Padua Prediction Score was Inappropriate for Venous Thromboembolism Risk Assessment in Acute Medical Inpatients: A Cohort Study

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Abstract

Background

Padua Prediction Score (PPS) still lacks of effectively external validation in Chinese population. To assess the accuracy of PPS to predict venous thromboembolism (VTE) risk in acute medical inpatients, and to compare the predictive value with Caprini risk assessment model (RAM).

Methods

This consecutive cohort study included acute internal medicine inpatients in Beijing Institute of Respiratory Medicine, Beijing, China from January to August 2019. The PPS and Caprini RAM were assessed for all the patients. The occurrence rate of VTE predicted by PPS and Caprini RAM was compared using Chi-squared test. Discrimination was evaluated by the area under curve using the Delong tests. Reclassification parameters were also used to compare the PPS's clinical utility with that of the Caprini RAM.

Results:

A total of 1647 inpatients of internal medicine were retrospectively registered. The overall incidence of VTE during hospitalization was 13.2%. The incidence of VTE in low-risk patients was 6.5% assessed by PPS, which was significantly higher than that by Caprini RAM (2.6%, $p < 0.001$). The area under the receiver operating characteristic curve (ROC) for PPS and Caprini RAM was 0.747 (95%CI, 0.725–0.768) and 0.773 (95%CI, 0.752–0.793), respectively ($p = 0.0453$). Based on the best cut-off, the specificity of the PPS appeared higher than that of the Caprini RAM (82.45 vs 60.07, $p < 0.001$), but its sensitivity was lower (59.45 vs 83.87, $p < 0.001$). Compared with Caprini RAM, the net reclassification index was estimated at 0.094 ($p = 0.016$) and integrated discrimination improvement was 0.037 ($p = 0.098$) by PPS. The ROC curve of the Caprini RAM and PPS in the subgroup of patients without pharmacological prophylaxis during their hospitalization was 0.776 of the Caprini RAM, which was significantly higher than that of the PPS ($p = 0.005$).

Conclusions

PPS seems inappropriately to predict VTE risk in acute internal medicine inpatients. It has limitations not only in the performance of identifying “VTE high-risk” patients, but also in the ability of discrimination. An accurate, widely applicable, validated RAM for prediction of the VTE risk needs to be further constructed in Chinese hospitalized medical patients.

Background

Venous thromboembolism (VTE), comprising deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), remains the third most common cardiovascular disease, and is also the most common preventable cause of hospital death [1]. The risk of VTE ranges from 40–60% in both surgical and medical inpatients [2, 3]. Nearly 60% of VTE events are related to recent hospitalization history [4, 5]. In particular, patients of internal medicine suffer from VTE events more frequently than surgical patients [6]. But the rate of standard thromboprophylaxis ranges from 10.3–20.2% in medical patients [2, 7, 8], that is insufficiently implemented. Researches in China suggest that more than 50% of hospitalized patients have ≥ 2 risk factors for thrombosis on admission [2], which highlights the significance of identifying inpatients at risk of VTE. The ideal risk assessment models (RAMs) make it possible to evaluate the risk stratification of VTE accurately, which in turn guides thromboprophylaxis [9].

Padua Prediction Score (PPS), including 11 items that were assigned 1 to 3 points respectively, was derived from a single cohort study carried out in Italy [10]. The 9th edition of the American College of Chest Physicians (ACCP) guidelines recommended that estimate hospitalized patients at risk of VTE using the PPS for inpatients of internal medicine [11]. Caprini RAM was developed based on expert consensus and clinical experience, consisted of 39 independent VTE risk factors that were given 1 to 5 points each and used a point-scoring system [12]. It was suggested for the 9th edition of the ACCP guidelines that the Caprini RAM was used to assess the VTE risk in non-orthopedic surgical patients [13, 14] .

At present, the PPS still lacks of external validation in Chinese population currently, whereas the Caprini RAM has been validated effectively in hospitalized patients of internal medicine [5, 14, 15]. Several case-control studies in China have compared the capabilities of Caprini RAM and the PPS in medical and surgical inpatients to evaluate which model can predict VTE risk better. It was found that the predictive performance of the Caprini RAM seemed to be better than the PPS [16, 17]. However, since most domestic studies were designed as case-control studies that cannot represent real-world scenario [5, 16, 17]. Therefore, the purpose of our study is to evaluate the accuracy of PPS to predict VTE risk in hospitalized patients of internal medicine in a Chinese cohort, and to further clarify whether PPS is applicable comparing with Caprini RAM.

Methods

Study population

This study was a single-center retrospective cohort study with patients diagnosed with acute medical diseases admitted to Beijing Institute of Respiratory Medicine, Beijing Chao-Yang Hospital, Capital Medical University from January to August 2019. Patients who had performed any of the compression venous ultrasonography, computed tomography pulmonary angiogram, and lung ventilation perfusion scan after 48 hours in hospital were eligible in our study. All the patients aged at least 40 years old and had been hospitalized for not less than 3 days. Critically ill patients admitted to the respiratory intensive

care unit (RICU) were also enrolled. Patients were excluded if they diagnosed with VTE (including PTE and DVT) or received anticoagulant treatment on admission.

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

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 Record. 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 to 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 at high-risk group. For Caprini RAM, the guidelines recommended that “low risk” if score 0–1; “intermediate risk” if score 2; “high risk” if score 3–4; “highest risk” if score ≥ 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, it was recommended anticoagulant prophylaxis [13]. In order to simplify the calculation and take into account the difference in preventive measures, we adopted dichotomous classification and defined patients with the Caprini score ≥ 3 was considered at high risk of VTE. The primary outcome was the occurrence of VTE events.

Sample size calculation

The sample size estimation was obtained by the module “Comparison of two ROC curves” in MedCalc. Based on the previous study, the average area under curve (AUC) of PPS and Caprini RAM were 0.66 and 0.73, respectively [16–18]. Correlation in positive and negative group calculated in the pre-experiment were 0.529 and 0.378. It is reported that VTE incidence ranges from 10%-40% in hospitalized patients of internal medicine [2, 19], so we assumed that the ratio of sample size in non-VTE / VTE group was 7. This resulted in a sample size of at least 1512 patients (189 VTE cases and 1323 non-VTE cases) corresponding with a 5% alpha error and a 20% beta error.

Statistical analyses

All statistical analyses were performed with R version 3.5.1 and MedCalc. The Shapiro-Wilk test was used to assess the normality of continuous variables. Results were described by their proportion and 95% confidence interval (CI) for categorical variables. Mean and standard deviation or median and interquartile range were used to describe continuous variables as appropriate. The comparison of the occurrence rate of VTE in different categories was using Chi-squared test. Assessment of discrimination between the PPS and the Caprini RAM, irrespective of cutoffs, was evaluated by the AUC using the Delong

tests [20]. Then, sensitivity, specificity and Youden index were calculated to performed diagnostic test statistics. Sensitivity analysis excluding the patients with anticoagulant prophylaxis was conducted. We examined the proportion of patients who would be reclassified into higher or lower-risk categories between the PPS and the Caprini RAM. The Kappa value was calculated to assess consistency. Reclassification parameters consisting of 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, complete-case analysis was used. Statistical significance was defined as a two-tailed P-value of < 0.05 for all analyses.

Results

Demographic and clinical characteristics

Of 3849 screened participants, a total of 1647 hospitalized patients (1008 male and 639 female) were retrospectively registered from January to August 2019. 2202 patients were excluded, because 432 patients didn't undergo confirmed examination for VTE, 540 were less than 40 years old, 961 were less than 3-day hospitalization, 186 were diagnosed with VTE on admission, and 83 were receiving anticoagulant treatment on admission because of other reasons. 217 (13.2%) patients were objectively confirmed with VTE during hospitalization, of which 3 patients (1.38%) were diagnosed with DVT and PTE, 16 patients (7.37%) had PTE only, 20 patients (9.22%) had proximal DVT and 178 patients (82.03%) had isolated distal DVT only (Fig. 1). Supplementary table 1 showed the main reasons for admission were acute exacerbation of chronic obstructive pulmonary disease (18.5%), pulmonary infection (17.7%), interstitial lung disease (16.2%), lung cancer (14.8%).

Table 1 provided the demographic and clinical characteristics of all the patients on admission. The median age was 65.0 years (interquartile range [IQR], 57.0–73.0). Patients in the VTE group were older than non-VTE group (median 70.0 vs 64.0, $p < 0.001$), and there were more men (71.4% vs 59.7%, $p < 0.001$) and RICU patients (21.7% vs 1.8%, $p < 0.001$). The median scores of PPS (5.0 vs 2.0, $p < 0.001$) and Caprini RAM (5.0 vs 3.0, $p < 0.001$) were higher in the VTE group. As for laboratory tests on admission, patients in the VTE group had higher levels of white blood count (7.6×10^9/L vs 6.4×10^9/L, $p < 0.001$), neutrophils (74.6% vs 63.0%, $p < 0.001$), D-dimer (2095.4 ng/ml vs 520.0 ng/ml, $p < 0.001$), C-reactive protein (1.85 mg/dl vs 0.74 mg/dl, $p < 0.001$), prothrombin time (12.2s vs 11.8s, $p < 0.001$) and activated partial thromboplastin time (25.5s vs 24.9s, $p < 0.001$); and lower levels of hemoglobin (123g/L vs 130g/L, $p < 0.001$), hematocrit (HCT, 36.3% vs 38.1%, $p < 0.001$) and platelet count (PLT, 200×10^9/L vs 219×10^9/L, $p = 0.004$).

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

	Total (n = 1647)	VTE (n = 217)	non-VTE (n = 1430)	*P* value
Demography				
Age (years)	65.0 (57.0–73.0)	70.0 (63.0–78.0)	64.0 (57.0–72.0)	<0.001
Male, n (%)	1008 (61.2%)	155 (71.4%)	853 (59.7%)	0.001
BMI* (kg/m2)	24.1 ± 3.9	23.7 ± 3.8	24.2 ± 3.9	0.478
Smoke history, n (%)	860 (52.2%)	122 (56.2%)	738 (51.6%)	0.205
RICU, n (%)	73 (4.4%)	47 (21.7%)	26 (1.8%)	<0.001
PPS (score)	2.0 (1.0, 4.0)	5.0 (2.0, 6.0)	2.0 (1.0, 4.0)	<0.001
Caprini RAM (score)	3.0 (2.0, 5.0)	5.0 (4.0, 7.0)	3.0 (2.0, 5.0)	<0.001
Thromboprophylaxis, n (%)	395 (24.0%)	152 (70.0%)	243 (17.0%)	<0.001
Laboratory tests on admission				
WBC ($\times 10^9$/L)	6.6 (5.2, 8.6)	7.6 (5.7, 9.9)	6.4 (5.1, 8.3)	<0.001
Neutrophils (%)	64.2 (56.0, 73.7)	74.6 (63.2, 83.7)	63.0 (55.0, 71.6)	<0.001
HGB (g/L)	129 (116, 141)	123 (107, 135)	130 (117, 142)	<0.001
HCT (%)	37.9 (34.6, 41.3)	36.3 (32.0, 39.8)	38.1 (34.9, 41.5)	<0.001
PLT ($\times 10^9$/L)	218 (172, 270)	200 (150, 267)	219 (174, 270)	0.004
PT§ (s)	11.8 (11.2, 12.6)	12.2 (11.4, 13.2)	11.8 (11.2, 12.4)	<0.001
APTT§ (s)	24.9 (23.0, 27.3)	25.5 (23.2, 29.3)	24.9 (23.0, 27.2)	0.001
D-dimer¶ (ng/ml)	600.0 (310.0, 1520.0)	2095.4 (1008.3, 4808.3)	520.0 (286.9, 1181.8)	<0.001

Data are presented as number of patients (%), mean ± SD, median (interquartile range).

Abbreviation: VTE: venous thromboembolism; BMI: body mass index; RICU: respiratory intensive care unit; 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 1375 total ,150 VTE and 1225 non-VTE. § Available in 1634 total ,217 VTE and 1417 non-VTE. ¶ Available in 1623 total ,216 VTE and 1407 non-VTE. Ψ Available in 1595 total ,208 VTE and 1387 non-VTE. ♣ Available in 1577 total ,213 VTE and 1364 non-VTE.

	Total (n = 1647)	VTE (n = 217)	non-VTE (n = 1430)	*P* value
ESR[Ψ] (mmol/h)	17.0 (7.0, 34.0)	19.0 (9.0, 34.8)	16.0 (6.0, 34.0)	0.192
CRP[♣] (mg/dl)	0.7 (0.3, 3.1)	1.9 (0.6, 8.2)	0.7 (0.3, 2.4)	<0.001
Data are presented as number of patients (%), mean ± SD, median (interquartile range).				
Abbreviation: VTE: venous thromboembolism; BMI: body mass index; RICU: respiratory intensive care unit; 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 1375 total ,150 VTE and 1225 non-VTE. [§] Available in 1634 total ,217 VTE and 1417 non-VTE. [¶] Available in 1623 total ,216 VTE and 1407 non-VTE. [Ψ] Available in 1595 total ,208 VTE and 1387 non-VTE. [♣] Available in 1577 total ,213 VTE and 1364 non-VTE.				

VTE events assessed by PPS and Caprini RAM

We divided all the patients into two groups: VTE low-risk group and VTE high-risk group, using the Caprini RAM and the PPS respectively. In 1647 patients, 1129 (68.5%) were in VTE low-risk group (< 4 points) by the PPS, and 73 out of 1129 patients (6.5%; 95% CI, 5.0%-7.9%) experienced VTE events during hospitalization, accounting for 33.6% of all the VTE events. According to the Caprini RAM, 547 patients were VTE low-risk (< 3 points), and only 14 patients had VTE events (2.6%; 95% CI, 1.2%-3.9%), which was significantly less than that in the low-risk group by the PPS ($p < 0.001$, Fig. 2). For patients at high risk, the incidence of VTE on the basis of the PPS was higher than that of the Caprini RAM (27.8% vs 18.5%, $p < 0.001$, Fig. 2).

Discriminative ability of PPS and Caprini RAM

For all the patients, the AUC of the ROC curve of Caprini RAM was 0.773 (95%CI, 0.752–0.793), which was significantly larger than that of the PPS [0.747 (95%CI, 0.725–0.768), $p = 0.0453$, 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 (82.45 vs 60.07, $p < 0.001$), but its sensitivity was lower (59.45 vs 83.87, $p < 0.001$). On the whole, Caprini RAM had a larger Youden index than PPS.

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

	AUC	Sensitivity, %	Specificity, %	Youden index
Caprini RAM	0.77 (0.75–0.79)	83.87 (78.3–88.5)	60.07 (57.5–62.6)	0.4394
PPS	0.75 (0.73–0.77)	59.45 (52.6–66.0)	82.45 (80.4–84.4)	0.4189
P value	0.0453	<0.001	<0.001	-
Abbreviation: RAM: risk assessment model; PPS: Padua prediction score; AUC: area under curve.				

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 1029 patients (n = 529 at low risk; n = 500 at high risk). 518 out of 1647 patients (31.5%) were at high risk determined by the PPS, while the rate of high-risk patients by the Caprini RAM was 66.8% (n = 1100, $p < 0.001$). The Kappa test was 0.33 corresponding to a low agreement.

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	Low-risk (< 4 points)	14	59	73
	High-risk (≥ 4 points)	0	144	144
	Total	14	203	217
Non-VTE patients	Low-risk (< 4 points)	515	541	1056
	High-risk (≥ 4 points)	18	356	374
	Total	533	897	1430
All the patients	Low-risk (< 4 points)	529	600	1129
	High-risk (≥4 points)	18	500	518
	Total	547	1100	1647
Kappa test = 0.33				
Abbreviation: VTE, venous thromboembolism; PPS, Padua prediction score; RAM, risk assessment model.				

For patients who developed VTE (n = 217), 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 59 (27.2%) patients from the high-risk by the Caprini RAM into the low-risk group by the PPS. So that the net decrease was 27.2%. For patients without VTE (n = 1430), the PPS correctly reclassified 541 patients into low-risk but incorrectly reclassified 18 patients into high-risk group, resulting in a net correct classification of 36.6% compared with the Caprini RAM. Therefore, the overall NRI was 0.094 ($p = 0.016$) by the PPS comparing with Caprini RAM. Furthermore, the IDI of PPS was 0.037 ($p = 0.098$) in comparison to Caprini RAM.

Thromboprophylaxis rate

There were 395 out of 1647 patients (24.0%) received anticoagulant prophylaxis. Of them, 371 patients received low molecular weight heparin, 21 fondaparinux sodium and 3 unfractionated heparin. There was a higher rate of thromboprophylaxis in the VTE group than the non-VTE group (70.0% vs 17.0%, p<0.001, Table 1). In patients who received prophylaxis, 38.5% (152/395) of patients developed VTE, which was higher than the occurrence rate of VTE in patients without prevention measures (65/1252, 5.2%, p<0.001). The median duration of thromboprophylaxis was 10 (7–15) days. The proportion of patients receiving thromboprophylaxis in the high-risk group was also significantly different, with PPS being 51.4% and Caprini RAM being 33.3% (p < 0.001, Supplementary Table 2).

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, 1252 patients were included in the sensitivity analysis. The AUC for predicting VTE was 0.776 (95% CI, 0.752 – 0.696) of the Caprini RAM, which was significantly higher than that of the PPS [0.696 (95% CI 0.670–0.721), $p = 0.005$, Fig. 3b].

Discussion

To the best of our knowledge, this study is the first cohort study to validate the PPS in predicting the risk of VTE in Chinese internal medicine inpatients. We found that the PPS had limitations not only in the ability of identifying the VTE risk of patients, but also in the performance of discrimination. This retrospective cohort study provided new insights into the risk prediction of VTE in Chinese hospitalized medical patients by comparing PPS and Caprini RAM.

In our study, 217 (13.2%) patients were objectively confirmed with VTE during hospitalization. In the low-risk group, the rate of VTE events was 6.5% by PPS, which was obviously higher than that assessed by Caprini RAM. That is to say, 33.6% of VTE events were not recognized by the PPS in the present setting. The sensitivity of the PPS appears to be lower than that of Caprini RAM. Our findings were consistent with other researches. Zhou et al. found that Caprini RAM assessed 82.3% of VTE patients as high risk,

whereas only 30.1% of VTE patients was identified as having high risk by PPS in a Chinese case-control study [5]. It was thought that the Caprini RAM may be considered as the first choice in a general hospital because of higher sensitivity when compared with PPS [18]. Higher specificity was noted when PPS compared with Caprini RAM in our study. However, lower Youden index demonstrated that PPS was inferior to Caprini RAM in authenticity, which is consistent with other studies[16, 17]. As Liu et al. reported previously, PPS has higher specificity (85.6% vs 73.4%) and lower Youden index (0.443 vs 0.010) in a retrospective study [16].

Our study suggested that the AUC of the Caprini RAM was larger than that of PPS for either all the patients or those without pharmacological prophylaxis, which was fully consistent with existing literatures even if the study design was different [5, 16, 17, 21, 22]. Chen et al found that, in Chinese hospitalized patients, the AUC of the Caprini RAM (0.779) was significantly higher than the value of PPS (0.635, $p < 0.05$), and concluded that Caprini RAM has a better predictive ability [18]. Although, another Chinese case-control study showed that there was no significant difference between the AUCs of the Caprini RAM and PPS, Caprini RAM was still recommended as the first choice in a general hospital because of its incorporation of comprehensive risk factors, higher sensitivity, and potential for prediction of mortality [17]. In addition, in terms of study design, the case-control study artificially increased the incidence of the disease and modified the tests properties. Therefore, the results of our cohort study are more convincing to reflect the real-world scenario.

The NRI and IDI were proposed by Pencina et al in 2008 to evaluate the added prediction performance of a new marker originally [23], and they have been advocated and adopted widely in point-based risk scores [24]. In our study, the value of NRI was 0.094, which was calculated by measuring the net change in risk classification in VTE and non-VTE patients, representing 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 (0.366) and a lower proportion in the VTE group (-0.272). These indicated that the recognition ability 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 [25]. In our study, although IDI was positive, there was no statistical difference between the two RAMs. To the best of our knowledge, this is the first study to employ NRI and IDI to evaluate predictive ability of VTE events by the PPS and Caprini RAM in Chinese inpatients. Considering the three indicators of AUC, NRI and IDI comprehensively, Caprini RAM had a better predictive ability than PPS. Although the current guidelines recommend that estimate hospitalized patients at risk of VTE using the PPS for nonsurgical inpatients [11], the predictive value of PPS in our study is still unsatisfactory.

These differences may be attributed to the flaws of the PPS, which were originally derived from a single center among Caucasian population and included 11 risk factors [10]. The cut-off of BMI (≥ 30) might not be optimal for Asian population. Studies suggested that there was considerable variation in body fat and fat-free mass among various ethnic groups [26]. The factor for "reduced mobility" appeared arduous to anticipate on admission, but it had a high weight (+ 3) and moderate repeatability owing to the variability of clinicians' comprehension. And some of the thrombophilia were not routinely examined in

clinical practice. Therefore, it is rational to infer that the PPS lacks an advantage in predicting VTE risk for Chinese internal medicine inpatients.

In our study, the Caprini RAM showed a better predictive ability and accuracy than PPS. Caprini RAM had been validated efficiently in more than 200 studies, especially for surgical patients [15, 27, 28]. The better prediction performance of Caprini RAM was attributed mostly to the comprehensive risk factors it incorporated. Meanwhile, it's somewhat cumbersome to implement for medical inpatients. Since it contains information that is difficult to obtain in internal medicine, such as surgery, obstetrics and gynecology, as well as some rare thrombophilia in Chinese population. Additionally, the complex variables of Caprini RAM bring challenges to the feasibility and convenience of clinical work. Furthermore, we found that the specificity of Caprini RAM was lower than that of PPS, which may lead to the occurrence of relatively excessive prevention such as bleeding.

Our study found that the real thromboprophylaxis rate of VTE high-risk patients remains discouraging, which was similar with previously domestic researches [8]. Most of the reasons were due to the non-standard formulation of prevention strategies, insufficient knowledge of physician 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 the occurrence of VTE, which accords with another study in VTE prophylaxis among acute medically ill patients [29]. However, in our cohort, there was no lethal VTE, and 82% of patients had isolated distal DVT. These indicated that although thromboprophylaxis could not avoid the development of VTE, it could effectively reduce the occurrence of fatal VTE. It is reported that a range of 5–10% incidence of fatal VTE in hospitalized patients without prophylaxis [6, 30].

To our knowledge, this study is the first consecutive cohort study to predict VTE risk among hospitalized medical patients. Systematic screening of hospitalized patients for the occurrence of VTE resulted in a more realistic incidence and decreased misdiagnosis of asymptomatic patients. That's also the main reason why the overall VTE incidence of our study is higher than other researches worldwide [31–33]. Though the diagnosis and treatment of patients with asymptomatic VTE remain controversial [32, 34], 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. However, our researchers are systematically trained to maximize the quality of the data. Secondly, there is a confounder 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 are limited.

In conclusion, PPS seems to be inappropriate to assess VTE risk for internal medicine inpatients in our center. By contrast, Caprini RAM showed greater advantages in predicting VTE risk in terms of sensitivity

and accuracy. However, both of these two scoring systems have some deficiencies in our study. Therefore, we need to establish an accurate and more efficient VTE prediction model for Chinese populations in the future.

Abbreviations

PPS
Padua Prediction Score
VTE
venous thromboembolism
RAM
risk assessment model
ROC
receiver operating characteristic curve
DVT
deep vein thrombosis
PTE
pulmonary thromboembolism
ACCP
American College of Chest Physicians
RICU
respiratory intensive care unit
BMI
body mass index
AUC
area under curve
CI
confidence interval
NRI
reclassification index
IDI
integrated discrimination improvement
IQR
interquartile range
HCT
hematocrit
PLT
platelet count.

Declarations

Acknowledgements: Not applicable.

Authors' contributions: Y. Yang, S. Yang and Y. Zhang conceived and designed the study. Y. Yang, S. Yang and Y. Zhang contributed to the statistical analysis and manuscript preparation. Y. Zhang wrote the first manuscript draft. S. Yang, Y. Yang, Y. Zhang, X. Jiao, J. Liu, W. Wang, T. Kuang, J. Gong and J. Li participated in the collection of patients' data. All authors reviewed the manuscript.

Conflict of interest: None declared.

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Ethics approval and consent to participate

Permission for data analysis was approved to the ethics committees of Beijing Chao-Yang Hospital, Beijing Institute of Respiratory Medicine, Capital Medical University, Beijing, China. Written informed consents were not obtained from individual patients because of the retrospective design.

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

Not applicable.

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Figures

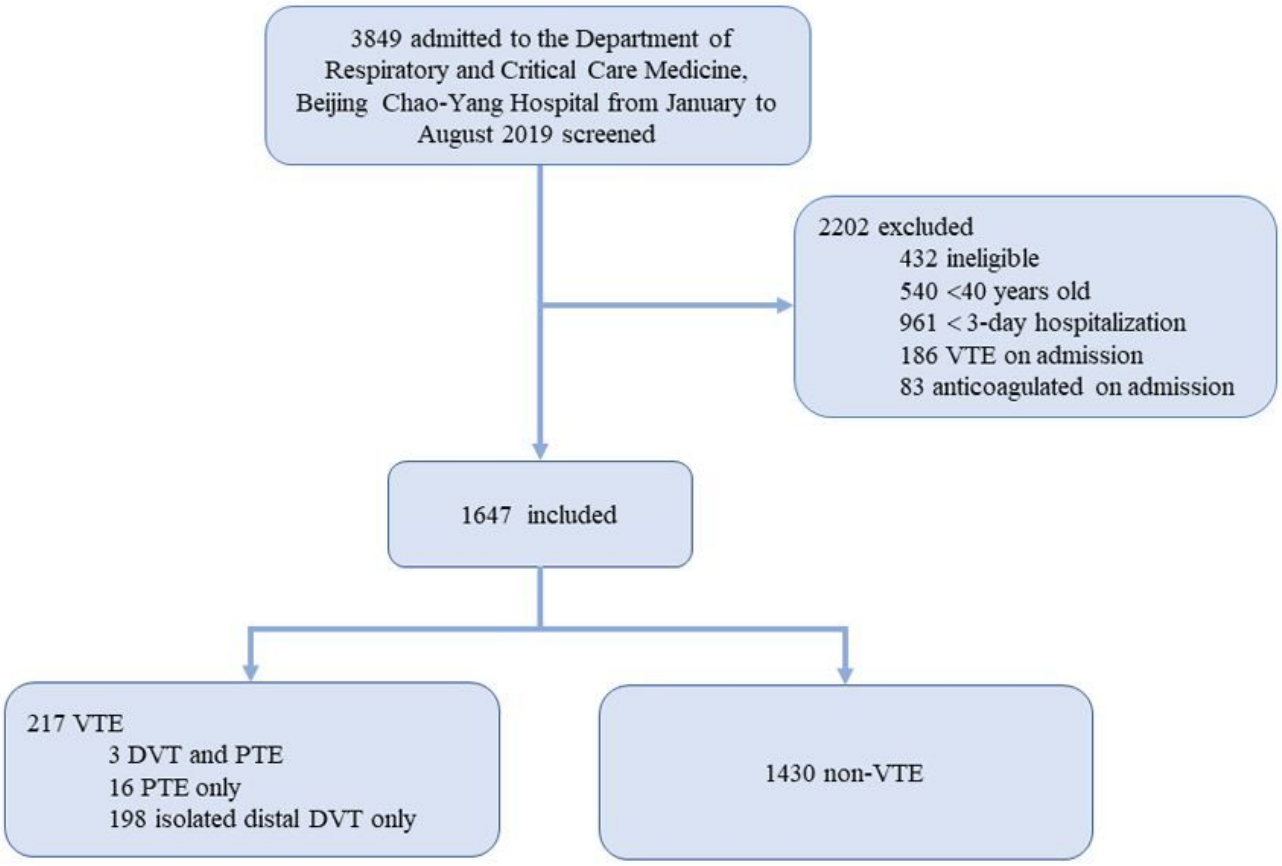

Figure 1

Patient disposition.

Abbreviation: VTE: venous thromboembolism; DVT: deep vein thrombosis; PTE: pulmonary thromboembolism.

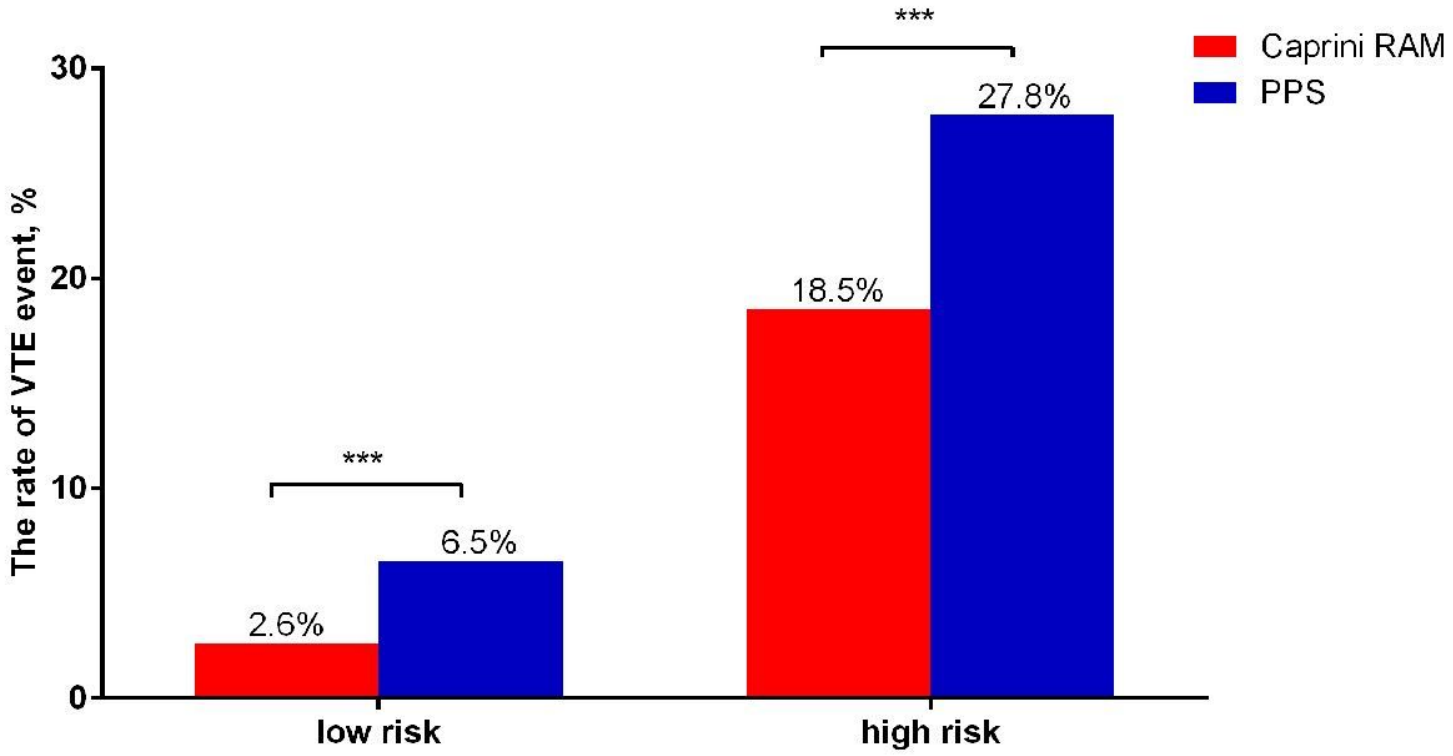

Figure 2

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.

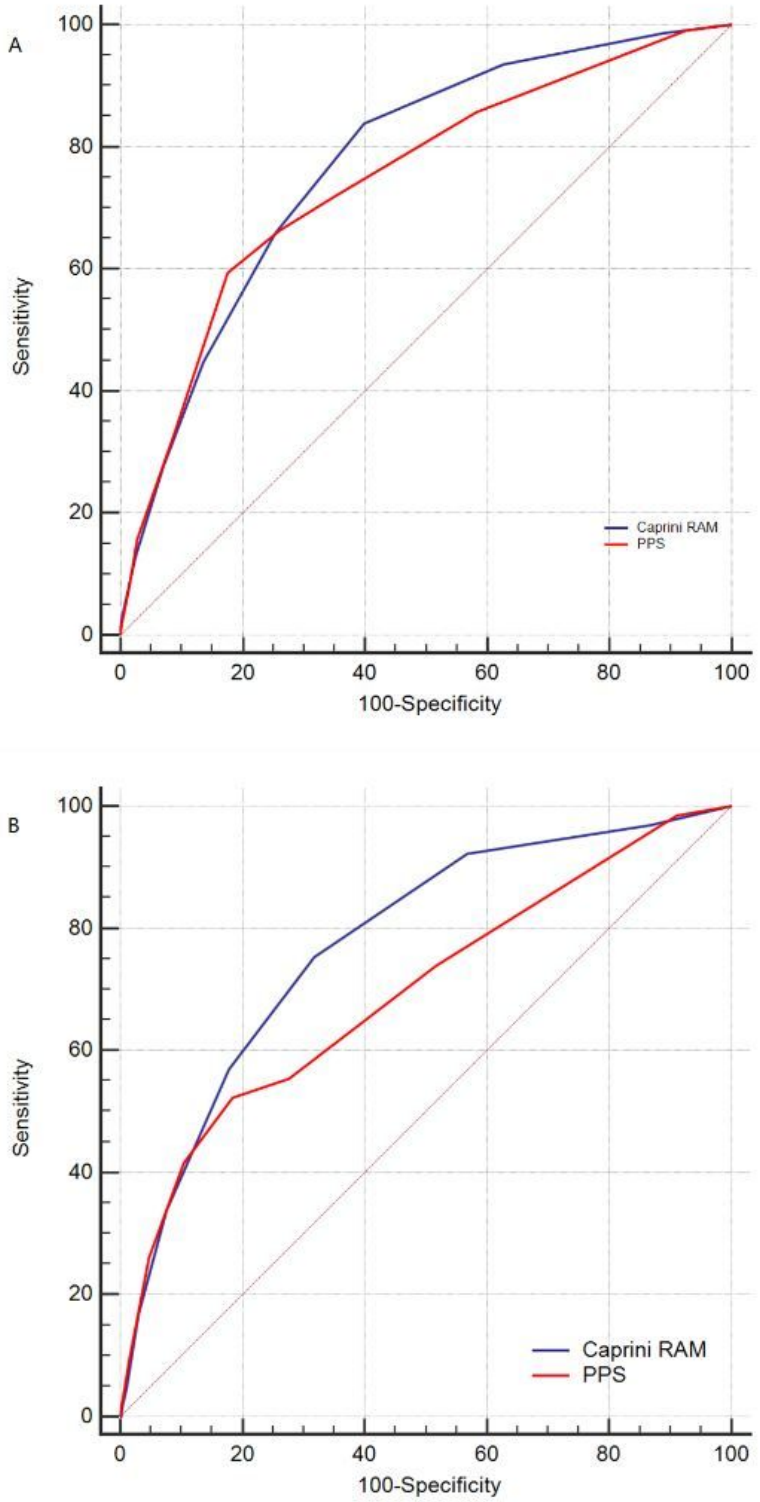

Figure 3

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 0.773 (95%CI, 0.752-0.793), which was significantly larger than the AUC of PPS [0.747 (95%CI, 0.725-0.768), p = 0.0453]; (b) For

patients without thromboprophylaxis, the AUC for predicting VTE was 0.776 (95% CI, 0.752-0.696) of the Caprini RAM, which was significantly higher than that of the PPS [0.696 (95% CI, 0.670-0.721), p = 0.005].

Abbreviation: RAM: risk assessment model; PPS: Padua prediction score; AUC: area under curve; VTE: venous thromboembolism.

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