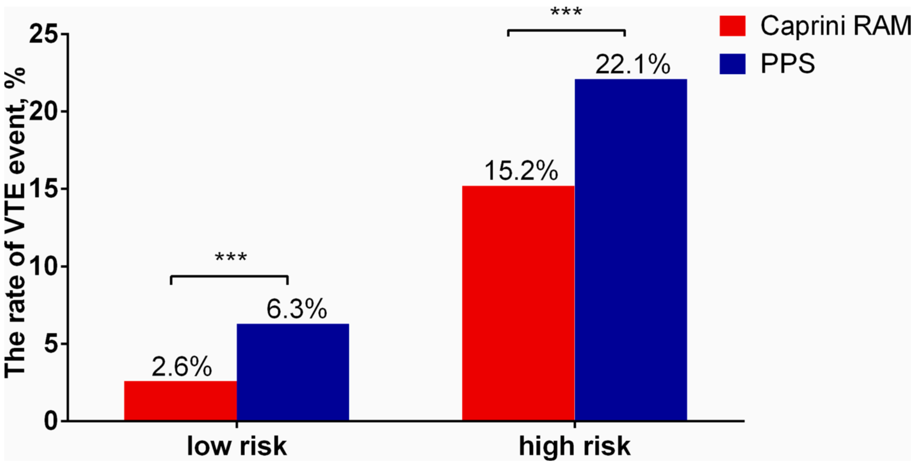

Fig. 2. The rate of VTE event in different risk categories by PPS and Caprini RAM. Abbreviation: VTE: venous thromboembolism; PPS: Padua prediction score; RAM: risk assessment model.

$p = 0.002$, Fig. 3b].

3.5. Reclassification of the study patients

Table 3 showed the reclassification of the patients with or without VTE by the PPS and Caprini RAM. The two predictive assessment methods resulted in identical classifications for 961 patients (n = 530 at low risk; n = 431 at high risk). 448 out of 1,574 patients (28.5%) were at high risk determined by the PPS, while the rate of high-risk patients by the Caprini RAM was 65.2% (n = 1,027, $p < 0.001$). The Kappa test was 0.31 corresponding to a low agreement.

For patients who developed VTE (n = 170), none of the patients were classified upward from low-risk by the Caprini RAM to high-risk category by the PPS. The trade-off was the reclassification of 57 (33.5%) patients from the high-risk by the Caprini RAM into the low-risk group by the PPS. So the net decrease was 33.5%. For patients without VTE (n = 1,404), the PPS correctly reclassified 539 patients into low-risk but incorrectly reclassified 17 patients into the high-risk group, resulting in a net correct classification of 37.2% compared with the Caprini RAM. Therefore, the overall NRI was 0.037 ($p = 0.436$) by the PPS compared with Caprini RAM. Furthermore, the IDI of PPS was 0.015 ($p = 0.495$) in comparison to Caprini RAM.

3.6. Modified classification of PPS

If a cumulative score of ≥ 3 for PPS was defined as an increased risk of VTE, the sensitivity (72.59) was improved but the trade-off was decreased specificity (57.80) when compared to the model with ≥ 4 cut-offs. The AUC of the ROC curve of modified PPS was 0.652 (95%CI, 0.604 to 0.700) and the Youden index was 0.304. Compared with Caprini RAM with the best cut-off value, there were no increases in reclassification as assessed by the NRI 0.010 ($p = 0.815$) and IDI 0.001 ($p = 0.959$).

3.7. Thromboprophylaxis rate

283 out of 1574 patients (18.0%) received anticoagulant prophylaxis. Of them, 267 patients received low molecular weight heparin and 16 fondaparinux sodium. There was a higher rate of thromboprophylaxis in the VTE group than in the non-VTE group (35.9% vs 15.8%, $p < 0.001$, Table 1). In patients who received prophylaxis, 21.6% (61/283) of patients developed VTE, which was higher than the occurrence rate of VTE in patients without prevention measures (109/1291, 8.4%, $p < 0.001$). The median duration of thromboprophylaxis was 10 (7–14) days. The proportion of patients receiving thromboprophylaxis in the high-risk group was also significantly different, with PPS being 40.0% and Caprini RAM being 25.3% ($p < 0.001$, Supplementary Table 4).

4. Discussion

To the best of our knowledge, this study is the first cohort study to validate the PPS in predicting VTE risk among hospitalized patients with acute respiratory conditions in China. The PPS was less discriminative than Caprini RAM in all the patients or patients without pharmacological prophylaxis. This study provided more solid and favorable evidence for the risk prediction of VTE in patients with acute respiratory conditions by comparing PPS and Caprini RAM.

In our study, 170 (10.8%) patients were objectively confirmed VTE during hospitalization, which was different from the rate reported in MAGNET AECOPD [20,21]. The most prominent cause of this increase is that MAGNET AECOPD focuses on the rate of symptomatic VTE while this study performed screening tests for VTE in patients with a high probability Wells score. The recalculated sample size for our cohort is 470, with a power of 0.902, based on the incidence of VTE (10.8%). In the low-risk group, the rate of VTE events was 6.3% by PPS, which was higher than the rate determined by the Caprini RAM. This implies that the sensitivity of the PPS appears to be lower than that of Caprini RAM. Zhou et al. found that Caprini RAM assessed 82.3 % of VTE patients as high risk, whereas only 30.1 % of VTE patients were identified as having high risk by PPS in a Chinese case-control study [13]. In our study, although higher specificity was noted when PPS compared with Caprini RAM, the lower Youden index demonstrated that PPS was inferior to Caprini RAM in authenticity, which is consistent with previous studies [15,16]. Importantly, Greg Maynard suggested that a risk score of ≥ 3 was warranted for those adopting PPS [23]. Therefore, we investigated whether PPS ≥ 3 as high-risk could be more useful in our center. But the results revealed that the modified classification of PPS is not a better predictor of VTE in our hospital.

It was suggested to use the PPS to stratify nonsurgical inpatients at risk of VTE by the ACCP guideline [8]. We reasoned that the inconsistency between the guideline and our results lies in some factors. The PPS, proposed by Paolo Prandoni, was empirically generated after substantial modification of the Kucher model and assessed its value in a single-center cohort study carried out among the Caucasian population. Moreover, it has not been validated externally worldwide [11]. Barbar et al. diagnosed VTE events in the cases with clinical symptoms while we performed VTE screening tests irrespective of symptoms. And the demographic characteristics, such as sex, age, and race, and the disease distribution of recruited patients were different. The difference may be also attributed to the limitations of the PPS items. The cut-off of BMI

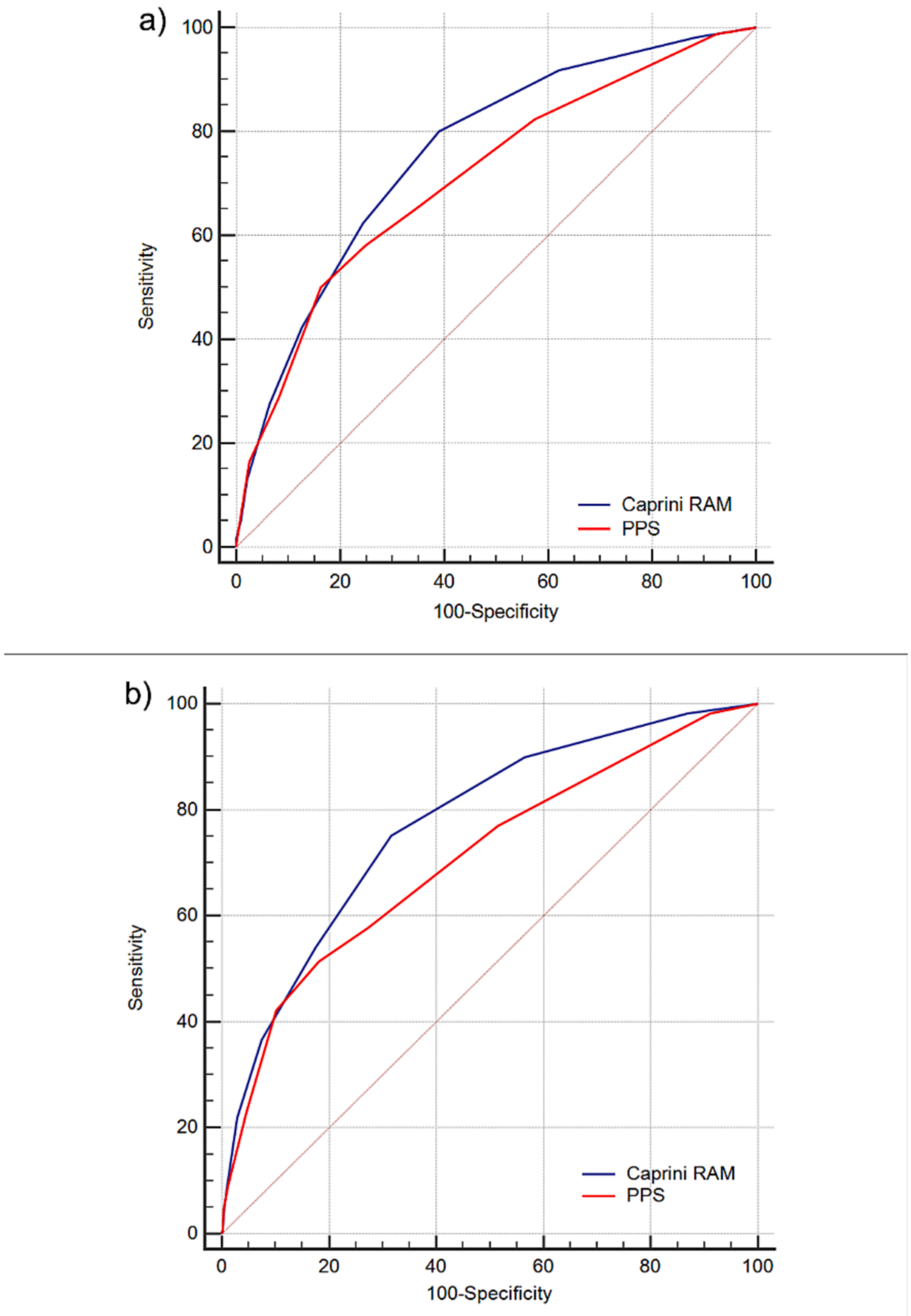

Fig. 3. ROC curves of the Caprini RAM and PPS for patients. (A) For all the patients, the AUC of the ROC curve of the Caprini RAM was 0.760 (95%CI, 0.724–0.797), which was significantly larger than the AUC of PPS [0.714 (95%CI, 0.672–0.756), p = 0.003; (B) For patients without thromboprophylaxis, the AUC for predicting VTE was 0.774 (95% CI, 0.729–0.819) of the Caprini RAM, which was significantly higher than that of the PPS [0.709 (95% CI, 0.656–0.763), p = 0.002]. Abbreviation: RAM: risk assessment model; PPS: Padua prediction score; AUC: area under the curve; VTE: venous thromboembolism.

Table 2
Predictive validity of the Carprini RAM and PPS in medical inpatients.

	AUC	Sensitivity (%)	Specificity (%)	Youden index
Caprini RAM	0.76 (0.72–0.80)	80.00 (73.20—85.70)	60.97 (58.40—63.50)	0.41 (0.34–0.47)
PPS	0.71 (0.67–0.76)	50.00 (42.20—57.80)	83.69 (81.70—85.60)	0.34 (0.25–0.41)
P value	0.0025	<0.001	<0.001	< 0.0001

RAM: risk assessment model; PPS: Padua prediction score; AUC: area under the curve.

(≥30) might not be optimal for the Asian population [24]. The factor “reduced mobility” carries a high weight (+3) but seems arduous to anticipate on admission. And some of the thrombophilia were not routinely examined in clinical practice.

In terms of study design, it was reported that a cohort study is the better way to ascertain the incidence of a disorder and reduce the risk of bias [25]. Case-control studies artificially increased the incidence of the disease and modified the properties of the tests. Previous domestic studies on the prediction of VTE were case-control studies. Thus, the results of our cohort study are more convincing to reflect the real-world scenario. Our study suggested that the AUC of the Caprini RAM was larger than that of PPS for either all the patients or those without

Table 3
Reclassification of the patients with or without VTE.

Classification of patients	PPS	Caprini RAM		
	VTE risk	Low-risk (<3 points)	High-risk (≥3 points)	Total
VTE patients (n = 170)	Low-risk (<4 points)	14(8.2%)	57(33.5%)	71(41.8%)
	High-risk (≥4 points)	0	99(58.2%)	99(58.2%)
	Total	14(8.2%)	156 (91.8%)	170 (100.0%)
Non-VTE patients (n = 1404)	Low-risk (<4 points)	516 (36.8%)	539 (38.4%)	1055 (75.1%)
	High-risk (≥4 points)	17(1.2%)	332 (23.6%)	349(24.9%)
	Total	533 (38.0%)	871 (62.0%)	1404 (100.0%)
All the patients	Low-risk (<4 points)	530 (33.7%)	596 (37.9%)	1126 (71.5%)
	High-risk (≥4 points)	17(1.1%)	431 (27.4%)	448(28.5%)
	Total	547 (34.8%)	1027 (65.2%)	1574 (100.0%)
Kappa test = 0.31				

VTE, venous thromboembolism; PPS, Padua prediction score; RAM, risk assessment model.

pharmacological prophylaxis, which was consistent with existing literature even when the study design was different [13,15,16,26,27].

The NRI and IDI were originally proposed by Pencina et al in 2008 to evaluate the added prediction performance of a new marker [28], and they have been advocated and adopted widely in point-based risk scores [29]. In our study, the value of NRI was 0.037, which was calculated by measuring the net change in risk classification in VTE and non-VTE patients, representing an improvement in the power of risk prediction. However, this was due to a higher proportion of patients with correct classification in the non-VTE group (0.372) and a lower proportion in the VTE group (-0.335). These indicated that the recognition capability of PPS was still inferior to Caprini RAM in the VTE group. The IDI is a measurement of improvement in differentiation, regardless of risk categories, and can be viewed as an integrated difference in Youden's indices [30]. In our study, although IDI was positive, there was no statistical difference between the two RAMs. To the best of our knowledge, there have been limited studies utilizing NRI and IDI to evaluate the predictive performance of the PPS and Caprini RAM for VTE events among Chinese inpatients. Considering the three performance indicators – AUC, NRI, and IDI – it can be concluded that Caprini RAM has exhibited superior predictive capability than PPS.

Our study found that the real thromboprophylaxis rate of VTE high-risk patients remains discouraging, which was similar to previous domestic research [6]. Most of the reasons were due to the non-standard formulation of prevention strategies, insufficient knowledge of physicians, and fear of bleeding risk associated with prophylaxis. Therefore, it is critical to enhance medical education and establish VTE risk-assessment systems for Chinese internal medicine inpatients. In addition, VTE events still occurred in 38.5% of patients who received pharmacologic prophylaxis. That is to say, thromboprophylaxis was not associated with a reduction in VTE occurrence, which accords with another study in VTE prophylaxis among acute medically ill patients [31]. However, in our cohort, there was no lethal VTE, and 79.4% of patients had isolated distal DVT. It is reported that a range of 5% to 10% incidence of fatal VTE in hospitalized patients is without prophylaxis [32,33]. These indicated that although thromboprophylaxis could not avoid the development of VTE, it could effectively reduce the occurrence of fatal VTE.

In our cohort study, systematic screening of hospitalized patients for VTE resulted in a more accurate incidence measurement and decreased misdiagnosis of asymptomatic patients. That's also the main reason why the overall VTE incidence of our study is higher than other research worldwide [34–36]. Moreover, our study was intended to observe the predictive value of the models, rather than focusing on the incidence and thromboprophylaxis rates of VTE in the real world. Though the diagnosis and treatment of patients with asymptomatic VTE remain controversial [35,37], correct diagnosis of these patients is essential for enhanced surveillance and management, such as ultrasonic monitoring of isolated distal DVT.

There are a few limitations in our study. Firstly, it was a single-center, retrospective cohort study. As with all retrospective studies, there may be challenges in identifying risk factors and estimating the incidence of VTE due to selective bias. Secondly, there is a confounding factor that some of the patients received thromboprophylaxis at the beginning of hospitalization, but we have adjusted it. Moreover, the patients evaluated in this study may be less representative owing to the diseases involved being limited.

5. Conclusions

PPS seems to be inappropriate to assess VTE risk for hospitalized patients with acute respiratory conditions in our center. We need to establish an accurate and more efficient VTE prediction model for Chinese populations in the future.

6. Author statement

Y. Yang, S. Yang and Y. Zhang conceived and designed the study. Y. Yang and S. Yang contributed to funding acquisition and supervision. Y. Yang, S. Yang and Y. Zhang contributed to the data curation, formal analysis, investigation, methodology, project administration, writing original draft and writing review & editing. Y. Zhang contributed to software and visualization. S. Yang, Y. Yang, Y. Zhang, X. Jiao, J. Liu, W. Wang, T. Kuang, J. Gong and J. Li contributed to resources and validation. All authors confirmed the final version of the paper.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2023.101301.

References

[1] S.V. Konstantinides, G. Meyer, C. Becattini, et al., 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS), Eur. Heart J. 41 (4) (2020) 543–603.
[2] J. Ge, Y. Li, X. Jin, J. Zhou, Venous thromboembolism risk assessment and thromboprophylaxis among hospitalized acute medical patients in China–the RAMP study, Thromb. Res. 126 (4) (2010) 270–275.
[3] A.T. Cohen, V.F. Tapson, J.F. Bergmann, et al., Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study, Lancet 371 (9610) (2008) 387–394.
[4] A.J. Darzi, S.G. Karam, R. Charide, et al., Prognostic factors for VTE and bleeding in hospitalized medical patients: a systematic review and meta-analysis, Blood 135 (20) (2020) 1788–1810.
[5] M. Vardi, N.O. Ghanem-Zoubi, R. Zidan, V. Yurin, H. Bitterman, Venous thromboembolism and the utility of the Padua Prediction Score in patients with sepsis admitted to internal medicine departments, J. Thromb. Haemost. 11 (3) (2013) 467–473.
[6] Z. Zhai, Q. Kan, W. Li, et al., VTE Risk Profiles and Prophylaxis in Medical and Surgical Inpatients: The Identification of Chinese Hospitalized Patients' Risk Profile for Venous Thromboembolism (DissolVE-2)-A Cross-sectional Study, Chest 155 (1) (2019) 114–122.
[7] M.E. DeWitt, D.M. Herrington, J.W. Sanders, Venous or arterial thrombosis in COVID-19 cases in the North Carolina COVID-19 Community Research Partnership (NC-CCRP), Res Pract Thromb Haemost 7 (2) (2023), 100080.
[8] S.R. Kahn, W. Lim, A.S. Dunn, et al., Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, Chest 141 (2 Suppl) (2012) e195S–e226.
[9] M.K. Gould, D.A. Garcia, S.M. Wren, et al., Prevention of VTE in nonorthopedic surgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines, Chest 141 (2 Suppl) (2012) e227S–e277s.
[10] P.J. Grant, M.T. Greene, V. Chopra, et al., Assessing the Caprini Score for Risk Assessment of Venous Thromboembolism in Hospitalized Medical Patients, Am. J. Med. 129 (5) (2016) 528–535.
[11] S. Barbar, F. Noventa, V. Rossetto, et al., A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padua Prediction Score, J. Thromb. Haemost. 8 (11) (2010) 2450–2457.
[12] J.A. Caprini, J.I. Arcelus, J.H. Hasty, A.C. Tamhane, F. Fabrega, Clinical assessment of venous thromboembolic risk in surgical patients, Semin. Thromb. Hemostas. 17 (Suppl 3) (1991) 304–312.
[13] H. Zhou, L. Wang, X. Wu, et al., Validation of a venous thromboembolism risk assessment model in hospitalized chinese patients: a case-control study, J. Atheroscler. Thromb. 21 (3) (2014) 261–272.
[14] M.M. Shang, R. Yan, X.L. Wang, W.P. Gong, Z.Q. Guo, Comparison of 2013 and 2009 versions of Caprini risk assessment models for predicting VTE in Chinese cancer patients: a retrospective study, J. Thromb. Thrombol. 50 (2) (2020) 446–451.
[15] X. Liu, C. Liu, X. Chen, W. Wu, G. Lu, Comparison between Caprini and Padua risk assessment models for hospitalized medical patients at risk for venous thromboembolism: a retrospective study, Interact. Cardiovasc. Thorac. Surg. 23 (4) (2016) 538–543.
[16] H. Zhou, Y. Hu, X. Li, et al., Assessment of the Risk of Venous Thromboembolism in Medical Inpatients using the Padua Prediction Score and Caprini Risk Assessment Model, J. Atheroscler. Thromb. 25 (11) (2018) 1091–1104.
[17] F. Khan, T. Tritschler, S.R. Kahn, M.A. Rodger, Venous thromboembolism, Lancet 398 (10294) (2021) 64–77.
[18] L. Needleman, J.J. Cronan, M.P. Lilly, et al., Ultrasound for Lower Extremity Deep Venous Thrombosis: Multidisciplinary Recommendations From the Society of Radiologists in Ultrasound Consensus Conference, Circulation 137 (14) (2018) 1505–1515.
[19] X. Chen, L. Pan, H. Deng, et al., Risk Assessment in Chinese Hospitalized Patients Comparing the Padua and Caprini Scoring Algorithms, Clin. Appl. Thromb. Hemostas. 24 (9_suppl) (2018) 127s–135s.
[20] C. Zhou, Q. Yi, H. Ge, et al., Validation of Risk Assessment Models Predicting Venous Thromboembolism in Inpatients with Acute Exacerbation Of Chronic Obstructive Pulmonary Disease: A Multicenter Cohort Study in China, Thromb. Haemost. 122 (7) (2022) 1177–1185.
[21] C. Zhou, Y. Guang, Y. Luo, et al., Superior Predictive Value of D-Dimer to the Padua Prediction Score for Venous Thromboembolism in Inpatients with AECOPD: A Multicenter Cohort Study, Int. J. Chron. Obstruct. Pulmon. Dis. 17 (2022) 2711–2722.
[22] A.C. Alba, T. Agoritsas, M. Walsh, et al., Discrimination and Calibration of Clinical Prediction Models: Users' Guides to the Medical Literature, J. Am. Med. Assoc. 318 (14) (2017) 1377–1384.
[23] G. Maynard, I.H. Jenkins, G.J. Merli, Venous thromboembolism prevention guidelines for medical inpatients: mind the (implementation) gap, J. Hosp. Med. 8 (10) (2013) 582–588.
[24] A. Misra, Ethnic-Specific Criteria for Classification of Body Mass Index: A Perspective for Asian Indians and American Diabetes Association Position Statement, Diabetes Technol. Ther. 17 (9) (2015) 667–671.
[25] D.A. Grimes, K.F. Schulz, Cohort studies: marching towards outcomes, Lancet 359 (9303) (2002) 341–345.
[26] M.T. Greene, A.C. Spyropoulos, V. Chopra, et al., Validation of Risk Assessment Models of Venous Thromboembolism in Hospitalized Medical Patients, Am. J. Med. 129 (9) (2016).
[27] L. He, L. Luo, X. Hou, et al., Predicting venous thromboembolism in hospitalized trauma patients: a combination of the Caprini score and data-driven machine learning model, BMC Emerg. Med. 21 (1) (2021) 60.
[28] M.J. Pencina, R.B. D'Agostino Sr., R.B. D'Agostino Jr., R.S. Vasan, Evaluating the added predictive ability of a new marker: from area under the ROC curve to reclassification and beyond, Stat. Med. 27 (2) (2008).
[29] L.E. Thomas, E.C. O'Brien, J.P. Piccini, R.B. D'Agostino, M.J. Pencina, Application of net reclassification index to non-nested and point-based risk prediction models: a review, Eur. Heart J. 40 (23) (2019).
[30] W.J. Youden, Index for rating diagnostic tests, Cancer 3 (1) (1950) 32–35.
[31] A. Gafter-Gvili, G. Drozdinsky, O. Zusman, S. Kushnir, L. Leibovici, Venous Thromboembolism Prophylaxis in Acute Medically Ill Patients: A Retrospective Cohort Study, The American journal of medicine 133 (12) (2020).
[32] D.A. Flevas, P.D. Megaloikonomos, L. Dimopoulos, et al., Thromboembolism prophylaxis in orthopaedics: an update, EFORT Open Rev 3 (4) (2018) 136–148.
[33] R. Alikhan, F. Peters, R. Wilmott, A.T. Cohen, Fatal pulmonary embolism in hospitalised patients: a necropsy review, J. Clin. Pathol. 57 (12) (2004) 1254–1257.
[34] H. Bo, Y. Li, G. Liu, et al., Assessing the Risk for Development of Deep Vein Thrombosis among Chinese Patients using the 2010 Caprini Risk Assessment Model: A Prospective Multicenter Study, J. Atheroscler. Thromb. 27 (8) (2020).
[35] G.H. Utter, T.S. Dhillon, E.S. Salcedo, et al., Therapeutic Anticoagulation for Isolated Calf Deep Vein Thrombosis, JAMA Surg. 151 (9) (2016) e161770.
[36] T. Moumneh, J. Riou, D. Douillet, et al., Validation of risk assessment models predicting venous thromboembolism in acutely ill medical inpatients: A cohort study, J. Thromb. Haemost. 18 (6) (2020) 1398–1407.
[37] A. Brateanu, K. Patel, K. Chagin, et al., Probability of developing proximal deep-vein thrombosis and/or pulmonary embolism after distal deep-vein thrombosis, Thromb. Haemostas. 115 (3) (2016) 608–614.