Application of the RCOG Risk Assessment Model for Evaluating Postpartum Venous Thromboembolism in Chinese Women: A Case-Control Study

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: Since China has not yet constructed its own risk assessment model (RAM) for pregnancy-related venous thromboembolism (VTE), more and more hospitals use the RCOG RAM for VTE risk prediction. However, the RCOG RAM was established based on Western populations, and its applicability in China is still uncertain. Thus, we aimed to evaluate the validity of the RCOG RAM in predicting postpartum VTE in Chinese maternity.

Material/Methods: This retrospective case-control study was conducted at the International Peace Maternity and Child Health Hospital (IPMCHH) from June 2016 to June 2020. The VTE group consisted of 38 women with postpartum VTE. For each VTE patient, 4 women without VTE who gave birth on the same day were randomly selected as the control group (n=152). The receiver operating characteristic (ROC) curve, calibration curve, and decision curve analysis (DCA) were used to evaluate the discrimination, accuracy, and validity of the RCOG RAM. Univariable analysis and multivariable logistic regression analysis were used to identify other related factors for postpartum VTE.

Results: Compared with the low-risk group, the risk of VTE was 9.75-fold greater in the intermediate-risk group, and 90.00-fold greater in the high-risk group. The area under curve (AUC) of the model was 0.828 (95% CI: 0.762-0.894), with a score of 2 as its best cut-off value, which exactly matched the criterion recommended by the RCOG guidelines for pharmacological thromboprophylaxis. The calibration curves and DCA of the model also showed good accuracy. In addition to the factors included in the RCOG RAM, glucocorticoid therapy during pregnancy (adjusted OR=6.72, 95% CI: 1.56-28.91) and previous use of IUD (adjusted OR=7.11, 95% CI: 1.45-34.93) were associated with increased risk of postpartum VTE.

Conclusions: The RCOG RAM was found to be effective in predicting postpartum VTE, and has certain guiding significance for postpartum thromboprophylaxis in China.

Keywords: Chemoprevention • Glucocorticoids • Intrauterine Devices • Risk Assessment • Venous Thromboembolism

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Background

Venous thromboembolism (VTE) comprises deep venous thrombosis (DVT) and pulmonary embolism (PE). Because of increased concentrations of coagulation factors, decreased anticoagulant and fibrinolytic components, and increased compression of the uterus to the iliac vein and inferior vena cava [1], the risk of VTE for women during pregnancy and the puerperium period is approximately 4-5 times higher than that in non-pregnant women of the same age [2,3]. Meanwhile, the risk of postpartum VTE is 20 times higher than that of antepartum VTE [4]. The incidence of VTE is 1-2 per 1000 pregnancies in Europe and America [5,6]. Nearly 80% of pregnancy-related VTEs are isolated DVTs, and 20% are PEs or coexisting PE and DVT [7], whose fatality rate can be as high as 15% [8]. Currently, VTE has become one of the leading causes of maternal mortality worldwide [9].

In the past, insufficient attention was given to the prevention of pregnancy-related VTE in China, and until now, there has been no epidemiological analysis based on national data. The Wells score and the Caprini score are usually used in clinical practice for VTE risk assessment in the obstetric department, but neither is designed specifically for pregnant women [10]. In 2015, the Royal College of Obstetricians and Gynecologists (RCOG) released the latest edition of guidelines for the prevention of VTE during pregnancy and puerperium and updated the VTE risk scoring method (mentioned as RCOG risk assessment model below). The detailed scoring method for VTE is shown in **Supplementary Table 1**. This model has been widely used in Western countries for the assessment of the risk of pregnancy-related VTE in both the antenatal and postnatal periods, and a thromboprophylaxis management process based on the results of the model has been recommended by the RCOG guidelines. If the total score is ≥2 postnatally, thromboprophylaxis for at least 10 days is recommended [11]. However, the data used for building the RCOG RAM were mostly obtained from Western countries. At present, whether this model is suitable for Chinese maternity care remains poorly understood. In view of the higher prevalence of VTE during the postnatal period, this study aimed to evaluate the predictive value of the RCOG RAM for postpartum VTE and its guiding significance in postpartum thromboprophylaxis in China. Furthermore, we aimed to explore related factors for postpartum VTE other than those already included in the model.

Material and Methods

Study Population

This retrospective case-control study was conducted at the International Peace Maternity and Child Health Hospital (IPMCHH), a specialized hospital of obstetrics and genecology in Shanghai, from June 2016 to June 2020. Women diagnosed with VTE during the postpartum period constituted the VTE group. For each VTE patient, 4 women who gave birth at the same day and confirmed as without VTE were randomly selected as the control group. Inclusion criteria included women who gave birth beyond 28 weeks of gestation, regardless of delivery mode, and completed regular antenatal and postnatal examinations as well as diagnostic examinations for VTE. Exclusion criteria were missing or untraceable previous medical records.

The diagnosis of DVT was confirmed by compression ultrasonography of the lower limb veins [12,13], and once thrombotic events were detected, the patient was routinely checked by echocardiography and computer tomography pulmonary angiography (CTPA) to investigate the presence of PE. All women were encouraged to walk as soon as possible after delivery. For those who underwent cesarean section, a pneumatic compression device was routinely used. Very few women received pharmacological prophylaxis, which was mainly based on empirical medication.

Data Collection

Data collected from medical records included socio-demographic characteristics, reproductive history, gynecologic history, previous contraceptive use, obstetric characteristics, and the results of laboratory tests (coagulation-related parameters) and imaging examinations. All women returned to the hospital for routine check-ups 42 days after delivery, and relevant data were also collected.

Assessment of Postpartum VTE Risk

Based on the above information, the RCOG RAM was used to assess the risk score and risk level of postpartum VTE. The risk of postpartum VTE was divided into 3 levels: low risk (<2 points and without intermediate or high-risk factors, no need for thromboprophylaxis), intermediate risk (≥2 points and without high-risk factors, need for thromboprophylaxis), and high risk (with at least 1 high-risk factor, need for thromboprophylaxis) [11]. All scores were calculated independently by 2 researchers. If any difference in the RCOG score was present, a third researcher recalculated the score.

Ethical Considerations

This study was approved by the Institutional Review Board of IPMCHH (GKLW-2020-03).
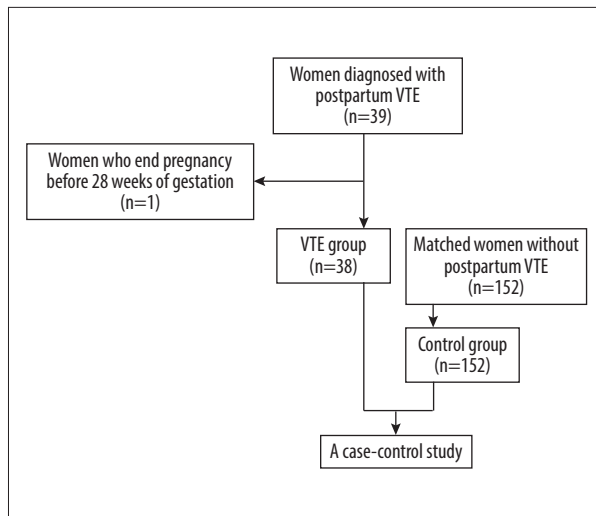
Figure 1. Flow chart.

A 2-sided *P* value <0.05 was considered statistically significant. All statistical analyses were performed using SPSS (version 22.0; SPSS, Inc., Chicago, IL, USA) and R statistical software version 4.0.2 (packages 'pROC', 'caTools', 'rms', 'rmda').

Results

VTE events and the use of anticoagulant

A total of 65 501 women gave birth in our hospital during the study period, and 39 thrombotic events occurred. The incidence of DVT was 0.060% and the incidence of PE was 0.018%. Among the VTE cases, 1 patient was excluded because delivery occurred at less than 28 gestational weeks. Therefore, 38 VTE cases (VTE group) and 152 women without VTE (control group) were finally included in this study (**Figure 1**).

Two women in the control group used low-molecular-weight heparin (LMWH) during pregnancy, one due to significant elevation in D-dimer and the other due to a history of 3 spontaneous abortions. In the VTE group, 1 woman with antiphospholipid syndrome (APS) used unfractionated heparin prenatally. Three women with antenatal DVT used LMWH during pregnancy, and the thrombus was dissolved before delivery. Among the 190 women, only the 3 with antenatal DVT used LMWH for thromboprophylaxis after delivery. Details of the VTE events are shown in **Supplementary Table 2**.

Table 1 shows the comparison of socio-demographic characteristics of the women in the 2 groups. There were no significant differences in BMI, educational level, and occupation

Statistical Analysis

The Kolmogorov-Smirnov test was used to evaluate the normal distribution. Continuous variables were assessed using the *t* test or Mann-Whitney U test. Categorical data were analyzed using chi-square tests or Fisher's exact test. RCOG risk stratification and factors (not included in the RCOG model) that were significantly different according to the univariable analysis were entered into a multivariable logistic regression analysis by stepwise selection. ROC curve analysis, calibration curve, and decision curve analysis (DCA) were used to evaluate the predictive value of the RCOG RAM for postpartum VTE, as well as the applicability of the thromboprophylaxis recommended by the RCOG guidelines.

Table 1. Socio-demographic characteristics of women in the VTE group and control group.

Variable	VTE group* n=38		Control group* n=152		χ^2/t	p Value
Age, year	33.92±1.65		31.40±0.66		3.23	0.006
BMI, kg/m²	22.78±0.97		21.88±0.56		1.47	0.144
Birthplace					5.13	0.024
Shanghai	23	(60.53)	61	(40.13)		
Outside of Shanghai	15	(39.47)	91	(59.87)		
Educational level					4.41	0.111
University or above	20	(52.63)	103	(67.76)		
High school	13	(34.21)	41	(26.97)		
Middle school or lower	5	(13.16)	8	(5.26)		
Occupation					2.26	0.133
Employed	32	(84.21)	142	(93.42)		
Unemployed	6	(15.79)	10	(6.58)		

VTE – venous thromboembolism; BMI – body mass index. * Data are presented as mean ± standard deviation or number (percentage).

Table 2. Risk factors for postpartum VTE contained in the RCOG risk assessment model.

Variable*	VTE group** n=38		Control group** n=152		χ^2	p Value
Pre-existing risk factors						
Previous VTE not related to major surgery	4	(10.53)	0	(0.00)	10.35	0.001
Medical comorbidities	2	(5.26)	3	(1.97)	1.19	0.276
Family history of VTE	8	(21.05)	10	(6.58)	6.68	0.010
Known low-risk thrombophilia	4	(10.53)	2	(1.32)	6.03	0.014
Age >35 years	14	(36.84)	25	(16.45)	7.33	0.007
Obesity					0.05	0.978
BMI ≥30	1	(2.63)	5	(3.29)		
BMI ≥40	0	(0.00)	1	(0.66)		
Parity >3	1	(2.63)	4	(2.63)	0.00	1.000
Smoker	3	(7.89)	2	(1.32)	3.99	0.046
Gross varicose veins	1	(2.63)	1	(0.66)	0.97	0.324
Obstetric risk factors						
Pre-eclampsia	2	(5.26)	10	(6.58)	0.09	0.766
Multiple pregnancy	4	(10.53)	3	(1.97)	5.03	0.025
Cesarean section in labor	18	(47.37)	20	(13.16)	19.46	<0.001
Elective cesarean section	17	(44.74)	71	(46.71)	0.05	0.827
Mid-cavity or rotational operative delivery	0	(0.00)	9	(5.92)	1.23	0.267
Prolonged labor (>24 hours)	0	(0.00)	3	(1.97)	0.00	1.000
PPH (>1 litre or transfusion)	1	(2.63)	5	(3.29)	0.04	0.836
Preterm birth <37+0 weeks	4	(10.53)	5	(3.29)	3.17	0.075
Transient risk factors						
Surgical procedure in pregnancy or puerperium	6	(15.79)	4	(2.63)	8.25	0.004
Current systemic infection	4	(10.53)	7	(4.61)	1.85	0.174
Immobility, dehydration	2	(5.26)	2	(1.32)	1.97	0.161

VTE – venous thromboembolism; BMI – body mass index; PPH – postpartum hemorrhage. * Previous VTE provoked by major surgery, known high-risk thrombophilia, stillbirth, and hyperemesis are also factors contained in the RCOG risk assessment model, but they did not exist in our study population, thus they are not included in the table. ** data are presented as number (percentage).

between the 2 groups. Significant differences in age (*P*=0.006) and birthplace (*P*=0.024) were observed.

Univariable Analysis of Risk Factors in the RCOG RAM

Risk factors contained in the RCOG RAM were compared between the 2 groups (**Table 2**). We found that the proportions of women in the VTE group with previous VTE (*P*=0.001), a family history of VTE (*P*=0.010), known low-risk thrombophilia (*P*=0.014), age >35 (*P*=0.007), smoking habit (*P*=0.046), multiple pregnancy (*P*=0.025), cesarean section in labor (*P*<0.001), and surgical procedure in pregnancy or puerperium (*P*=0.004) were higher than those in the control group. Other risk factors showed no significant differences between the 2 groups.

Among the 190 women, the most common risk factors were elective cesarean section (88/190), age >35 years (39/190), cesarean section in labor (38/190), and family history of VTE (18/190).

Table 3. RCOG risk score and risk level of women in the VTE group and control group.

	VTE group n=38	Control group n=152	OR	95% CI	p Value
Score (mean±SD)	3.74±0.74	1.49±0.22	2.04	[1.57, 2.64]	<0.001
Risk level, n (%)					<0.001
Low risk	4 (10.53)	90 (59.21)	Reference		
Intermediate risk	26 (68.42)	60 (39.47)	9.75	[3.24, 29.36]	
High risk	8 (21.05)	2 (1.32)	90.00	[14.22, 569.52]	

VTE – venous thromboembolism; SD – standard deviation; OR – odd ratio; CI – confidence interval.
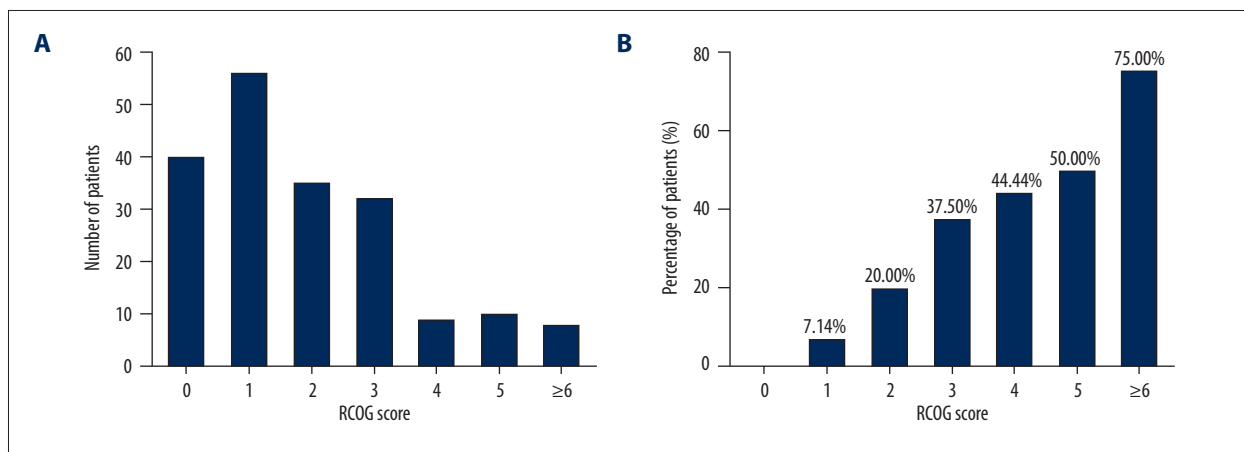
Figure 2. The distribution of the women in each score segment according to the RCOG assessment model. (**A**) Histogram of RCOG score (n=190). (**B**) Rates of VTE in each RCOG score segment.

**Risk Scoring and Risk Stratification Based on the RCOG RAM**

Table 3 shows that the RCOG scores of women in the VTE group were much higher than that of the control group (3.74±0.74 vs 1.49±0.22, *P*<0.001). A difference in risk stratification was also found between the 2 groups (*P*<0.001). The univariable logistic regression analysis revealed that the risk of postpartum VTE was 9.75-fold greater in the intermediate-risk group, and 90.00-fold greater in the high-risk group than in the low-risk group. Meanwhile, as the RCOG score increased, the risk of developing postpartum VTE increased almost linearly (**Figure 2**).

The ROC curve analysis determined that the AUC of the RCOG RAM was 0.828 (95% CI: 0.762-0.894, **Figure 3A**), and the Youden index was 0.50, with the best cut-off value being 2, which exactly matches the cut-off value recommended by the RCOG guidelines for pharmacological thromboprophylaxis after delivery. The sensitivity of the model was 89.47%, and its specificity was 60.53%. The positive predictive value was 36.17%, and the negative predictive value was 95.83%. In addition, the calibration plot showed good agreement between the prediction of the RCOG RAM and actual observation of VTE events (Hosmer-Lemeshow test p=0.214, see **Figure 3B**). The DCA also showed a certain net benefit value when the threshold probability is between 0.05-0.74 and 0.87-0.99, indicating that clinical decisions based on the predicted result of this model can benefit patients (**Figure 3C**).

Univariable Analysis of Other Clinical Dactors and D-dimer

Other factors that might be associated with postpartum VTE were also analyzed. We found that endometriosis (*P*=0.024), a family history of diabetes (*P*=0.010), recurrent pregnancy loss (*P*=0.024), glucocorticoid therapy during pregnancy (*P*=0.004), previous use of oral contraceptive pills (*P*=0.005), and intrauterine devices (*P*=0.001) for contraception were more common in women with postpartum VTE, while the previous use of condoms, calendar rhythm method, or withdrawal method for contraception (*P*=0.009) was more common in the control group (**Table 4**). Women in the VTE group had significantly higher D-dimer levels before delivery, and on the first and third day after delivery (*P*<0.05, **Table 4**).
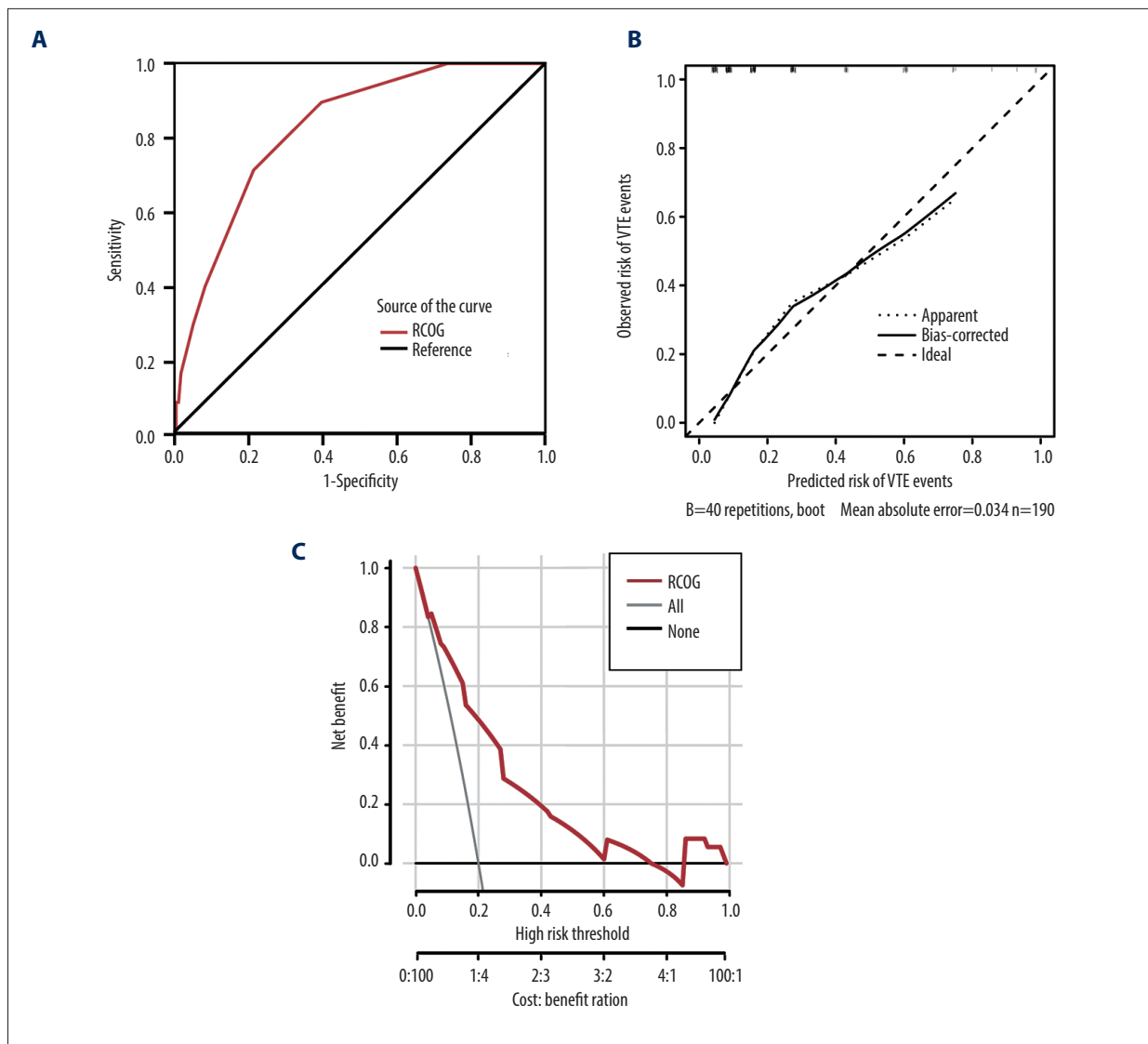
Figure 3. ROC curve, calibration plot and DCA of the RCOG risk assessment model. (**A**) ROC curve of the RCOG RAM. The AUC was 0.828 (95% CI: 0.762-0.894), and the Youden index was 0.50. (**B**) Calibration plot of the RCOG RAM. The apparent (thin dotted line) and bias-corrected (black solid line) nonparametric smoothed calibration curves are shown. (**C**) DCA of the RCOG RAM. The gray and black solid lines represent the net benefit of the strategy of treating all patients and no patients, respectively.

Multivariable Analysis

RCOG risk stratification and factors (not included in the RCOG model) found to be significantly different in the univariable analysis were further entered into a multivariable logistic regression analysis. The results show that RCOG intermediate risk (adjusted OR=8.39, 95% CI: 2.64-26.60), RCOG high risk (adjusted OR=118.23, 95% CI: 18.05-774.46), previous use of IUD (adjusted OR=7.11, 95% CI: 1.45-34.93), and glucocorticoid therapy during pregnancy (adjusted OR=6.72, 95% CI: 1.56-28.91) were associated with elevated risk of postpartum VTE (**Table 5**).

Discussion

The RCOG risk assessment model is one of the most complex scales for pregnancy-related VTE. Since its first publication in 2004, it has been demonstrated to be effective in reducing the maternal mortality rate from PE in the UK [11], but its applicability in Chinese maternity care is uncertain. The traditional conception is that Asian people have a relatively low risk of VTE compared with people in Western countries [14]. As the data used to establish the RCOG model were obtained from Western countries, it is worrying that the use of RCOG RAM in China might lead to the overestimation of VTE risk as well as the overuse of LMWH.

Table 4. Other clinical features and D-dimer of women in the VTE group and control group.

Variable	VTE group* n=38		Control group* n=152		χ^2/Z	p Value
Reproductive history						
Gravidity					3.20	0.202
1	15	(39.47)	80	(52.63)		
2	10	(26.32)	40	(26.32)		
≥3	13	(34.21)	32	(21.05)		
Number of spontaneous abortions					7.42	0.024
0	31	(81.58)	127	(83.55)		
1	2	(5.26)	21	(13.82)		
≥2	5	(13.16)	4	(2.63)		
Number of voluntary termination of pregnancy					1.17	0.559
0	28	(73.68)	113	(74.34)		
1	6	(15.79)	30	(19.74)		
≥2	4	(10.53)	9	(5.92)		
Gynecologic history						
Endometriosis	5	(13.16)	5	(3.29)	5.11	0.024
PCOS	1	(2.63)	6	(3.95)	0.15	0.702
Previous contraceptive use						
Never/condoms/calendar rhythm method/ withdrawal method	24	(63.16)	126	(82.89)	6.77	0.009
Oral contraceptive pills	13	(34.21)	21	(13.82)	8.04	0.005
IUD	7	(18.42)	3	(1.97)	11.34	0.001
Obstetric characteristics						
ART	5	(13.16)	19	(12.50)	0.01	0.913
Progesterone therapy during early pregnancy	13	(34.21)	36	(23.68)	1.74	0.187
Glucocorticoid therapy during pregnancy	7	(18.42)	6	(3.95)	8.33	0.004
GDM	8	(21.05)	33	(21.71)	0.01	0.930
Gestational hypertension	5	(13.16)	13	(8.55)	0.74	0.390
Family history						
Family history of diabetes	8	(21.05)	10	(6.58)	6.68	0.010
Family history of hypertension	8	(21.05)	30	(19.74)	0.03	0.856
D-dimer						
D-dimer at 12 weeks (mg/ml)	0.67	(0.50-0.99)	0.66	(0.50-0.79)		0.300
D-dimer at 34 weeks (mg/ml)	1.29	(0.94-1.72)	1.16	(0.88-1.74)		0.305
D-dimer before delivery (mg/ml)	2.13	(1.32-3.15)	1.72	(1.17-2.66)		0.043
D-dimer at 1st day after delivery (mg/ml)	4.86	(3.36-7.11)	3.74	(2.53-5.13)		0.006
D-dimer at 3rd day after delivery (mg/ml)	2.71	(1.65-4.09)	1.99	(1.38-2.74)		0.008

VTE – venous thromboembolism; PCOS – polycystic ovarian syndrome; IUD – intrauterine device; ART – assisted reproductive technology; GDM – gestational diabetes mellitus. * Data are presented as number (percentage) or median (interquartile range).

Table 5. Multivariable logistic regression analysis of risk factors for postpartum VTE.

	Adjusted OR	95% CI	p Value
RCOG risk level			<0.001
Low risk	Reference		
Intermediate risk	8.39	[2.64, 26.60]	
High risk	118.23	[18.05, 774.46]	
IUD			0.016
No	Reference		
Yes	7.11	[1.45, 34.93]	
Glucocorticoid therapy during pregnancy			0.010
No	Reference		
Yes	6.72	[1.56, 28.91]	

VTE – venous thromboembolism; IUD – intrauterine device; OR – odd ratio; CI – confidence interval.

Several domestic studies have compared the RCOG RAM and other VTE scoring models not specifically designed for pregnant women. Liang et al found that the discrimination and accuracy of the Wells score were better than that of the RCOG RAM, but they used the 2009 version of the RCOG model [15]. At the same time, Zhang et al came up with an opposite result [16]. Moreover, a prospective observational study has been carried out in Beijing to evaluate the feasibility of the RCOG RAM [17]. In our case-control study, we found that the RCOG RAM could screen out the majority of patients who eventually developed postpartum VTE (34/38), and for those assessed as low-risk by the model, nearly 96% would not develop VTE (90/94). Therefore, this model has a clear predictive value for postpartum VTE in Chinese women.

During its application in other Asian countries, it was found that the RCOG RAM might lead to the overuse of anticoagulant drugs in women who are less likely to develop postpartum VTE. A retrospective study in Malaysia suggested that 30.62% of postpartum women without VTE met the criteria for thromboprophylaxis [18]. Our study reached a similar conclusion.

Currently, the main concerns for the large-scale use of LMWH are its high price and the increased risk of hemorrhage and poor wound healing. However, compared with other anticoagulants such as heparin, LMWH is much safer [19]. Some studies have also confirmed that the use of LMWH does not increase the risk of postpartum hemorrhage and wound complications [20,21]. In view of the fatal consequences of VTE, it is critical to ensure that as many women as possible with potential risks of VTE receive anticoagulation treatment.

In our study, elective cesarean section, age >35 years, cesarean section in labor, and family history of VTE were the most common risk factors for postpartum VTE. Therefore, to reduce the incidence of VTE events, we strongly recommended that efforts should be made to prevent cesarean sections without indication and to avoid pregnancy in advanced age. We also found that in addition to the factors already contained in the RCOG RAM, previous use of IUD and glucocorticoid therapy during pregnancy might also increase the risk of postpartum VTE.

IUDs containing levonorgestrel (Mirena) are thought to increase the risk of VTE, but a copper IUD seems to be a safe alternative for contraception, even for people with a history of DVT or PE [22,23]. However, we surprisingly found that previous use of a copper IUD might increase the risk of postpartum VTE. Among the 7 women who had used IUD in the VTE group, only 1 used Mirena, and the rest used copper IUDs. Previous studies have not detected changes in coagulation-related parameters in IUD users, but the placement of an IUD has been shown to cause abnormal uterine bleeding by elevating fibrinolysis [24], which might cause further potential abnormalities in coagulation function that lead to thrombosis during pregnancy and the peripartum period. Furthermore, extensive microthrombosis in stromal capillaries has been observed in the endometrium in contact with an IUD [25].

The main purpose of using glucocorticoids during pregnancy is to promote fetal lung maturity in women who are at risk of preterm birth, or to treat thrombocytopenia during pregnancy. The use of glucocorticoids can cause the increased circulation level of fibrinogen, Factor VII, Factor VIII, and other hemostatic components [26]. Previous epidemiological studies also found that the use of systemic glucocorticoids can increase the risk of VTE by up to 3 times [27]. However, in the currently widely used risk assessment models for VTE, whether designed for pregnant women or not, the use of glucocorticoids is not regarded as a risk factor [10]. Therefore, it is recommended that clinicians strengthen the prevention and treatment of VTE in women who use glucocorticoids.

To our knowledge, this study is one of the few to assess the applicability of the RCOG RAM in China, and contains a relatively large number of VTE cases. At the same time, our study also has some limitations. Due to the low prevalence of postpartum VTE and the single-center design, although we enrolled all VTE cases within 4 years, the number of VTE events was relatively small. Additionally, the retrospective study design may limit the interpretation of the results and make it difficult to establish causal conclusions. To solve these problems, a prospective, large-sample, multicenter study will be required in the future. As far as we know, a large prospective observational study on the applicability of the RCOG RAM in Chinese women has already been carried out in Beijing, and the researchers hope to revise the model based on the study results to make it more suitable for Chinese population [17]. We hope that this study can provide a reference for the use of the RCOG RAM in Chinese maternity care, and provide valuable experience for subsequent large-scale studies.

Conclusions

Our results indicate that the RCOG RAM is effective in identifying women who were at risk of postpartum VTE, and that following the thromboprophylaxis methods recommended by the RCOG guidelines can effectively reduce the risk of VTE. But at the same time, we found that previous use of IUD and use of glucocorticoid during pregnancy might also increase the risk of postpartum VTE. Therefore, for the better prevention of pregnancy-related VTE, a risk assessment model based on national data needs to be established in the future.

Acknowledgements

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Conflict of Interest

None.

Supplementary Data

Supplementary Table 1. The RCOG risk assessment model for VTE.

Risk factors for VTE	Score*
Pre-existing risk factors	
Previous VTE (except a single event related to major surgery)	4
Previous VTE provoked by major surgery	3
Known high-risk thrombophilia	3
Medical comorbidities (e.g. cancer, heart failure; active systemic lupus erythematosus, Inflammatory polyarthropathy or inflammatory bowel disease; nephrotic syndrome; type I diabetes mellitus with nephropathy; sickle cell disease; current intravenous drug user)	3
Family history of unprovoked or estrogen-related VTE in first-degree relative	1
Known low-risk thrombophilia (no VTE)	1
Age (>35 years)	1
Obesity	
BMI ≥30	1
BMI ≥40	2
Parity ≥3	1
Smoker	1
Gross varicose veins	1
Obstetric risk factors	
Pre-eclampsia in current pregnancy	1
ART/IVF (antenatal only)**	1

Supplementary Table 1 continued. The RCOG risk assessment model for VTE.

Risk factors for VTE	Score*
Multiple pregnancy	1
Cesarean section in labor	2
Elective cesarean section	1
Mid-cavity or rotational operative delivery	1
Prolonged labor (>24 hours)	1
PPH (>1 litre or transfusion)	1
Preterm birth <37^{+0} weeks in current pregnancy	1
Stillbirth in current pregnancy	1
Transient risk factors	
Any surgical procedure in pregnancy or puerperium except immediate repair of the perineum, e.g. appendicectomy, postpartum sterilisation	3
Hyperemesis	3
OHSS (first trimester only)**	4
Current systemic infection	1
Immobility, dehydration	1

VTE – venous thromboembolism; BMI – body mass index; ART – assisted reproductive technology; IVF – in vitro fertilization; PPH – postpartum hemorrhage. * Risk factors with score ≥4 are considered as high-risk factor; risk factors with score of 2-3 are considered as intermediate-risk factors; risk factors with score of 1 are considered as low-risk factors. ** ART/IVF is regarded as a risk factor for antenatal VTE, and ovarian hyperstimulation syndrome (OHSS) is regarded as a risk factor for VTE only in the first trimester.

Supplementary Table 2. VTE events.

Patient	VTE event	Confirmed time*	RCOG score	Risk factor**	Anticoagulant during pregnancy
1	DVT (both)	Day 2	5	Age >35 years, elective caesarean section, surgical procedure in pregnancy or puerperium	No
2	DVT (left)	Day 2	1	Elective caesarean section	No
3	DVT (right) +PE	Day 3	8	Previous VTE (PE during puerperium), family history of VTE, age >35 years, elective caesarean section, preterm birth	No
4	DVT (both) +PE	Day 2	3	Caesarean section in labour, immobility	No
5	DVT (left) +PE	Day 2	2	Smoker, elective caesarean section	No
6	DVT (left)	Day 4	6	Low-risk thrombophilia (APS), age >35 years, elective caesarean section, surgical procedure in pregnancy or puerperium	Heparin since 1st trimester
7	DVT (left)	Day 3	5	Family history of VTE, age >35 years, BMI >30, gross varicose veins, elective caesarean section	No
8	DVT (left) +PE	Day 3	3	Age >35 years, caesarean section in labour	No
9	DVT (both) +PE	Day 2	1	Elective caesarean section	No

Supplementary Table 2 continued. VTE events.

Patient	VTE event	Confirmed time*	RCOG score	Risk factor**	Anticoagulant during pregnancy
10	DVT (both)	Day 2	4	Medical comorbidities, elective caesarean section	No
11	DVT (both)	Day 3	4	Elective caesarean section, surgical procedure in pregnancy or puerperium	No
12	DVT (both)	10+ weeks, Day 2	5	Smoker, previous VTE (DVT found in 1st trimester in this pregnancy)	LMWH since 1st trimester
13	DVT (left)	Day 3	2	Family history of VTE, elective caesarean section	No
14	DVT (both)	Day 2	2	Caesarean section in labour	No
15	DVT (right)	Day 2	6	Age >35 years, current systemic infection, caesarean section in labour, preterm birth, immobility	No
16	DVT (both)	Day 3	2	Caesarean section in labour	No
17	DVT (left)	Day 3	3	Age >35 years, caesarean section in labour	No
18	DVT (right)	Day 2	5	Age >35 years, elective caesarean section, surgical procedure in pregnancy or puerperium	No
19	DVT (both) +PE	7+ weeks, Day 3	6	Previous VTE (non-surgical DVT, and DVT found in 1st trimester in this pregnancy), family history of VTE, low-risk thrombophilia (APS)	LMWH since 1st trimester
20	DVT (left)	Day 2	4	Family history of VTE, pre-eclampsia, caesarean section in labour	No
21	DVT (left)	Day 4	3	Low-risk thrombophilia (APS), caesarean section in labour	No
22	DVT (left)	Day 3	4	Smoker, age >35 years, caesarean section in labour	No
23	DVT (left) +PE	Day 3	2	Caesarean section in labour	No
24	DVT (left) +PE	Day 2	3	Age >35 years, caesarean section in labour	No
25	DVT (left) +PE	Day 2	2	Family history of VTE, elective caesarean section	No
26	DVT (left)	Day 3	1	Elective caesarean section	No
27	DVT (left) +PE	Day 3	2	Multiple pregnancy, elective caesarean section	No
28	DVT (right) +PE	Day 4	10	Age >35 years, pre-eclampsia, multiple pregnancy, caesarean section in labour, PPH, preterm birth, surgical procedure in pregnancy or puerperium	No
29	DVT (both)	Day 2	3	Age >35 years, caesarean section in labour	No
30	DVT (left)	Day 5	5	Age >35 years, parity >3, caesarean section in labour, current systemic infection	No

Supplementary Table 2 continued. VTE events.

Patient	VTE event	Confirmed time*	RCOG score	Risk factor**	Anticoagulant during pregnancy
31	DVT (left)	Day 2	3	Medical comorbidities	No
32	DVT (both)	30+weeks, Day 2	11	Previous VTE (prenatal DVT in this pregnancy), low-risk thrombophilia (APS), family history of VTE, multiple pregnancy, elective caesarean section, surgical procedure in pregnancy or puerperium	LMWH since 3rd trimester
33	DVT (left) +PE	Day 3	3	Age >35 years, caesarean section in labour	No
34	DVT (left)	Day 3	1	Elective caesarean section	No
35	DVT (left)	Day 6	3	Multiple pregnancy, elective caesarean section, preterm birth	No
36	DVT (left)	Day 4	3	Caesarean section in labour, current systemic infection	No
37	DVT (right)	Day 2	3	Caesarean section in labour, current systemic infection	No
38	DVT (right)	Day 2	3	Family history of VTE, caesarean section in labour	No

VTE – venous thromboembolism; DVT – deep venous thrombosis; PE – pulmonary embolism; APS – antiphospholipid syndrome; LMWH – low-molecular-weight heparin. * "Confirmed Time" refers to the time of initial diagnosis of VTE before and/or after delivery. Day 2, Day 3, etc. indicate the second or third day, respectively, after childbirth. ** Artificial reproductive technology/in vitro fertilization and ovarian hyperstimulation syndrome are risk factors for VTE antenatally, so they are not included in this table for postpartum VTE assessment.

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