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在线全文

妇科手术后静脉血栓栓塞的独立危险因素及术后D-二聚体预测价值研究*

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【摘要】 目的 探讨妇科手术后静脉血栓栓塞（venous thromboembolism, VTE）的独立危险因素，评估术后D-二聚体（D-dimer）对VTE的预测价值，为制定个体化抗凝策略提供依据。**方法** 收集2020年3月—2022年3月于四川大学华西上锦南府医院接受妇科手术的307例女性患者的围术期资料，纳入标准为Caprini评分≥3分且未接受VTE预防。收集资料包括年龄、体质指数（body mass index, BMI）、绝经状态、合并症（高血压等）、术前及术后凝血指标（凝血酶原时间、活化部分凝血活酶时间、纤维蛋白原、D-二聚体等）、手术入路、麻醉时间、手术时间、美国麻醉医师协会（American Society of Anesthesiologists, ASA）分级，以及术后VTE发生情况（经影像学确诊）。根据术后是否发生VTE进行分组，单因素分析比较组间差异，二元logistic回归筛选独立危险因素，绘制受试者工作特征（receiver operating characteristic, ROC）曲线，计算曲线下面积（area under the curve, AUC）、灵敏度、特异度及约登指数，评估D-二聚体的诊断效能。**结果** 307例患者中，42例术后发生VTE，发生率为13.68%（42/307），其中深静脉血栓（deep vein thrombosis, DVT）30例（9.77%, 30/307），肺栓塞（pulmonary embolism, PE）12例（3.91%, 12/307）。多因素logistic回归分析显示，术后VTE的独立危险因素包括：年龄（OR=1.122/岁，95% CI：1.070~1.176）、BMI升高（OR=1.180，95% CI：1.031~1.351）、绝经状态（OR=13.753，95% CI：3.692~51.229）、高血压（OR=3.951，95% CI：1.837~8.498）、手术时间延长（OR=1.047/min，95% CI：1.013~1.082）、麻醉时间延长（OR=1.007/min，95% CI：1.002~1.011）、ASA分级升高（OR=8.122，95% CI：2.973~22.184）及术后D-二聚体升高（OR=1.177/mg/L，95% CI：1.029~1.346）。VTE组Caprini评分高于非VTE组（4.57±1.21 vs. 3.64±1.11，P<0.001），但多因素分析中Caprini评分无统计学意义（P=0.877）。术后D-二聚体为1.50 mg/L时，诊断VTE的灵敏度为54.76%，特异度为73.58%；术前后D-二聚体差值为2.50 mg/L时的灵敏度为26.19%，特异度为94.72%。**结论** 年龄增加、BMI升高、绝经状态、高血压、手术时间延长、麻醉时间延长及ASA分级升高是妇科术后VTE的独立危险因素。术后D-二聚体≥1.50 mg/L及术前后D-二聚体差值≥2.50 mg/L可作为VTE筛查与预警的实用指标，建议纳入术后常规监测。Caprini评分在该人群中预测价值有限，需整合上述因素构建面向妇科手术患者的专属风险评估模型。

【关键词】 妇科手术 静脉血栓栓塞 危险因素 D-二聚体 Caprini评分 预测模型

Independent Risk Factors for Venous Thromboembolism After Gynecological Surgery and the Predictive Value of Postoperative D-Dimer

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[Abstract] Objective To investigate the independent risk factors for venous thromboembolism (VTE) after gynecological surgery, evaluate the predictive performance of postoperative D-dimer levels for VTE, and inform the development of individualized anticoagulation strategies. **Methods** Perioperative data were collected from 307 female patients who underwent gynecological surgeries at West China Shangjin Nanfu Hospital, Sichuan University between March 2020 and March 2022. The inclusion criteria were a Caprini score ≥ 3 and the absence of any VTE prophylaxis. The data collected included age, body mass index (BMI), menopause, comorbidities (e.g., hypertension), preoperative and postoperative coagulation parameters (prothrombin time, activated partial thromboplastin time, fibrinogen, D-dimer, etc.), the surgical approach, anesthesia duration, surgery duration, American Society of Anesthesiologists (ASA) physical status classification, and postoperative VTE occurrence confirmed by imaging examinations. Patients were divided into

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VTE and non-VTE groups according to postoperative imaging findings. Univariate analysis was performed to compare differences between groups. Binary logistic regression was performed to identify independent risk factors. The receiver operating characteristic (ROC) curve was plotted, and the area under the curve (AUC), sensitivity, specificity, and Youden index were calculated to evaluate the predictive performance of D-dimer levels. **Results** Among the 307 patients, 42 (13.68%) developed postoperative VTE, including 30 cases (9.77%) of deep vein thrombosis (DVT) and 12 cases (3.91%) of pulmonary embolism (PE). Multivariable logistic regression analysis showed that independent risk factors for postoperative VTE included age (odds ratio [OR] = 1.122 per year, 95% CI: 1.070-1.176), increased BMI (OR = 1.180, 95% CI: 1.031-1.351), menopause (OR = 13.753, 95% CI: 3.692-51.229), hypertension (OR = 3.951, 95% CI: 1.837-8.498), prolonged surgery duration (OR = 1.047 per minute, 95% CI: 1.013-1.082), prolonged anesthesia duration (OR = 1.007 per minute, 95% CI: 1.002-1.011), higher ASA classification (OR = 8.122, 95% CI: 2.973-22.184), and elevated postoperative D-dimer levels (OR = 1.177 per mg/L, 95% CI: 1.029-1.346). Although the Caprini score was significantly higher in the VTE group than that in the non-VTE group (4.57 ± 1.21 vs. 3.64 ± 1.11, $P < 0.001$), binary logistic regression analysis revealed no statistically significant association ($P = 0.877$). A postoperative D-dimer level = 1.50 mg/L was the optimal threshold for diagnosing VTE, yielding a sensitivity of 54.76%, specificity of 73.58%. A preoperative-to-postoperative D-dimer change = 2.50 mg/L showed a sensitivity of 26.19%, specificity of 94.72%. **Conclusion** Increased age, higher BMI, menopause, hypertension, prolonged surgery duration and anesthesia duration, and higher ASA classification are independent risk factors for VTE after gynecological surgery. A postoperative D-dimer level ⩾ 1.50 mg/L and a preoperative-to-postoperative D-dimer change ⩾ 2.50 mg/L may serve as practical indicators for VTE screening and early risk identification and should be incorporated into routine postoperative monitoring. The Caprini score demonstrated limited predictive value for VTE risk in this gynecological patient cohort. Therefore, a risk assessment model tailored to patients undergoing gynecological surgery should be developed by incorporating these risk factors.

[Key words] Gynecological surgery Venous thromboembolism Risk factors D-dimer Caprini score Predictive model

静脉血栓栓塞症(venous thromboembolism, VTE)是一种常见的严重心血管疾病,包括深静脉血栓形成(deep vein thrombosis, DVT)和肺栓塞(pulmonary embolism, PE)。DVT指血液在深静脉内异常凝结,多发生于下肢,导致血管阻塞;PE则由静脉系统或右心的血栓脱落阻塞肺动脉及其分支,可引起肺循环和呼吸功能障碍。VTE的主要病理机制为Virchow三联征,涵盖血管内皮损伤、血流瘀滞及血液高凝状态[1]。手术是住院患者发生VTE的重要诱因。美国资料显示,术后VTE年发生率可达30%~60%[2];国内报道为32.7%~53.4%,且呈逐年上升趋势[3-4]。VTE一旦发生,后果严重。文献报道VTE患者7 d、30 d及1年的平均生存率分别为74.8%、72.0%和63.6%;若发生PE,生存率进一步降至59.1%、55.6%和47.7%,显著低于无VTE者[5]。此外,术后VTE显著增加医疗负担:美国VTE患者的预估住院费用为62 838美元,远高于非VTE患者的24 464美元[6];即使急性期处理成功,复发和再入院风险仍较高[7]。

妇科手术患者是VTE的高危群体。大型妇科手术后VTE发生率为15%~40%[8],尤其是盆腔器官脱垂和妇科肿瘤患者,因年龄更大、BMI更高、常处于血液高凝状态,风险尤为突出。尽管术后VTE风险因素研究已较广泛,但针对妇科手术人群的专门研究仍相对不足。尽管1991年提出的Caprini评分是目前应用最为广泛的VTE风险预测指标[9],但其在妇科领域的应用仍存在不足之处[10]。本研究拟通过回顾性队列分析,探讨妇科患者术后VTE的危险因素,为制定个体化抗凝策略、降低VTE相关并发症及疾病负担提供循证依据。

1 资料与方法

1.1 临床资料

收集2020年3月—2022年3月于四川大学华西上锦南府医院接受妇科手术的女性患者临床资料,根据纳排标准共纳入307例,用于术后VTE风险因素分析。纳入标准:①接受妇科手术的女性患者;②Caprini评分≥3分;③术后未接受VTE预防措施;④临床资料完整。排除标准:①术前已确诊VTE;②术前1周内接受过抗凝治疗;③合并凝血功能障碍;④合并心、肝、肾等重要脏器明显功能障碍;⑤临床资料不完整。本研究经四川大学华西第二医院医学科研伦理委员会批准〔医学科研2024伦审批第(026)号〕。

1.2 数据收集

1.2.1 术前一般情况

收集患者年龄、性别、体质指数(body mass index, BMI)等一般资料,以及入院诊断、激素替代疗法(hormone

replacement therapy, HRT)使用史、妊娠史、血栓相关病史、内外科合并症等临床资料。同时收集术前凝血指标,包括血小板计数(platelet count, PLT)、凝血酶原时间(prothrombin time, PT)、活化部分凝血活酶时间(activated partial thromboplastin time, APTT)、纤维蛋白原(fibrinogen, FIB)、凝血酶时间(thrombin time, TT)及D-二聚体(D-dimer)水平,以及下肢静脉超声、胸部X线/CT和心电图等影像学检查结果。

1.2.2　手术相关指标

收集患者手术相关资料,包括手术方式、麻醉时间、手术时间、术中出血量及美国麻醉医师协会(American Society of Anesthesiologists, ASA)分级。

麻醉时间:指从给予第一种麻醉药物开始至麻醉终止的时间段,包括诱导期、维持期和苏醒期,由手术记录获取。

手术时间:指从手术切口开始至切口缝合完毕的时间段,仅涵盖手术操作本身,不包括术前准备及术后复苏时间,由手术记录获取。

术中出血量:由术者通过称量吸引瓶内血液、计数饱含血液的纱布数量及计算引流管收集血量综合评估,由手术记录获取。

1.2.3　术后相关指标

收集患者术后24~72 h的临床资料,包括Caprini评分、PLT、PT、APTT、FIB、TT、D-二聚体水平、下肢静脉超声结果及术后预防措施使用情况。如有计算机断层扫描肺动脉造影(computed tomography pulmonary angiography, CTPA)结果,一并收集。根据术后影像学结果判断患者是否发生静脉血栓栓塞症,并据此将患者分为VTE组与非VTE组,进行后续统计学分析。

Caprini评分评估:于术后24 h内根据Caprini评分量表[9](附表)计算患者评分,评估妇科手术患者VTE风险等级。

1.3　统计学方法

使用IBM SPSS Statistics 24.0 软件(IBM, 阿蒙克, 纽约, 美国)进行统计学分析。对于符合正态分布的连续变量,组间比较采用独立样本t检验,结果以均值±标准差表示。对于不符合正态分布的连续变量,采用秩和检验,结果以中位数(四分位数间距)表示。对于分类变量,采用χ^2检验,当期望频数<5时使用Fisher精确检验,结果以例数(百分比)表示。将单因素分析中$P < 0.05$的变量纳入二元logistic回归模型,以筛选VTE的独立危险因素,结果以比值比(odds ratio, OR)和95%置信区间(confidence interval, CI)表示。计算灵敏度(sensitivity)、特异度(specificity)、阳性预测值(positive predictive value, PPV)及阴性预测值(negative predictive value, NPV),并绘制受试者工作特征(eceiver operating characteristic, ROC)曲线来评估D-二聚体等指标对VTE的预测价值,并计算曲线下面积(area under the curve, AUC),通过约登指数确定最佳截断值。P<0.05被认为具有统计学意义。

2　结果

2.1　VTE与非VTE患者一般情况比较

本研究共纳入307例患者,其中42例(13.68%)术后发生VTE(纳入VTE组),265例(86.31%)术后未发生VTE(纳入非VTE组);VTE组中深静脉血栓(DVT)30例(9.77%),肺栓塞(PE)12例(3.91%)。如表1所示,两组患者在年龄、BMI、绝经状态、高血压、Caprini评分及住院时间方

表 1　VTE及非VTE患者一般情况比较

Table 1　Comparison of general characteristics between VTE and non-VTE groups

Characteristic	Non-VTE (n = 265)	VTE (n = 42)	t/χ^2	P
Age/yr.	45.77 ± 12.89	60.55 ± 12.59	−6.924	< 0.001
BMI/(kg/m^2)	23.43 ± 3.17	24.49 ± 3.06	−2.021	0.044
Menopause/case (%)	90 (33.96)	18 (42.86)	21.155	< 0.001
Hypertension/case (%)	27 (10.19)	13 (30.95)	17.702	< 0.001
Diabetes mellitus/case (%)	26 (9.81)	4 (9.52)	0.251	0.618
COPD/case (%)	4 (1.5)	1 (2.38)	0.172	0.680
Smoking/case (%)	16 (6.04)	1 (2.38)	0.360	0.549
Hormone replacement therapy/case (%)	42 (15.85)	6 (14.29)	0.067	0.796
Caprini score	3.64 ± 1.11	4.57 ± 1.21	−4.958	< 0.001
Length-of-stay/d	7.50 ± 3.76	9.21 ± 5.09	−2.602	0.010

VTE: venous thromboembolism; BMI: body mass index; COPD: chronic obstructive pulmonary disease.

面差异均有统计学意义(P<0.05)，VTE组患者的平均年龄、BMI、Caprini评分及住院时间均高于非VTE组，绝经后及合并高血压的患者比例亦高于非VTE组。

2.2 VTE与非VTE患者术前后凝血指标比较

如表2所示，非VTE组患者术后PT、APTT、TT、FIB及D-dimer水平均较术前升高，而PLT及HGB水平较术前降低，差异均有统计学意义(P<0.05)；VTE组患者术后PT、TT、FIB及D-dimer水平均高于术前，PLT及HGB水平低于术前，差异亦均有统计学意义(P<0.05)。术前两组间各凝血指标差异均无统计学意义，而术后VTE组FIB及D-dimer水平显著高于非VTE组(P<0.05)。进一步对术前后差值进行分析(表3)发现，VTE组术后D-dimer升高幅度较非VTE组更为显著(P<0.05)。

2.3 VTE与非VTE患者手术相关因素比较

两组患者手术相关因素比较见表4。VTE组患者的麻醉时间(152.62±67.06 min)和手术时间(135.40±61.16 min)均长于非VTE组(121.94±59.72 min、100.28±55.17 min)，差异有统计学意义(P<0.05)。ASA分级方面，VTE组Ⅱ级患者比例低于非VTE组，Ⅳ级患者比例高于非VTE组，差异亦有统计学意义(P<0.05)。两组手术入路及术中出血量差异无统计学意义(P>0.05)。

2.4 术后VTE风险因素二元logistic分析

单因素分析显示，VTE组与非VTE组在年龄、BMI、绝经状态、高血压、Caprini评分、手术时间、麻醉时间、ASA分级及术后D-dimer水平方面差异均有统计学意义。将上述因素纳入二元logistic回归模型进行分析(表5, 图1)，

表 2 VTE与非VTE患者术前后凝血指标比较

Table 2 Comparison of coagulation parameters between VTE and non-VTE groups before and after surgery

Parameter	Time point	Non-VTE (n = 265)	t_1	P_1^*	VTE (n = 42)	t_2	$P_2^\dagger$	t_3	$P_3^\ddagger$
PT/s	Pre-op	11.04 ± 0.73	−7.476	< 0.001	10.86 ± 0.52	−6.519	< 0.001	1.524	0.129
	Post-op	11.51 ± 0.92			11.50 ± 0.63			0.116	0.908
APTT/s	Pre-op	27.16 ± 2.24	−2.023	0.044	26.53 ± 2.09	−1.845	0.072	1.709	0.089
	Post-op	27.52 ± 2.61			27.33 ± 2.64			0.421	0.674
TT/s	Pre-op	16.70 ± 8.44	3.163	0.002	16.51 ± 1.08	7.218	< 0.001	0.145	0.885
	Post-op	15.04 ± 1.25			15.29 ± 0.97			−1.222	0.223
FIB/(g/L)	Pre-op	3.04 ± 1.49	−8.363	< 0.001	3.25 ± 0.96	−10.385	< 0.001	−0.860	0.390
	Post-op	4.03 ± 1.27			4.54 ± 1.41			−2.399	0.017
D-dimer/(mg/L)	Pre-op	0.63 ± 1.73	−5.955	< 0.001	0.61 ± 0.72	−3.290	0.002	0.068	0.946
	Post-op	1.40 ± 1.78			3.34 ± 5.41			−4.528	< 0.001
PLT/(× 10^9 L^{-1})	Pre-op	230.69 ± 77.38	5.397	< 0.001	215.60 ± 41.72	2.561	0.014	1.235	0.218
	Post-op	212.25 ± 71.14			202.14 ± 47.30			0.889	0.375
HGB/(g/L)	Pre-op	127.54 ± 17.97	15.200	< 0.001	125.38 ± 15.72	7.986	< 0.001	0.735	0.463
	Post-op	115.68 ± 15.60			111.24 ± 13.13			1.747	0.082

PT: prothrombin time; APTT: activated partial thromboplastin time; TT: thrombin time; FIB: fibrinogen; PLT: platelet count; HGB: hemoglobin; Pre-op: preoperative; Post-op: postoperative. * represents paired t-test within the non-VTE group (Pre-op vs. Post-op); † represents paired t-test within the VTE group (Pre-op vs. Post-op); ‡ represents independent-samples t-test between groups (for the Pre-op rows, pre-op values are compared between groups; for the Post-op rows, post-op values are compared between groups).

表 3 VTE与非VTE患者术前后凝血指标变化程度比较

Table 3 Comparison of preoperative-to-postoperative changes in coagulation parameters between VTE and non-VTE groups

Parameter	Non-VTE (n = 265)	VTE (n = 42)	t	P
PT/s	0.47 ± 1.03	0.63 ± 0.63	−0.990	0.323
APTT/s	0.36 ± 2.88	0.80 ± 2.83	−0.934	0.351
TT/s	−1.66 ± 8.52	−1.22 ± 1.09	−0.331	0.741
FIB /(g/L)	0.98 ± 1.91	1.29 ± 0.81	−1.038	0.300
D-dimer /(mg/L)	0.77 ± 2.10	2.73 ± 5.38	−4.248	< 0.001
PLT/(× 10^9 L^{-1})	−18.44 ± 55.62	−13.45 ± 34.04	−0.564	0.573
HGB/(g/L)	−11.86 ± 12.70	−14.14 ± 11.48	1.094	0.275

The abbreviations are explained in the note to Tablle 2.

表 4　VTE与非VTE患者手术相关因素比较

Table 4　Comparison of surgery-related factors between VTE and non-VTE groups

Factor	Non-VTE (n = 265)	VTE (n = 42)	t/χ^2	P
Surgical approach/case (%)				
Laparoscopy	154 (58.11)	20 (47.62)	2.761	0.252
Vaginal surgery	92 (34.72)	16 (38.10)		
Open surgery	19 (7.17)	6 (14.29)		
Anesthesia time/min	121.94 ± 59.72	152.62 ± 67.06	−3.040	0.003
Sugical duration/min	100.28 ± 55.17	135.40 ± 61.16	−3.776	< 0.001
Intraoperative blood loss/mL	84.87 ± 133.95	114.17 ± 196.15	−1.226	0.221
ASA grade/case (%)				
Grade Ⅱ	218 (82.26)[a]	25 (59.52)[b]	17.518	< 0.001
Grade Ⅲ	44 (16.60)[a]	11 (26.19)[a]		
Grade Ⅳ	3 (1.13)[a]	6 (14.29)[b]		

ASA: American Society of Anesthesiologists. [a and b] The same superscript letters indicate no statistically significant difference between subsets (at the 0.05 level).

结果显示：年龄（OR=1.122，95%CI：1.070~1.176，P<0.001）、BMI升高（OR=1.180，95%CI：1.031~1.351，P=0.016）、绝经状态（OR=13.753，95%CI：3.692~51.229，P<0.001）、高血压（OR=3.951，95%CI：1.837~8.498，P<0.001）、手术时间延长（OR=1.047/min，95%CI：1.013~1.082，P=0.006）、麻醉时间延长（OR=1.007/min，95%CI：1.002~1.011，P=0.004）、ASA分级升高（OR=8.122，95%CI：2.973~22.184，P<0.001）及术后D-dimer升高（OR=1.177/mg/L，95%CI：1.029~1.346，P=0.017）均为VTE的独立危险因素。Caprini评分在本模型中无统计学意义（OR=1.026，95%CI：0.737~1.430，P=0.877）。

表 5　术后VTE风险因素二元logistic分析

Table 5　Binary logistic regression analysis of risk factors for postoperative VTE

Variable	B	Wald	P	Exp(B)	95% CI	
					Lower	Upper
Age	0.115	22.775	< 0.001	1.122	1.070	1.176
BMI	0.166	5.803	0.016	1.180	1.031	1.351
Menopause	2.621	15.264	< 0.001	13.753	3.692	51.229
Hypertension	1.374	12.369	< 0.001	3.951	1.837	8.498
Caprini score	0.026	0.024	0.877	1.026	0.737	1.430
Operation time	0.046	7.546	0.006	1.047	1.013	1.082
Anesthesia time	0.007	8.425	0.004	1.007	1.002	1.011
ASA grade	2.095	16.690	< 0.001	8.122	2.973	22.184
Postoperative D-dimer	0.163	5.680	0.017	1.177	1.029	1.346

The abbreviations are explained in the notes to Tables 1 and 4.

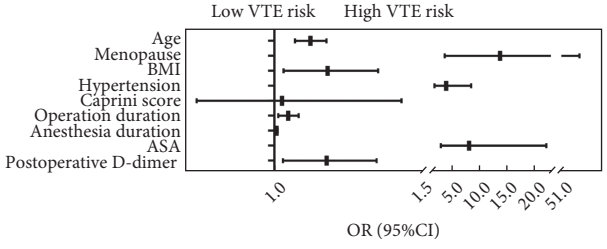


图 1　术后VTE风险因素二元logistic回归分析森林图

Fig 1　Forest plot of binary logistic regression analysis for risk factors of postoperative VTE

2.5　术后D-dimer水平及手术前后D-dimer差值诊断VTE发生ROC曲线

如图2所示。术后D-dimer水平诊断VTE的曲线下面积（AUC）为0.663（95%CI：0.571~0.755，P=0.001），提示其具有一定的临床诊断价值。当术后D-dimer取最佳截断值1.50 mg/L时，约登指数最高（28.34%），灵敏度为

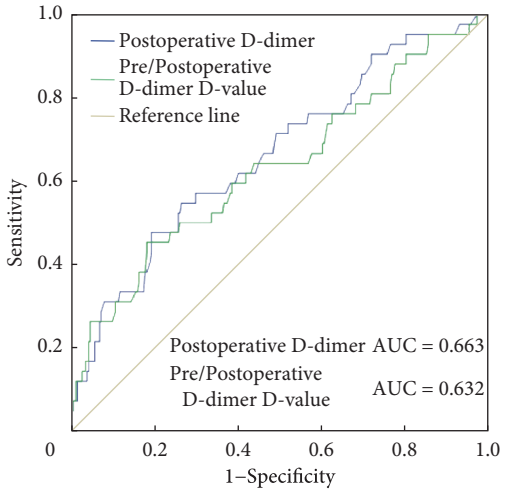


图 2　术后D-二聚体水平及术前后差值预测VTE的ROC曲线

Fig 2　ROC curves of postoperative D-dimer level and its preoperative-to-postoperative change for predicting VTE

54.76%, 特异度为73.58%(表6)。术前后D-dimer差值诊断VTE的AUC为0.632(95%CI: 0.533~0.730, *P*=0.006), 当差值取2.50 mg/L时, 约登指数最高(20.91%), 灵敏度为26.19%, 特异度为94.72%(表7)。

表 6 术后D-dimer水平诊断VTE发生灵敏度及特异度

Table 6 Sensitivity and specificity of postoperative D-dimer levels for diagnosing VTE

Postoperative D-dimer	PPV/%	NPV/%	Sensitivity/%	Specificity/%	Youden index/%
0.50 mg/L	15.66	94.83	92.86	20.75	13.61
1.00 mg/L	18.30	90.91	66.67	52.83	19.50
1.25 mg/L	20.17	90.43	57.14	64.15	21.29
1.50 mg/L	24.73	91.12	54.76	73.58	28.34
1.625 mg/L	23.81	90.13	47.62	75.85	23.47
1.75 mg/L	27.78	90.64	47.62	80.38	28.00
2.00 mg/L	27.45	89.06	33.33	86.04	19.37

PPV: positive predictive value; NPV: negative predictive value.

表 7 术前术后D-dimer差值诊断VTE发生灵敏度及特异度

Table 7 Sensitivity and specificity of preoperative-to-postoperative D-dimer change for diagnosing VTE

ΔD-dimer	PPV/%	NPV/%	Sensitivity/%	Specificity/%	Youden index/%
0.50 mg/L	15.17	88.37	64.29	43.02	7.31
1.00 mg/L	21.21	89.90	50.00	70.57	20.57
1.50 mg/L	27.66	88.85	30.95	87.17	18.12
2.00 mg/L	37.93	88.85	26.19	93.21	19.4
2.50 mg/L	44.00	89.01	26.19	94.72	20.91
3.00 mg/L	42.86	88.46	21.43	95.47	16.9

Δ: change; the other abbreviations are explained in the note to Table 6.

3 讨论

年龄增长作为住院患者VTE的独立危险因素已被多项研究证实, 是目前临床实践中VTE风险评估的重要考量指标。无论是否接受手术, 高龄患者发生VTE的风险均高于年轻患者, 其病理生理机制可能与老龄所致的静脉回流障碍、静脉瓣膜功能不全、全身慢性炎症状态及血管内皮损伤等因素有关[11-13]。多项研究表明, 年龄增长与妇科患者术后VTE风险呈正相关: 50岁以上患者妇科术后VTE风险显著增加[14-15], 年龄≥60岁是VTE的独立危险因素[16-17], 而针对接受盆底重建手术患者的研究则发现70岁及以上是VTE的风险阈值[18]。现有文献报告的年龄阈值存在一定异质性(50岁、60岁、70岁), 提示年龄与VTE风险之间可能呈连续剂量-效应关系而非简单的阈值效应。本研究同样发现年龄是妇科手术患者术后VTE的独立危险因素, 患者年龄每增加1岁, 术后VTE风险增加约12.2%(OR=1.122, 95%CI: 1.070~1.176), 进一步支持了上述结论。

与年龄因素类似, 肥胖亦是VTE的重要危险因素之一。相较于BMI正常者, 超重及肥胖患者因内脏脂肪压迫致下肢血流淤滞、脂肪组织释放促炎因子致血管内皮损伤, 以及脂肪因子水平升高所致的促血栓形成状态, 其VTE风险显著增加[19-21]。此外, 超重和肥胖可通过延长手术时间进一步增加VTE风险。无论内科还是外科患者, 超重及肥胖均显著增加VTE发生风险, 最高可达6.2倍[22-23]。妇科患者中, 多囊卵巢综合征及妊娠期患者因代谢改变等因素, BMI水平通常更高[24-25], 故肥胖亦是该人群VTE的重要影响因素。本研究中, VTE组平均BMI显著高于非VTE组(24.49±3.06 vs. 23.43±3.17), 多因素logistic回归分析确认BMI升高为VTE的独立危险因素(OR=1.180, 95%CI: 1.031~1.351), 即BMI每增加1单位, 妇科术后VTE风险升高约18.0%。这一结果提示妇科临床医师应高度重视肥胖患者术后VTE的预防。

绝经状态亦是妇科患者术后VTE风险增加的重要影响因素。本研究中, 已绝经妇女术后VTE风险较未绝经妇女增加约12.75倍(OR=13.753, 95%CI: 3.692~51.229)。绝经后妇女体内凝血系统的改变涉及血管内皮、血小板活性、凝血及纤溶等多个层面, 遗传背景及环境因素(如饮食习惯、吸烟、体力活动减少、慢性低度炎症等)均可影响止血相关蛋白的表达与功能[26], 这可能部分解释老年女性VTE发生率高于年轻女性的现象。雌孕激素在维持心血管系统功能方面发挥重要作用, 可通过调节血管内皮功能、促进前列环素合成、提高一氧化氮(NO)生物利用度, 以及直接作用于血小板表面雌激素受体抑制血小板活化与聚集[27-29]。绝经后体内雌孕激素水平下降, 可激活NADPH氧化酶(NOX)、降低NO生物利用度并增加活性氧(ROS)生成, 进而诱导血管内皮功能障碍[30]。上述机制提示, 临床工作者在对妇科患者进行术后VTE风险评估时, 应充分关注绝经状态这一重要因素, 以指导更精准的预防策略。

除患者自身因素外, 麻醉时间与手术时间延长均为术后VTE的独立危险因素。本研究中, 麻醉时间(OR=1.007, 95%CI: 1.002~1.011)及手术时间(OR=1.047, 95%CI: 1.013~1.082)均为妇科手术后VTE的独立危险因素。由于二者具有较强的相关性且致病机制相似, 故合并讨论。已有研究证实, 麻醉时间超过2 h可显著增加妇科手术后VTE风险[31-32], 手术时间每增加60 min, VTE发

生风险增加35%[33-34]。在腹腔镜和机器人辅助子宫切除术中, 手术时间≥240 min会导致包括VTE在内的总体并发症风险增加[35]。麻醉及手术时间延长导致VTE的机制可能包括: 全身麻醉状态下下肢肌肉松弛、“泵血”功能减弱致静脉回流减慢; 麻醉药物(如丙泊酚)所致剂量依赖性低血压进一步加重静脉淤滞; 手术中长时间截石位或俯卧位致腹内压升高、下腔静脉及髂静脉受压, 限制下肢静脉回流; 此外, 手术时间延长使组织暴露时间增加, 促炎因子(IL-6、TNF-α)及C反应蛋白(CRP)呈时间依赖性升高, 加重血管内皮损伤及功能障碍, 从而增加VTE发生风险[36]。

ASA分级(American Society of Anesthesiologists Physical Status Classification System)是美国麻醉医师协会制定的术前身体状况评估标准, 通过评估患者基础健康状况及合并症严重程度对围术期风险进行量化分级。ASA分级越高, 提示患者基础状况越差, 围术期并发症及死亡率亦越高[37]。本研究发现ASA分级是妇科手术后VTE的独立危险因素, 且随着分级升高VTE风险呈增加趋势。既往研究亦表明, ASA分级≥Ⅲ级是盆腔器官脱垂手术、妇科肿瘤手术、非恶性子宫切除手术术后VTE的预测因子[38-41]。然而, ASA分级作为单一指标在术后VTE风险评估中的价值有限: 一方面其缺乏实验室及影像学等客观量化参数, 评估结果受临床医师主观经验影响较大; 另一方面, Mrad等[42]的研究发现, 在整形外科手术患者中, ASA分级对于高风险患者术后VTE事件的预测效能弱于Caprini评分。因此, ASA分级虽可在一定程度上指导VTE预防决策, 但临床实践中仍需结合其他客观指标进行综合评估。

D-dimer(D-二聚体)是交联纤维蛋白(cross-linked fibrin)经纤溶酶降解后产生的特异性小分子片段, 是反映血栓形成与溶解过程的关键生物标志物。本研究中, 术后1 ~ 3 d患者D-dimer水平与VTE发生显著相关, D-dimer每升高1 mg/L, VTE发生风险增加17.7%(OR=1.177, 95% CI: 1.029~1.346)。术后D-dimer水平升高作为VTE的预测指标已被多项研究证实, 但其阈值在不同人群中存在差异[43-44]。此外, 有研究显示妇科手术前D-dimer 1.5 mg/L亦可用于预测VTE, 敏感度为87.5%, 特异度为93.8%[45]。本研究进一步分析显示, 术后D-dimer 1.50 mg/L时约登指数最高, 为最佳预测阈值; VTE组患者术前后D-dimer升高幅度亦显著大于非VTE组, 术后升高2.50 mg/L提示VTE风险增高。然而, 术后D-dimer及术前后差值的AUC分别为0.663和0.632, 判别能力中等偏低。以D-dimer 1.50 mg/L为阈值时特异性较高(73.58%)但灵敏度偏低(54.76%), 提示有近半数VTE患者可能漏诊; 而D-dimer差值2.50 mg/L虽特异性高达94.72%, 但灵敏度仅26.19%, 不适宜作为普适筛查指标。综上, D-dimer单项指标可作为高危信号用于识别需紧急干预的患者, 但不宜作为独立诊断工具。临床实践中应警惕D-dimer≥1.50 mg/L的风险信号, 对差值显著升高者及时干预, 未来研究应探索将D-dimer动态变化与其他危险因素整合, 以构建更适合妇科患者的VTE风险预测模型。

值得注意的是, 本研究中单因素分析显示VTE组Caprini评分高于非VTE组, 但多因素logistic回归分析未显示其与术后VTE风险存在统计学关联(OR=1.026, 95% CI: 0.737~1.430, *P*=0.877)。究其原因, 可能与本研究所纳入患者Caprini评分均≥3分、均为中危及以上风险有关, 基线VTE风险本身处于相对较高且狭窄的范围, 限制了评分的区分效能。尽管如此, 单因素分析中VTE组评分仍显著高于非VTE组, 提示Caprini评分在中高危人群中仍具一定的风险分层能力; 但在多因素模型中, 年龄、BMI等评分构成条目被作为独立变量纳入后, Caprini评分的额外预测贡献有限。此外, 本研究发现高血压、绝经状态、麻醉时间、ASA分级及术后D-dimer水平等Caprini评分未涵盖的因素亦与VTE发生相关。2017年《妇科手术后深静脉血栓形成及肺栓塞预防专家共识》提出的G-Caprini(Gynecological Caprini)评分体系, 纳入了“年龄≥50岁、高血压、静脉曲张、手术时间≥3 h、术后卧床时间≥48 h、开腹手术”6项妇科手术后DVT独立危险因素[46]。本研究在上述因素之外, 还发现绝经状态、麻醉时间、ASA分级及术后D-dimer水平等因素对VTE发生亦有较大影响。因此, 建议在妇科手术患者中探索建立更具针对性的VTE风险评估模型, 以指导更加精准的个体化预防策略。

本研究通过回顾性分析307例妇科手术患者资料, 明确了年龄、BMI、绝经状态、麻醉时间、手术时间、ASA分级及术后D-dimer水平为术后VTE的独立危险因素, 并量化了各因素的风险效应。本研究为单中心设计, 所有手术由同一位术者完成, 有效控制了手术技术差异。但本研究亦存在一定局限性: 回顾性设计可能导致选择偏倚和信息偏倚; 单中心样本限制结果的外推性; 未纳入的混杂因素可能影响因果推断; 样本量有限, 可能不足以检测出效应较小的风险差异。未来应开展多中心、大样本前瞻性研究, 进一步验证和完善妇科患者VTE风险预测模型。

妇科患者术后VTE的发生与年龄增长、BMI升高、绝经状态、高血压、手术时间延长、麻醉时间延长及ASA分级升高显著相关, 其中绝经状态与ASA分级对VTE风险的贡献尤为突出。高龄、肥胖、绝经后、合并高血压且全

身状况较差(ASA≥Ⅲ级)的患者为VTE高危人群,应予重点防控。术后24~72 h的D-dimer水平是VTE的有效诊断指标,以1.50 mg/L为阈值时诊断效能最优。现有Caprini评分在本研究人群中预测价值有限,建议整合绝经状态、高血压等风险因素构建妇科专属VTE风险评估模型。针对高危患者,临床可动态监测D-dimer水平、优化手术流程以缩短时间,并及早采取预防措施。

* * *

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