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ORIGINAL RESEARCH

Development of Risk Prediction Model for Muscular Calf Vein Thrombosis with Acute Exacerbation of Chronic Obstructive Pulmonary Disease

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Purpose: This study aims to establish a risk prediction model for muscular calf vein thrombosis (MCVT) in patients with acute exacerbation of chronic obstructive pulmonary disease (AECOPD).

Methods: The research sample consisted of 248 patients with AECOPD and all of them underwent vascular ultrasounds of both lower limbs in this retrospective study. Univariate analysis and multivariate logistic regression analysis were conducted on factors with significant group differences to screen for the independent risk factors of MCVT. A nomogram to predict the risk of MCVT was constructed and validated with bootstrap resampling.

Results: According to the exclusion criteria, 240 patients were included for analysis, divided into the MCVT group (n = 81) and the non-MCVT group (n = 159). Multivariate logistic regression analyses showed that hypertension, elevated MPV, reduced albumin (ALB), elevated D-dimer and bed rest ≥3 days were independent risk factors for MCVT in AECOPD. A nomogram model for predicting AECOPD with MCVT was established based on them. The area under the curve (AUC) of receiver operating characteristic (ROC) curve for the prediction model and the simplified Wells score was 0.784 (95% CI: 0.722–0.847) and 0.659 (95% CI: 0.583–0.735), respectively. The cut-off value and Youden index of prediction model were 0.248 and 0.454, respectively. At the same time, the sensitivity, specificity, positive predictive value, and negative predictive value of the prediction model were 85.9%, 59.5%, 84.6%, and 77.4%, respectively. The sensitivity and specificity of the simplified Wells score were 67.9% and 56.3%, respectively. Validation by the use of bootstrap resampling revealed optimal discrimination and calibration, and the decision analysis curve (DAC) suggested that this prediction model involved high clinical practicability.

Conclusion: We developed a nomogram that can predict the risk of MCVT for AECOPD patients. This model has the potential to assist clinicians in making treatment recommendations and formulating corresponding prevention measures.

Keywords: acute exacerbation of chronic obstructive pulmonary disease, muscular calf vein thrombosis, risk factors, nomogram, model

Introduction

Chronic obstructive pulmonary disease (COPD) is a common respiratory disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities.[1] Nearly 3 million people die from COPD every year and COPD is currently the third-leading cause of death worldwide.[2] Most patients with COPD have persistent systemic inflammation, chronic hypoxia and impaired pulmonary function over a long time. Therefore, COPD patients show decreased exercise tolerance and lower limb movement, often accompanied by lower limb venous endothelial injury and blood stasis,[3,4] which create the pathophysiological conditions for forming deep vein thrombosis (DVT). Acute exacerbation of chronic obstructive pulmonary disease (AECOPD) refers to the deterioration of respiratory symptoms in a short period and requires additional treatment. It is reported that the risk of DVT in patients with AECOPD is up to 12.4% and the risk of pulmonary embolism (PE) is also increased accordingly, which can be highly life-threatening.[5–8]

Muscular calf vein thrombosis (MCVT) belonging to isolated distal deep vein thrombosis (IDDVT) refers to thrombosis in the calf muscle veins, most commonly found in halibut and fibula muscles. The incidence of MCVT accounts for 50% of IDDVT and 5.6–31.3% of DVT.[9] The symptoms of lower limb swelling and pain are often inconspicuous because the muscular calf vein branch is thin and the inflammatory stimulation caused by thrombosis is light, which patients and clinicians do not easily detect. Thus, patients with MCVT may miss the best timing of treatment and develop PE.[10,11]

The nomogram has been accepted as a reliable tool for creating a simple, intuitive graph of a statistical predictive model that quantifies the risk of a clinical event.[12] The nomogram risk prediction model is widely utilized in clinic. In contrast, research about the risk prediction model in AECOPD patients with MCVT is seldom reported, and there are discrepancies in the findings of studies. As a result, this study has constructed the risk prediction model of MCVT. It is designed to help clinicians identify patients at risk of MCVT and provide a theoretical and decision-making basis for early thromboprophylaxis.

Methods
Study Design
A total of 248 patients with AECOPD were hospitalized in the department of Respiratory Medicine at the Second Affiliated Hospital of Harbin Medical University from January 2017 to December 2020 with the simplified Wells score greater than or equal to 2. Then, all of them received vascular ultrasounds of both lower limbs and were screened for this study. Their data originated from the hospital information system (HIS) and the diagnostic criteria of the 2017 GOLD guidelines[1] are used to confirm the diagnosis and severity grading of AECOPD. According to the 2016 American College of Chest Physicians (ACCP) Antithrombotic Therapy for VTE Disease[13] and the vascular ultrasounds of both lower limbs, 89 patients were diagnosed DVT, among whom 81 with MCVT, 3 with common femoral vein thrombosis, 2 with superficial femoral vein thrombosis and 3 with popliteal vein thrombosis. A total of 240 patients were included in this research and divided into the MCVT group (81 cases) and the non-MCVT group (159 cases), see Figure 1 for details. The clinical data of these patients were retrospectively gathered for analysis and constructing a nomogram risk prediction model.

Inclusion criteria were as follows: (1) hospitalized patients with a confirmed diagnosis of AECOPD; (2) simplified Wells score greater than or equal to 2; (3) developed the vascular ultrasounds of both lower limbs.
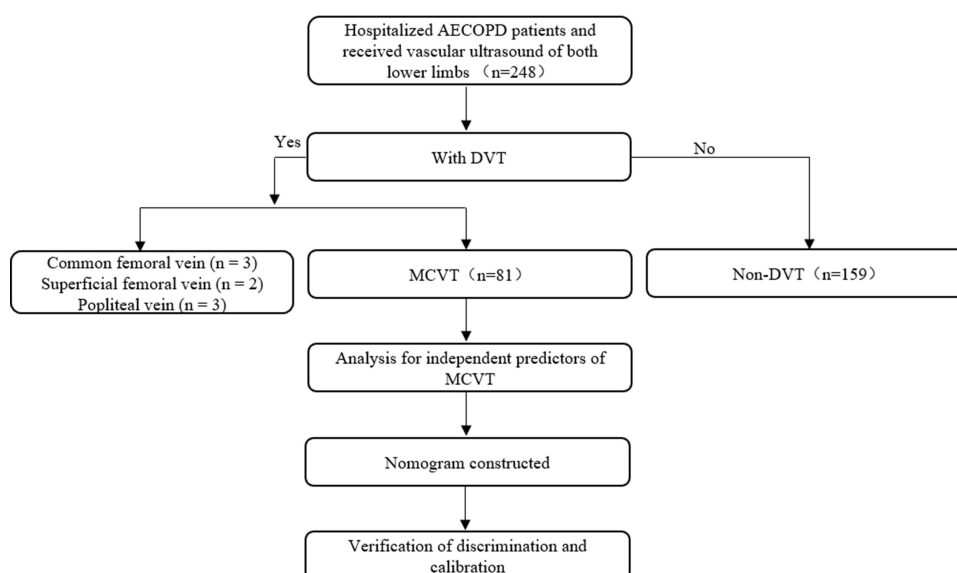
Figure 1 Flow chart describing the research method.
Abbreviations: AECOPD, acute exacerbation of chronic obstructive pulmonary disease; DVT, lower extremity deep vein thrombosis; MCVT, muscular calf vein thrombosis.

Exclusion criteria were as follows: (1) patients with lying in bed in the last 1 month because of surgery (such as hip arthroplasties) and trauma (such as femoral shaft fracture); (2) patients with severe hepatic and renal dysfunction, severe hematological system diseases, immune deficiency and severe neurological disease; (3) patients having a recent history of anticoagulation treatment (such as warfarin, low-molecular-weight heparin, or rivaroxaban); (4) patients diagnosed DVT, but the thrombus located beyond the calf muscle veins; (5) patients diagnosed with chronic MCVT. This study was approved by the ethical committee of the Second Affiliated Hospital of Harbin Medical University. All procedures involving human participants complied with the Declaration of Helsinki, and informed consents were exempted from all patients.

Data Collection

The baseline characteristics include age, gender, underlying diseases, the history of venous thromboembolism (VTE), severity grading, FEV1 in percent of the predicted value (FEV1% pred), bed rest ≥3 days. Clinical manifestations such as lower limb swelling and fever ≥3 days. Laboratory examination such as blood routine, biochemical series, hemogram, blood gas analysis; other data such as simplified Wells score, vascular ultrasounds of both lower limbs and complications. Blood samples and relevant examinations were collected during admission.

Statistical Analysis

Data were analyzed using SPSS 25.0 and R 3.6.3 software. The categorical variables were described by the number of cases (rate) and were compared using the chi-square test ($\chi 2$ test). Normally distributed variables were expressed as the mean ± standard deviation (mean ± SD), while non-normally distributed variables were shown as the median (M) and interquartile range (IQR). Univariate analysis and multivariate logistic regression analysis were performed on variables reaching statistical significance to determine the independent risk factors for MCVT. The independent risk factors were imported into R software for further analysis, and the "rms" program package in R software was used to establish the nomogram and correction diagram of MCVT occurrence. The performance of the nomogram was assessed by discrimination and calibration. The discriminative ability of the model was determined by the AUC of ROC analysis, which ranged from 0.5 (no discrimination) to 1 (perfect discrimination). The ROC analysis was also used to calculate the optimal cut-off values, which were determined by maximizing the Youden index (ie, sensitivity + specificity −1). The accuracy of the optimal cut-off value was assessed by sensitivity, specificity and predictive values. The calibration of the prediction model was performed by a visual calibration plot comparing the predicted and actual probability of MCVT. In addition, the nomogram was subjected to 1000 bootstrap resamples for internal validation to assess their predictive accuracies. The DAC was used to evaluate the nomogram's net benefit and clinical practicability. A value of $P < 0.05$ was considered to be statistically significant.

Results

Baseline Characteristics

The proportion of patients who exhibited hypertension and VTE in MCVT group was significantly higher than that in the non-MCVT group ($P < 0.05$). Compared with the MCVT group, fewer patients in the non-MCVT group had lower swelling of lower limbs and bed rest ≥ 3 days. No statistically significant differences were found in age, gender, smoking history, complication, severity grading and FEV1% pred between the two sets (Table 1).

Comparison of Laboratory Parameters

There was no statistical difference between the MCVT group and the non-MCVT group in terms of WBC, HCT, MCV, RDW-CV, PDW, FIB, PaO2 and PaCO2 (Table 2). The concentration of D-dimer (Figure 2B) and MPV (Figure 2C) in the MCVT group was significantly higher than in the non-MCVT group, but the MCVT group had a remarkable level of PLT (Figure 2A) and ALB (Figure 2D) than in the non-MCVT group.

Table 1 Baseline Characteristics

Characteristics	AECOPD-MCVT (n=81)	AECOPD-nMCVT (n=159)	P value
Age (year)	69.85±9.80	68.09±9.27	0.173
Gender			0.187
Man (case,%)	36(44.4)	85(53.5)	
Women (case,%)	45(55.6)	74(46.5)	
Smoking history (case,%)	39(48.1)	85(53.5)	0.436
Comorbidity (case,%)			
Hypertension	35(43.2)	40(25.2)	**0.004**
Diabetes	13(16.0)	18(11.3)	0.302
Cardiovascular disease	36(44.4)	59(39.7)	0.272
Cerebrovascular disease	15(18.5)	31(19.5)	0.856
History of VTE (cases, %)	6(7.4)	3(1.9)	**0.031**
Symptom (case,%)			
Swelling of lower limbs	39(48.1)	46(28.9)	**0.003**
Fever time ≥ 3 days	4(4.9)	18(11.3)	0.105
Bed rest ≥3 days	35(43.5)	22(13.8)	**P<0.001**
Complication (cases, %)			
Hypoxemia	16(19.8)	50(31.4)	0.055
Respiratory failure	44(54.3)	71(44.7)	0.156
Ion disorder	33(40.7)	66(41.5)	0.909
Cor pulmonale	20(8.30)	52(32.7)	0.074
Severity grading (cases, %)			0.666
Grade I	26(32.1)	56(35.2)	
Grade II	20(24.7)	51(32.1)	
Grade III	25(30.9)	46(28.9)	
FEV% pred (case,%)			0.285
≥80	3(3.7)	5(3.1)	
50–79	15(18.5)	28(17.6)	
30–49	12(14.8)	44(27.7)	
<30	9(11.1)	36(22.6)	

Note: Bold numbers in table indicates that there is statistical differences between the groups.
Abbreviations: VTE, venous thromboembolism; FEV% pred, FEV1 in percent of the predicted value.

Logistic Multivariate Regression Analysis of the Modeling Group

The results of the univariate analysis indicated that VTE, hypertension, swelling of lower limbs, bed rest ≥3 days, RDW-SD, MPV, ALB and D-dimer were predictors for MCVT. The statistically significant factors ($P < 0.05$) shown in the univariate analysis were selected as independent variables of the multivariate logistic regression analysis. The results suggested that hypertension, elevated MPV, reduced ALB, elevated D-dimer and bed rest ≥3 days were independent risk factors for MCVT with AECOPD (Figure 3); however, VTE, swelling of lower limbs and RDW-SD were not significant.

Predictive Nomogram for the Probability of MCVT

Based on the final regression analysis, a nomogram was constructed that incorporated the 5 significant risk factors for predicting MCVT (Figure 4). A total score was calculated using hypertension, MPV, ALB, D-dimer, and bed rest ≥3 days. The value of each of these variables was given a score on the point scale axis. A total score could be easily calculated by adding each single score and, by projecting the total score to the lower total point scale, we were able to estimate the probability of MCVT.

Distinguishing Degree, Calibration and Clinical Effectiveness of the Predictive Model

The ROC curve of the nomogram model and simplified Wells score are shown in Figure 5. The prediction model and simplified Wells score had AUC value of 0.784 (95% CI: 0.722–0.847) and 0.659 (95% CI: 0.583–0.735), respectively.

Table 2 Laboratory Parameters

| Parameters	AECOPD-MCVT (n=81)	AECOPD-nMCVT (n=159)	P value
WBC(×10^9/L)	7.90(6.00,9.00)	7.40(5.90,9.10)	0.207
HGB(g/L)	137.86±23.88	139.30±23.16	0.653
HCT (%)	41.40(37.30,46.85)	41.80(38.30,46.00)	0.643
MCV(fl)	94.50(89.70,98.05)	93.30(90.20,96.60)	0.379
RDW-CV (%)	14.10(13.10,15.05)	13.70(13.00,14.90)	0.110
RDW-SD (fl)	49.57±9.52	47.76±5.67	0.052
PLT(×10^{12}/L)	198.00(138.00,255.00)	224.00(173.00,282.00)	**0.025**
MPV (fl)	10.92±1.14	10.52±1.11	**0.009**
PDW (fl)	12.60(11.40,15.10)	12.40(11.00,14.20)	0.171
ALB(g/L)	35.68±4.90	38.28±5.87	**0.001**
FIB(g/L)	3.59±1.08	3.53±1.09	0.682
D-dimer(ng/mL)	470.00(213.50,777.50)	171.00(102.75,294.00)	**P<0.001**
PaO$_2$(mmHg)	71.14±27.82	70.03±22.41	0.799
PaCO$_2$(mmHg)	48.00(39.00,68.00)	48.00(42.75,66.00)	0.336

Note: Bold numbers in table indicates that there is statistical differences between the groups.
Abbreviations: WBC, white blood cell; HGB, hemoglobin; HCT, hematocrit; MCV, mean corpuscular volume; RDW-CV, red blood cell distribution width coefficient of variation; RDW-SD, red blood cell distribution width standard deviation; PLT, platelet; MPV,mean platelet volume; PDW, platelet distribution width; ALB, albumin; FIB, fibrinogen; PaO$_2$, partial pressure of oxygen; PaCO$_2$, partial pressure of carbon dioxide.
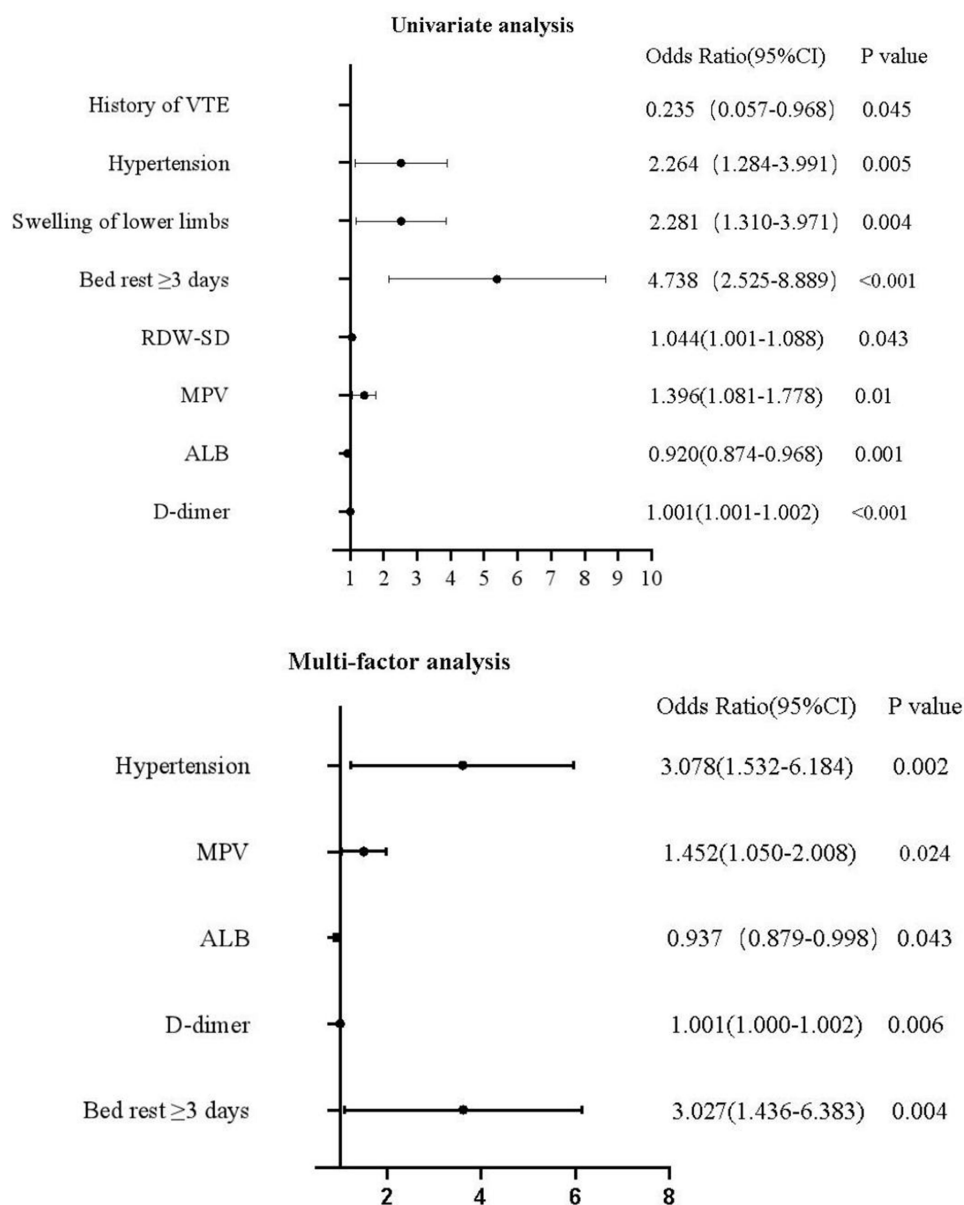
The sensitivity, specificity, positive predictive value, negative predictive value, cut-off value and Youden index of the model were 85.9%, 59.5%, 84.6%, 77.4%, 0.248, 0.454, accordingly. The sensitivity and specificity of the simplified Wells score were 67.9% and 56.3%, respectively. A calibration curve of the nomogram is presented in Figure 6, which shows that the MCVT probabilities predicted by the nomogram agreed well with the actual probabilities. In other words, this model had a high prediction accuracy. The performance of the nomogram was internally validated with Bootstrap resampling (1000 times) analysis, and it showed that the model had good predictive performances. Results of the DAC of the nomogram are shown in Figure 7. This model had good clinical utility, and it was feasible for making useful judgments because the decision curve was far from the 2 extreme curves.

Discussion

COPD is the most common chronic respiratory disease. The total number of patients with COPD is more than 100 million in China, causing substantial social and family economic burdens.[14] Owing to the existence of systemic inflammation, platelet activation and oxidative stress in COPD pathogenesis, patients are prone to developing DVT and PE, and have a higher risk of DVT and PE in acute exacerbation.[15–17] According to previous reports, the incidence of
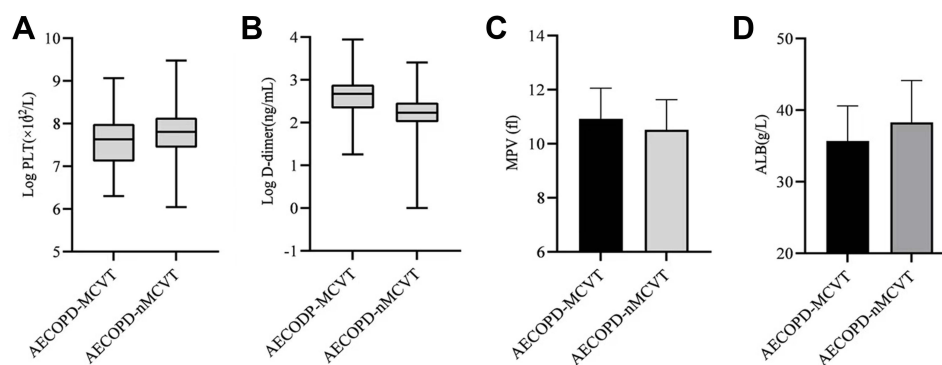

Figure 2 Laboratory examination results of the modeling group. The variables of (**A**) and (**B**) were presented as Log transformed values. The variables of (**C**) and (**D**) were presented as regime values.

Univariate analysis

	Odds Ratio(95%CI)	P value
History of VTE	0.235 (0.057-0.968)	0.045
Hypertension	2.264 (1.284-3.991)	0.005
Swelling of lower limbs	2.281 (1.310-3.971)	0.004
Bed rest ≥3 days	4.738 (2.525-8.889)	<0.001
RDW-SD	1.044(1.001-1.088)	0.043
MPV	1.396(1.081-1.778)	0.01
ALB	0.920(0.874-0.968)	0.001
D-dimer	1.001(1.001-1.002)	<0.001

1 2 3 4 5 6 7 8 9 10

Multi-factor analysis

|	Odds Ratio(95%CI)	P value
Hypertension	3.078(1.532-6.184)	0.002
MPV	1.452(1.050-2.008)	0.024
ALB	0.937 (0.879-0.998)	0.043
D-dimer	1.001(1.000-1.002)	0.006
Bed rest ≥3 days	3.027(1.436-6.383)	0.004

2 4 6 8

Figure 3 Univariate analysis and multi-factor analysis shows the risk factors of MCVT in AECOPD patients.
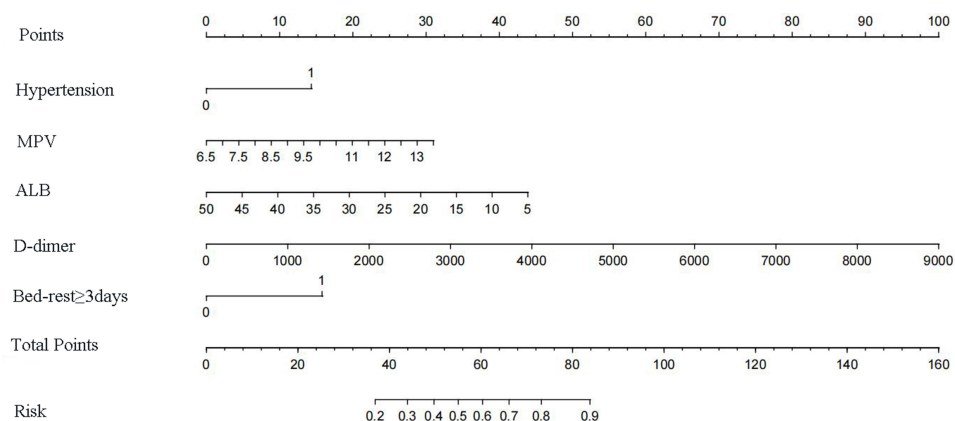
Figure 4 Risk nomogram model for predicting the occurrence of MCVT in AECOPD patients. The value of each of variable was given a score on the point scale axis. A total score could be easily calculated by adding each single score and, by projecting the total score to the lower total point scale, we were able to estimate the probability of MCVT.
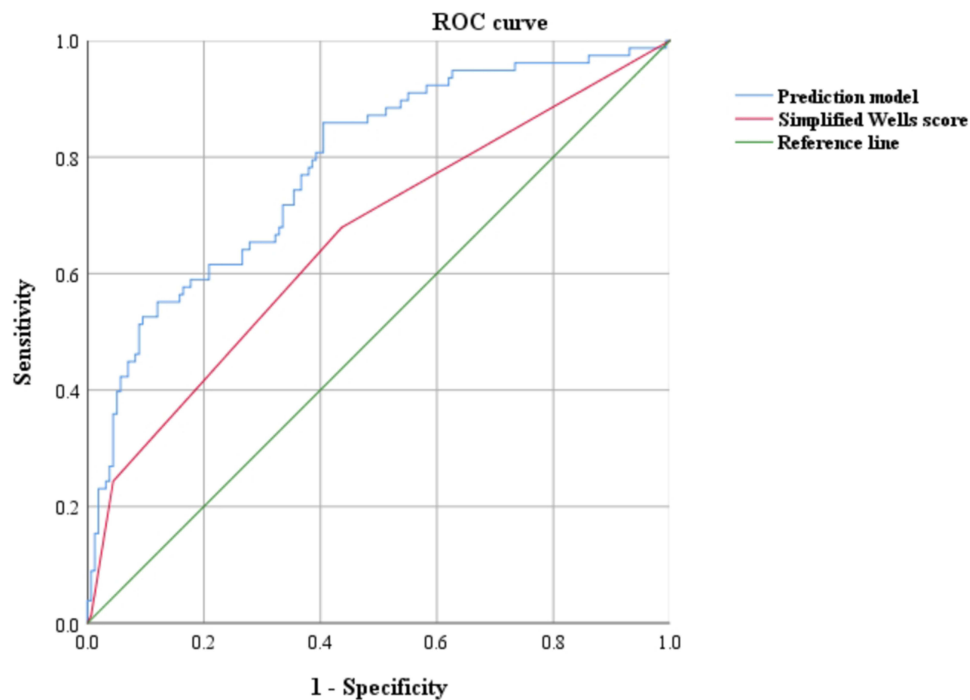
Figure 5 The ROC of the prediction model and simplified Wells score.
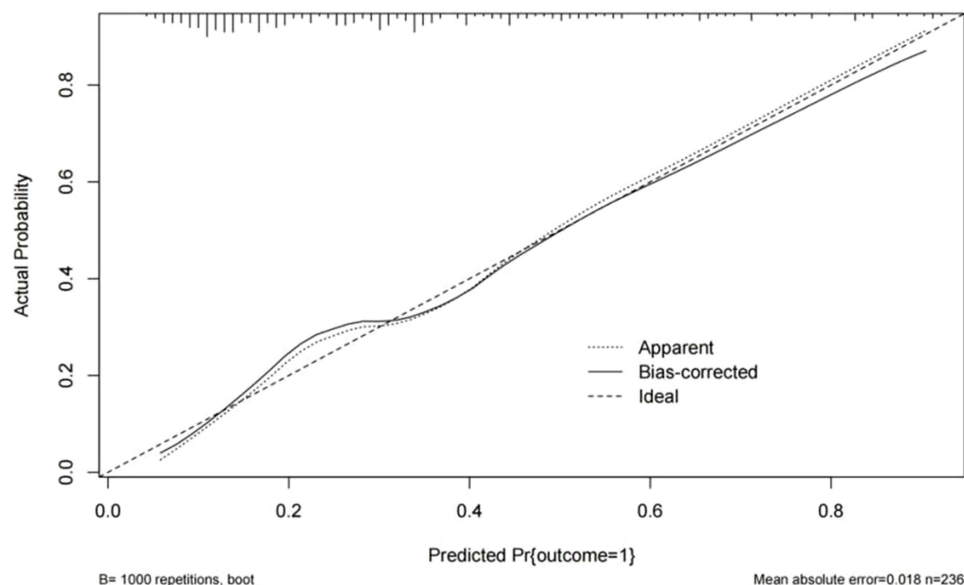

Figure 6 The calibration curves for the nomogram. The x-axis represents the nomogram-predicted probability and y-axis represents the actual probability of MCVT. Perfect prediction would correspond to the ideal line. The apparent line represents the entire cohort (n¼ 236), and the solid line is bias-corrected by bootstrapping (B¼1000 repetitions), indicating observed nomogram performance.

DVT and PE in AECOPD patients was 19–29%[11,18] and 3.3–29.1%,[19] respectively. DVT and PE have become the serious common comorbidity of AECOPD.

In the present study, we observed that the incidence of DVT with AECOPD who have perfected vascular ultrasounds of both lower limbs was 35.8% (89/240). This was higher than previous results. On the one hand, it might be due to having insufficient knowledge of the disease severity for AECOPD patients selected in the study, who had greater
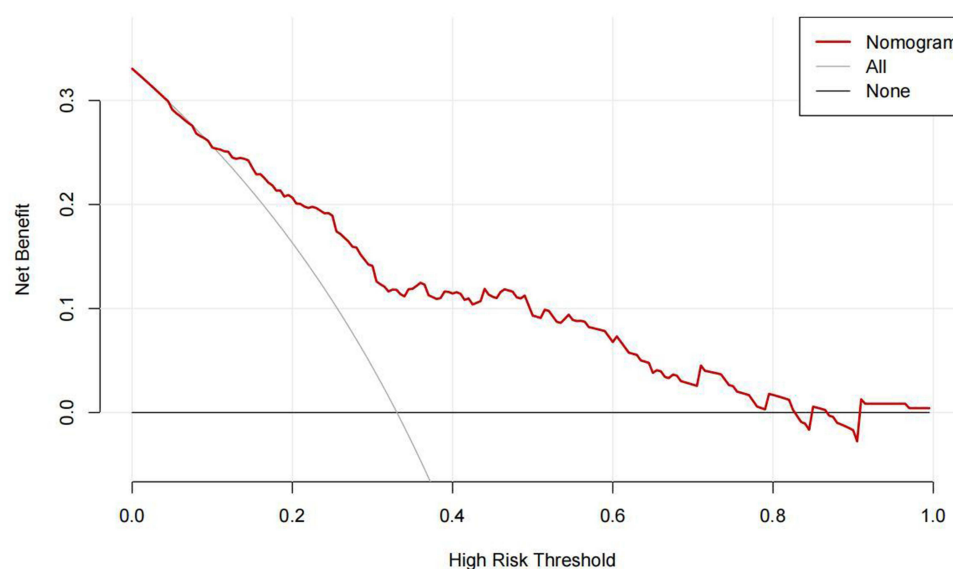
Figure 7 The decision curve analysis (DCA) of the prediction model. DCA was used to evaluate the availability and benefits of the prediction model. The abscissa represents the threshold probability and ordinate represents the net benefit (NB).

severity of illness at the time of hospital admission and prolonged bed time, with an increased risk of DVT, on the other hand, the difference possibly stemmed from the sample size included in other studies.

Compared with other venous in lower limb, the muscular calf vein is more subjected to thrombus due to multiple branches, small vein valve and slow blood flow.[20–22] However, it is worth noting that many patients may be missed because they are asymptomatic. In our study, MCVT made up 91% (81/89) of DVT, consistent with earlier reports. Previous studies suggested that MCVT might be the source of proximal DVT[23,24] and the probability of MCVT progression towards proximal DVT was 10–33%,[25] which could lead to increased incidence of PE.[26] Furthermore, we also observed that IDDVT accounted for 33.7% (89/240) of DVT. IDDVT could cause a high VTE recurrence rate and high mortality rate and was correlated with post-thrombotic syndrome (PTS).[26–28] Hence, MCVT served as the most common type of IDDVT, and the early identification of MCVT in AECOPD patients can contribute to reduce the occurrence of adverse events and improve the quality of life.

The study has imposed statistical analysis on baseline characteristics and laboratory findings in MCVT group and non-MCVT group. Univariate analysis revealed that VTE, hypertension, swelling of lower limbs, bed rest ≥3 days, RDW-SD, MPV, ALB and D-dimer were predictors for MCVT. A further multivariate logistic regression analysis indicated that hypertension, elevated MPV, reduced ALB, elevated D-dimer and bed rest ≥3 days were independent risk factors for MCVT in AECOPD patients. The VTE history as a risk factor for VTE was generally recognised at home and abroad. However, it was only found to be a predictor, rather than an independent risk factor for MCVT in this study. We hypothesized that the depreciated significance could be resulted from the interplay between the factors included in the analysis. Therefore, it is still necessary to be vigilant about the possibility of MCVT for AECOPD patients with a history of VTE in the clinic.

Patients with COPD often reduce their physical activity and extend relatively bed rest due to cardiopulmonary insufficiency during exacerbation, which leads to venous stasis. It has been demonstrated that bed rest more than 3 days increases the incidence of venous thromboembolism and also is a risk factor for promoting DVT.[29] Our results were in accordance with the findings. To remove this risk factor, physicians can guide them actively for rehabilitation exercise according to the current state of the organism, consequently decreasing the incidence of MCVT and improving the quality of life of patients.[30]

As the disease progresses, there are many comorbidities in AECOPD patients, among which hypertension is the most common. About 70.9% of AECOPD patients are accompanied by primary or secondary hypertension.[31,32] During periods

of acute COPD exacerbation, oxidative stress and inflammatory response presenting in the organism can induce airway epithelium injury and accelerate the progression of atherosclerosis, which leads to the occurrence of cardiovascular diseases such as hypertension.[33] Chang et al[34] found that MCVT existed easily in AECOPD patients complicated by hypertension. Long-term fluctuation of blood pressure easily causes vasodilator dysfunction, damaging the vascular endothelial cell, leading to the aggregation of platelet and fibrin, which in turn instigates venous thrombosis of the lower extremity.[35] In parallel, the nomogram model in this study demonstrated that the AECOPD patients with hypertension were associated with higher risks of MCVT. Moreover, hypertension with MCVT increases the risk of adverse cardiovascular events and death.[34] Consequently, well-controlled hypertension for managing the prognosis of AECOPD patients cannot be ignored.

As a multifunctional protein in the plasma, ALB is considered to be a negative acute-phase protein in inflammatory conditions.[36] It possesses important antioxidant properties, plays an important role in defense against oxidative stress,[37] and can serve as a biomarker for clinical evaluation of malnutrition.[38] The majority of patients with AECOPD are elderly and usually associated with underlying diseases, easily suffering from malnutrition.[39] Meanwhile, systemic inflammatory response and oxidative stress of them also result in a decline of ALB. The current study and Zinellu et al[40] detected that the ALB level in AECOPD patients was lower than normal. A decrease in albumin level is indicated as a trigger of elevated platelet and fibrinogen aggregation, negatively correlating with the risk of venous thromboembolism.[41] A prospective study[42] suggested that reduced ALB level was the risk factor for DVT. Lung et al[43] reported that lower ALB levels increased the prevalence of lower limb vein thrombosis dramatically. Consistent with these studies, our risk prediction model demonstrated that reduced ALB was the independent risk factor of AECOPD patients combined with MCVT. As a result, timely correcting the low level of ALB may play a positive role in preventing MCVT.

MPV represents the average size of platelets and correlates with platelet function and activation.[44] Elevated MPV marks platelet activation and enlarged platelet volume.[45] Large platelets with strong coagulation ability, fast aggregation and good mucoadhesion property can release more prothrombotic substances that are advantageous in venous thrombosis. They are also a predictor of venous thrombosis.[45,46] AECOPD patients are usually accompanied by hypoxia and tachycardia, which can stimulate platelet activation and lead to an increase in MPV.[47] Cui et al[48] and Farah et al[49] confirmed that elevated MPV was an independent predictor of DVT events. The model constructed in the current study revealed it was easy for AECOPD patients to develop MCVT when they present elevation of MPV. In addition, it was shown that elevated MPV could predict poor prognosis of AECOPD patients.[50] Aydınyılmaz et al[51] found that additional use of antiplatelet drug based on the above anticoagulant therapy reduced mortality for COVID-19 patients with MPV >10.45f/l. A systematic evaluation and meta-analysis study indicated that all-cause mortality in patients with AECOPD was decreased after taking antiplatelet therapy.[52] Further prospective studies are still needed to confirm whether giving prophylactic antiplatelet medications will diminish the risk of death for AECOPD patients.

D-dimer is not only the smallest fibrin degradation product but also a specific degradation product of the fibrous matrix of venous thrombosis. It is abnormally elevated in the case of blood hypercoagulability or secondary hyperfibrinolysis and is a highly sensitive indicator of thrombosis and dissolution.[53] Many studies have found that the level of D-dimer in MCVT with AECOPD patients was noticeably higher than those of the AECOPD without thrombosis, and that elevated D-dimer was the independent risk factor for MCVT.[53,54] Like our study, these studies revealed that D-dimer levels had strong association with venous thrombosis. However, D-dimer can be affected by many factors, such as infection, tumor, severe hepatorenal insufficiency and pregnancy. As a result, D-dimer elevation at the time of hospitalization for AECOPD may indicate whether MCVT exists while we must preclude the possibility of other factors. We can observe the dynamic level of D-dimer and refine interrelated examinations for reducing the occurrence of adverse events.

This study combined hypertension, elevated MPV, reduced ALB, elevated D-dimer and bed rest ≥3 days to establish a nomogram model. When the calculated score increased in the nomogram model, the corresponding risk of MCVT also increased significantly. The AUC of ROC curve is calculated to verify the predictive performance. The simplified Wells score is a commonly used clinical likelihood assessment scale for VTE. In this study, we used the nomogram model and simplified Wells score to make the predictive diagnosis of MCVT in AECOPD patients, respectively. We evaluated the predictive diagnostic potential of the nomogram model against simplified Wells score, the most widely used method, in

AECOPD patients. The AUC, sensitivity, and specificity of the prediction model ROC curve were found to be significantly higher than the simplified Wells score, suggesting that the model had good predictive value in estimating the probability of MCVT occurrence in AECOPD. Meanwhile, at the Youden index threshold value, the positive and negative predictive values were 84.6% and 77.4%, respectively, suggesting the effectiveness of the mode in predicting MCVT in AECOPD patients with certain high-risk factors. Furthermore, using the calibration curve and DAC to evaluate the model, it was found that the model had good calibration and clinical utility. These results indicate that the model may help clinicians recognize and prevent MCVT early in patients with AECOPD.

However, this study has some limitations. Firstly, this was a single-center retrospective study with a small sample size and a limited number of logistic multivariate regression analyses. Secondly, we did not conduct a follow-up of the patients after discharge. Thirdly, the model has not been verified in the external validation queue. Therefore, the sample size should be expanded, and the predictive value of the nomogram model should be verified by a multi-center study in future.

Conclusion

The present study found that hypertension, elevated MPV, reduced ALB, elevated D-dimer and bed rest≥3 days were independent risk factors of AECOPD patients with MCVT. Based on this, we have developed and internally validated a novel nomogram for predicting the risk of MCVT for patients with AECOPD. The nomogram is easy to use, is highly accurate, and exhibits excellent calibration. This nomogram might help clinicians to make individualized predictions of MCVT and to improve treatment recommendations for AECOPD patients with high-risk factors.

Author Contributions

All authors made a significant contribution to the original text, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

The authors declare no conflicts of interest.

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