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Evaluation of Risk Factors for Venous Thromboembolism in Patients Who Underwent Gynecological Surgery and Validation of a Fast-Rating Assessment Table

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Background: The aim of this study was to retrospectively analyze the risk factors for venous thromboembolism (VTE) in gynecological patients and verify the validity of a fast-rating assessment table.

Material/Methods: From October 2015 to October 2017, 53 patients complicated with VTE after gynecological operations were analyzed, and a total of 106 patients with 2 adjacent operations were selected as the control group. Factors such as age, body mass index (BMI), and tumor type were analyzed by univariate and multivariate analysis. A fast-rating assessment table of VTE risk factors was constructed. This fast-rating assessment table and the Caprini score table were used to compare the scores of all patients.

Results: In the univariate analysis, there were significant differences in BMI, tumor type, operation duration, blood loss, blood transfusion, bed rest time, and thrombus-related history between the 2 groups. In the multiple factor analysis, age >60 years old, BMI >28 kg/m^2, malignant tumors, operation duration ≥3 hours, laparoscopic surgery and thrombus-related history were independent risk factors for VTE in patients. Both the fast-rating assessment table and the Caprini score table identified 90% of VTE patients as high-risk and very high-risk, and there was no significant difference between the tables.

Conclusions: Patients with older age, high BMI, malignant tumors, longer operation duration, laparoscopic surgery, or history of thrombosis may be more prone to VTE after gynecologic surgery. The fast-rating assessment table is easy to operate and has a high recognition level for VTE. It can be applied widely.

MeSH Keywords: Gynecologic Surgical Procedures • Risk Factors • Venous Thromboembolism

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Background

Venous thromboembolism (VTE) ranks third in the most common acute cardiovascular syndrome, causing a large disease burden, and the incidence of VTE continues to increase as the global life expectancy increases [1]. Only 45% of people surveyed were aware that the majority of cases of VTE are preventable, with even smaller numbers of people aware that hospital admission for surgical and medical treatment is a major risk factor for VTE [2], including deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE is one of the most serious complications after gynecological pelvic surgery [3].

The formation of venous thrombosis is influenced by a variety of factors. In the mid-19th century, Virchow first proposed that blood stasis, hypercoagulability and vascular wall damage are the 3 major factors of thrombosis formation. Any cause that leads to the 3 pathological conditions aforementioned is a risk factor for the development of VTE. Blood concentration caused by pre-operative preparation for gynecological surgery, vasodilation after anesthesia during surgery, vascular injury, release of coagulation factors, postoperative immobilization, and non-standard use of hemostatic drugs are all factors promoting thrombosis in patients have undergone gynecological surgery [4].

Several individualized risk models have also been developed and clinically evaluated [5,6]. However, none of them is more widely validated than the risk assessment model of Caprini [7]. Since its revision in 2009, the Caprini risk model has undergone retrospective validation in a large number of western populations, confirming its effectiveness and feasibility in screening populations at high-risk of VTE [8]. It contains approximately 40 different risk factors, making it complicated and time-consuming, so we designed a fast-rating assessment table that is more in line with the characteristics of patients undergoing gynecological surgery.

This study retrospectively assessed the risk factors for VTE in gynecologic surgery and evaluate the validity of the established fast-rating assessment table.

Material and Methods

Clinical data

This mono-central, retrospective case-control study aimed to gynecologic tumor patients who had undergone laparotomic or laparoscopic surgery. Data of 53 patients complicated with VTE after being hospitalized and receiving surgical treatment in The First Hospital Affiliated to Xi'an Jiaotong University was collected. As for control group, a total of 106 non-VTE patients with time-adjacent gynecological surgeries were selected. Patients with grade one surgeries, such as curettage and hysteroscopy were excluded. DVT diagnostic criteria was that patients with limb swelling, pain, fatigue, or other clinical manifestations, with B-ultrasonographic-confirmed venous thrombosis. Diagnostic criteria for pulmonary embolism (PE) patients were in accordance with the ninth edition of Antithrombotic Therapy and Prevention of Thrombosis Guidelines published by American College of Chest physician (ACCP) [9].

Method

The study was designed as a retrospective case-control study, medical record information of VTE and non-VTE group was obtained through information from the department of hospital, mainly including age, body mass index (BMI), benign or malignant tumors, previous disease history, complications, surgical procedures, operation duration, blood loss and time of postoperative bed rest. These risk factors were analyzed by single-factor analysis, and multi-factors analysis was conducted using logistic regression model.

According to Caprini scale and Wells scale, Clinical Evaluation Scale of Gynecological Patients with Deep Venous Thrombosis (LDVT), combined with Clinical Guidelines: Prevention of Deep Venous Thrombosis and Pulmonary Embolism of American Society of Obstetricians and Gynecologists (ACOG), along with the results of multi-factors analysis, and the mean of the relevant parameters and the area under the receiver operating characteristic (ROC) curve, select the score of the parameter. A fast-rating assessment table of VTE risk factor was developed and all patients were scored. Then the evaluation outcomes of it in this study were compared with Caprini table widely.

Statistical method

SPSS 20.0 statistical software was utilized for analysis. In univariate analysis, the enumeration data is represented by the number of cases (constituent ratio); the chi-square test was used to compare the enumeration data between groups. As for multivariate analysis, the logistic regression model was adopted. $P<0.05$ was considered to have statistically significance. the ROC curve of model score was plotted to predict venous thrombosis and the cutoff value for predicting the venous thrombosis score was determined.

Results

Univariate analysis of risk factors for VTE in gynecologic patients

Comparisons between the 2 groups, after determining 10 risk factors that may lead to VTE, showed that there was a

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Table 1. Univariate analysis of risk factors for VTE in gynecologic surgery patients: n (%).

Factors	VTE group (n=53)		Control group (n=106)		P
Age years					0.69
<41 years	5	(9.4)	10	(9.4)	
41–60 years	21	(39.6)	37	(34.9)	
61–69 years	24	(45.3)	55	(51.9)	
>70 years	3	(5.7)	4	(3.8)	
BMI (kg/m^2)					<0.05
<25	26	(49.1)	79	(74.5)	
25–28	22	(41.5)	23	(21.7)	
>28	5	(9.4)	4	(3.8)	
Tumor					<0.05
Benign tumor	31	(58.5)	90	(84.9)	
Malignant tumor stage I–II	20	(37.7)	15	(14.1)	
Malignant tumor stage III–IV	2	(3.8)	1	(1.0)	
Surgical procedures					0.59
Laparoscopic surgery	32	(60.4)	41	(38.7)	
Open surgery	21	(39.6)	65	(61.3)	
Operation duration					<0.05
<3 hours	39	(73.6)	94	(88.7)	
≥3 hours	14	(26.4)	12	(11.3)	
Blood loss					<0.05
<500 mL	41	(77.4)	104	(98.1)	
≥500 mL	12	(22.6)	2	(1.9)	
Blood transfusion					<0.05
Yes	7	(13.2)	10	(9.4)	
No	46	(86.8)	96	(90.6)	
Medical complications					0.72
Hypertension	18	(34.0)	26	(24.5)	
Diabetes	16	(30.2)	12	(11.3)	
Other medical diseases	2	(3.8)	2	(1.9)	
No other medical diseases	17	(32.1)	66	(62.3)	
Time in bed					<0.05
<48 hours	11	(20.8)	55	(51.9)	
≥48 hours	42	(79.2)	51	(48.1)	
Thrombus related history					<0.05
Yes	9	(17.0)	1	(0.9)	
No	43	(83.0)	105	(99.1)	

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Table 2. Multivariate logistic regression analysis of risk factors for VTE in gynecologic surgery patients.

Variates	B	OR (95%CI)	P
Age >60 years	0.034	1.058 (1.032, 1.150)	0.010
BMI >28 kg/m^2	0.305	1.341 (1.201, 1.498)	0.000
Malignant tumor	2.043	1.948 (1.911, 1.974)	0.000
operation duration	0.030	1.035 (1.010, 1.064)	0.000
Blood loss	0.001	1.020 (1.014, 1.028)	0.873
Blood transfusion	0.396	1.386 (0.648, 1.942)	0.639
Time of bed rest	–0.358	0.738 (0.693, 0.801)	0.326
Laparoscopic surgery	3.482	28.94 (11.65, 42.84)	0.000
Thrombus related history	2.164	1.952 (1.931, 1.963)	0.000

Table 3. Simple asssessment form of risk factors for VTE patients.

Risk factors	0	1	2	3
Age (years)	<51	51–59	60–70	>70
BMI (kg/m^2)	<25	25–27	28–30	>30
Tumor properties	benign	–	Malignant	–
Operation duration (hours)	<1	1–2	2–3	>3
Thrombus related history	–	–	Yes	–
Hypercoagulable state of blood	–	–	Hyperlipidemia, diabetes, cardiovascular disease	–
Laparoscopic surgery	–	–	Yes	–

statistically significant difference between the 2 groups in terms of BMI, tumor type, operation duration, amount of blood loss, need for a blood transfusion, time in bed, and history of thrombosis (P<0.05). However, no difference was found in age, surgical procedures, or complications (P>0. 05). The results are shown in Table 1.

Multivariate logistic regression analysis of risk factors for VTE in gynecologic surgery patients

In total, 8 factors, including age, surgical methods, BMI, operation duration, amount of blood loss, need for a blood transfusion, time in bed, tumor type, and history of thrombosis, which had statistically significant differences in the univariate analysis, were analyzed by multivariate logistic regression. The results demonstrated that age >60 years old, BMI >28 kg/m^2, malignant tumor, surgery time ≥3 hours, laparoscopic surgery, and previous history of thrombosis are independent risk factors affecting gynecological surgery patients complicated with VTE (P<0.05). The results are shown in Table 2.

Combining the results of the multivariate logistic regression analysis, a fast-rating assessment table of risk factors for VTE patients was designed; it is shown in Table 3.

The area under the ROC curve for predicting venous thrombosis was 0.946 (95% confidence interval [CI]: 0.952–0.978). The optimal cutoff value for the area prediction was 5 points. The sensitivity of this cutoff value for predicting venous thrombosis was 86.2%. The specificity was 68.7%, and the Youden index was 0.73. Then, we established the criterion where low risk is 0–1, medium risk is 2, high risk is 3–4 and extremely high risk was >5 (Figure 1).

Comparing the results of the fast-rating assessment table of risk factors and the Caprini scoring table for VTE patients

All cases were evaluated using the fast-rating assessment table for VTE patients, and the score was compared with that of the Caprini scoring table. In total, 90.6% of VTE patients were classified in the high-risk and extremely high-risk groups using

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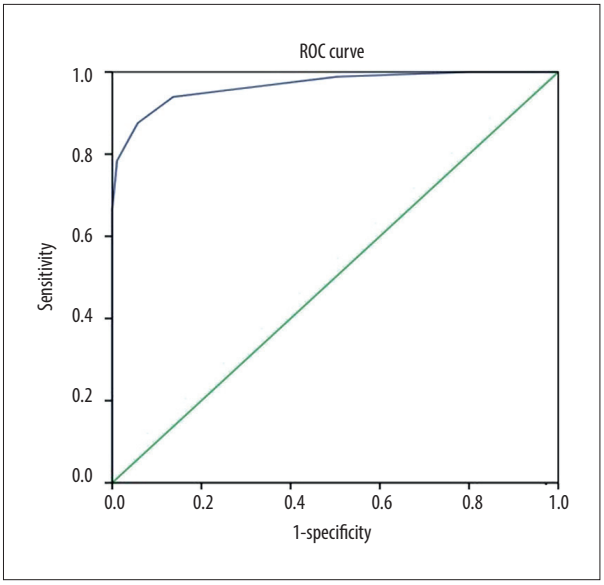

Figure 1. Simulated score predicts ROC curve of venous thrombosis.

the simple scoring table, and when using the Caprini scoring table, 88.7% of them were classified in the high-risk group and extremely high-risk group, indicating no statistically significant difference between the tables ($P>0.05$). The details are shown in Table 4.

Discussion

A systematic review found that in the Asian population, the venous thromboembolism (VTE) rates ranged from 11 to 88 cases per 10 000 admissions. Population-based estimates of postsurgical deep venous thrombosis (DVT) rates ranged from 0.15% to 1.35% [10]. The morbidity of DVT after pelvic surgery in western countries is 11% to 29%. In China, the occurrence of VTE after surgery has attracted increasing attention. First, this was because of the incidence rate of VTE after orthopedic surgery, then it was found that the incidence rate of venous thrombosis in gynecological pelvic surgery was also very high.

In this study, there were statistically significant differences between the VTE group and the control group for BMI, tumor type, operation duration, amount of blood loss, need for a blood transfusion, time in bed and history of thrombosis ($P<0.05$), while no significant differences were found for age, surgical procedures, or complications. Many studies have shown a significant increase in the incidence of thrombosis in patients with malignant tumors [11,12]. The surgical site for gynecological malignant tumors is located in the pelvic cavity, where the blood vessels are abundant, making it easy to cause vascular injury during the operation. In addition, the tumor tissue produces a large amount of thromboplastin, which promotes thrombosis. Our study indicated that patients with malignant tumors had a higher morbidity risk, which was consistent with previous reports. In patients with obesity and underlying diseases, endocrine disorders cause changes in blood viscosity and vascular intima damage, increasing the risk of venous thrombosis. It has been found that BMI ≥35 kg/m^2 is an independent risk factor for VTE in cancer patients [13]. Our study found that BMI ≥28 kg/m^2 was an independent risk factor for thrombosis but that there was no difference between the VTE group and the control group for patients with internal disease, which may be related to the failure to separate these risk factors and the limited sample size. Rahh et al. [14] found that age >60 years old is a high-risk factor for gynecological venous thrombosis. In the univariate analysis for the present study, there was no statistically significant difference in age between the 2 groups, while in the multivariate regression analysis, senior age was an independent risk factor, meaning that older patients are at higher risk. In addition, the longer operation time, the more bleeding, the more coagulation mechanisms and factors initiated by the coagulation system, the slower the postoperative recovery, the longer the bed rest time, the higher the risk of thrombosis. Davenport et al. [15] found that the incidence of VTE in patients with gynecological malignancies who had undergone laparoscopic surgery was lower than that in patients who had undergone laparotomy. However, Nick et al. [16] found that laparoscopic surgery can increase the incidence of VTE. The influence of pneumoperitoneum, hypercapnia and cystolithiasis in laparoscopic surgery may enable formation of venous thrombosis, and the long time in bed and slow recovery after laparotomy are also enable the formation of thrombosis;

Table 4. Comparison of VTE risk factor scores and Caprini scores.

	VTE (n=53)				Non-VET (n=106)			
	Low risk	Medium risk	High risk	Extremely high risk	Low risk	Medium risk	High risk	Extremely high risk
VTE risk factor scores	0	5 (9.43%)	8 (15.09%)	40 (75.48%)	52 (49.1%)	48 (45.2%)	4 (3.8%)	2 (1.9%)
Caprini scores	0	6 (11.3%)	8 (15.1%)	39 (73.6%)	54 (50.9%)	46 (43.4%)	4 (3.8%)	2 (1.9%)
P		0.53	0.82	0.86	0.78	0.67	0.87	0.81

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so, the results of various studies are different. As the single-factor analysis of risk factors in our study showed, there was no statistically significant difference in surgical methods between the 2 groups. In the multi-factor analysis, laparoscopic surgery was an independent risk factor, so a larger sample size and multi-center sample were required.

At present, the most commonly used venous thrombosis risk assessment scales are the Caprini rating scale and the Wells rating scale, of which the Caprini rating scale is more comprehensive and covers more items related to gynecological surgery. Therefore, Caprini score is the cornerstone of the most widely used guidelines for the prevention and treatment of VTE in gynecologic surgery in the United States [17]. The Caprini scale contains approximately 40 different risk factors, covering all the risk factors that may cause VTE in hospitalized patients, but the identification of these factors is mostly unrelated to gynecological surgery. Clinically, the workload and working time of clinicians have increased, so we formulated a fast-rating assessment table of VTE risk factors for gynecological applications, which is simple in design and filled in by checking boxes. The total score is simple and easy to obtain; meanwhile, it takes less time. Using the VTE risk factor table to score all cases and comparing the scores with the Caprini scores, the difference in scores was not statistically significant ($P>0.05$). In total, 90.6% of VTE patients were classified in the high-risk group and extremely high-risk group using the VTE risk factor table, and 88.7% were classified in these groups using the Caprini score table, indicating that the degree of recognition of the VTE risk factor table is similar to that of the Caprini score table. In view of its strong maneuverability and shorter time requirement, it is easier to use the VTE risk factor table widely in the clinic.

After the simple and rapid scoring, the relevant preventive measures should be taken for patients. The operation should be gentle, accurate and fast to reduce intraoperative bleeding and shorten the operation time. Hemostatic agents should be used meticulously during and after operations; and in the early stage after operations, passive or active lower limb muscle exercise should be advocated. Physical methods include graded pressurized elastic socks, intermittent inflatable pressurized devices and plantar venous pumps, which have the advantage of no drug-prevented risk of bleeding [18]. Drug prevention is now dominated by low molecular weight heparin [19].

Conclusions

In summary, age >60 years old, BMI >28 kg/m^2, malignant tumors, operation duration ≥3 hours, laparoscopic surgery, and thrombus-related history are independent risk factors for VTE in patients who underwent gynecological surgery. The fast-rating assessment table can identify 90.6% of patients as high-risk and very high-risk and can be applied widely to prevent and reduce the incidence of VTE in gynecological surgery patients.

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