

## · 临床研究 ·

# 北京协和医院外科老年患者术后静脉血栓栓塞症流行病学调查

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**【摘要】 目的** 调查北京协和医院外科老年患者术后静脉血栓栓塞症(VTE)的流行病学资料, 寻找老年患者术后发生VTE的危险因素。**方法** 回顾性分析2016年5月至7月在北京协和医院接受手术的4 819例患者的临床资料, 收集患者的基本信息、术后及出院后3个月内症状性VTE的发生及预防情况。根据年龄将患者分为老年组(≥65岁, 925例)和中青年组(<65岁, 3 894例), 比较2组的VTE发生、预防情况以及发生VTE相关危险因素的差异。采用SPSS 26.0软件进行数据分析。根据数据类型, 组间比较分别采用t检验、U检验、χ<sup>2</sup>检验及方差分析。**结果** 老年组和中青年组患者术后VTE的发病率分别为2.59%(24/925)、0.33%(13/3 894), 老年组VTE的发病风险约为中青年组的8倍( $RR = 7.952, 95\% CI 4.033 \sim 15.678, P < 0.001$ )。神经外科老年患者的VTE发病率最高(16.67%, 4/24), 且显著高于其他科室( $P = 0.003$ )。老年组有19项危险因素占比显著高于中青年组( $P < 0.01$ ), 其中占比最多的前3项危险因素分别为大手术(>45 min)、恶性肿瘤和肥胖(体质量指数>25 kg/m<sup>2</sup>)。多因素logistic回归分析显示下肢肿胀、当前吸烟和手术时间>2 h是老年患者术后发生VTE的独立危险因素( $P < 0.05$ )。老年高危人群使用机械预防和药物预防的比例均高于中青年高危人群[51.42%(399/776)和39.21%(567/1446),  $P < 0.001$ ; 31.44%(244/776)和20.95%(303/1446),  $P < 0.001$ ]。老年VTE患者中, 有70.83%(17/24)发病前未接受药物预防, 58.33%(14/24)仅接受机械预防仍发生症状性VTE。**结论** 老年外科手术患者术后VTE发病率高于中青年患者, 对于合并下肢肿胀、当前吸烟和手术时间>2 h的老年患者应加强围手术期VTE药物预防。

**【关键词】** 老年人; 外科; 静脉血栓栓塞症; 发病率; 危险因素; 预防

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## Epidemiological investigation of postoperative venous thromboembolism in elderly patients in Peking Union Medical College Hospital

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**【Abstract】 Objective** To investigate the epidemiological data of postoperative venous thromboembolism (VTE) in elderly surgical patients in Peking Union Medical College Hospital in order to explore the risk factors for the disease. **Methods** Clinical data of 4 819 patients who underwent surgery in Peking Union Medical College Hospital from May 2016 to July 2016 were collected and retrospectively analyzed. Their baseline information, and VTE prophylaxis and incidence of symptomatic VTE after the operation and in 3 months after discharge were recorded. According to their age, the patients were divided into the elderly group ( $\geq 65$  years old,  $n=925$ ) and the young and middle-age group ( $<65$  years old,  $n=3 894$ ). The differences in the occurrence and prevention of VTE were compared between the 2 groups, and the risk factors related to the occurrence of VTE were analyzed. SPSS statistics 26.0 was used for statistical analysis. Student's  $t$  test, U test, Chi-square test or Fisher exact test was employed for intergroup comparison depending on different date types. **Results** The incidence of postoperative VTE was 2.59% (24/925) in the elderly group and 0.33% (13/3 894) in the young and middle-age group, with the incidence in the elderly group about 8 times higher than that in the young and middle-age group ( $RR = 7.952, 95\% CI: 4.033 \sim 15.678, P < 0.001$ ). The incidence in the department of neurosurgery was the highest (16.67%, 4/24), significantly higher than that in other departments ( $P = 0.003$ ). The proportion of 19 risk factors in the elderly group was obviously higher

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than that in the young and middle-age group, and the most-accounted top 3 risk factors were major surgery ( $>45$  min), malignancy, and obesity (body mass index $>25$  kg/m $^2$ ). Multivariate logistic regression analysis showed that swollen legs, current smoking, and duration of surgery  $>2$  h were independent risk factors for postoperative VTE in elderly patients ( $P<0.05$ ). The proportions of receiving mechanical prophylaxis and pharmacologic prophylaxis for high-risk patients were statistically higher in the elderly group than the young and middle-age group [51.42% (399/776) vs 39.21% (567/1446),  $P<0.01$ ; 31.44% (244/776) vs 20.95% (303/1446),  $P<0.01$ ]. Among the elderly patients with VTE, 70.83% (17/24) did not receive pharmacologic prophylaxis before onset, and 58.33% (14/24) only received mechanical prophylaxis, but still had symptomatic VTE. **Conclusion** The incidence of postoperative VTE is high in elderly patients than the young and middle-age ones. Physicians should strengthen perioperative pharmacologic prophylaxis for VTE to the elderly patients with swollen legs, current smoking or duration of surgery  $>2$  h.

**[Key words]** aged; surgery; venous thromboembolism; incidence; risk factors; prophylaxis

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静脉血栓栓塞症(venous thromboembolism, VTE)包括深静脉血栓形成(deep vein thrombosis, DVT)和肺血栓栓塞症(pulmonary thromboembolism, PTE),是外科手术患者常见的术后并发症和围手术期死亡的重要原因之一<sup>[1]</sup>。未经预防的内外科患者中DVT的发病率高达约10%~40%,PTE与约10%的住院患者死亡有关<sup>[2]</sup>。VTE的发生与多种因素相关,其中手术和高龄是重要的危险因素<sup>[3]</sup>。有研究报道,随着年龄的增加VTE的发病率呈指数增长<sup>[4]</sup>。随着老龄化的进展,VTE的发病率也在逐渐升高<sup>[5]</sup>。合理的预防可降低VTE的发病率、死亡率及医疗费用<sup>[6]</sup>。因此,早期识别具有发生VTE高风险的患者进行预防十分重要。目前对外科患者术后VTE的危险因素研究虽较多,但针对老年患者的危险因素研究仍很少<sup>[7,8]</sup>。本研究旨在调查北京协和医院外科手术患者VTE的流行病学资料,分析老年患者术后VTE的临床特征,寻找老年患者术后发生VTE的危险因素,为临床制定VTE预防策略提供帮助。

## 1 对象与方法

### 1.1 研究对象

连续纳入2016年5月至7月在北京协和医院手术科室住院接受手术的患者。纳入标准:(1)年龄 $\geqslant 18$ 周岁;(2)住院时间 $\geqslant 2$  d;(3)在基本外科、肝脏外科、泌尿外科、妇科、乳腺外科、神经外科、心脏外科、胸外科、血管外科、整形美容外科及骨科接受手术治疗的患者。

排除标准:(1)入院时或手术前已确诊为VTE的患者;(2)入院疾病需要并且给予治疗性抗凝(如用低分子肝素治疗急性心肌梗死等),但不包括住院期间发生的症状性VTE;(3)信息缺失。多次入院的

患者选择第1次符合纳入排除标准的病历记录。

依据世界卫生组织标准,将患者分为年龄 $\geqslant 65$ 岁的老年组和 $<65$ 岁的中青年组<sup>[9]</sup>。本研究已获得北京协和医院伦理委员会批准(B164)。

### 1.2 方法

回顾性收集患者的一般资料,包括年龄、性别、体质量指数(body mass index,BMI)、科室、住院时间及慢性基础疾病等;患者住院期间及出院后3个月内的症状性VTE发生情况。收集2005年Caprini风险评估模型中的危险因素<sup>[10]</sup>,包括病史相关因素:VTE史、VTE家族史、恶性肿瘤、急性心肌梗死、炎症性肠病史、肝素诱发的血小板减少症、慢性阻塞性肺病以及1个月内的脓毒症、严重肺部疾病、充血性心力衰竭、脑卒中、急性脊髓损伤、髋部或骨盆或下肢骨折;手术相关因素:时长、类型及1个月内的既往大手术史;实验室检查指标:狼疮抗凝物、抗心磷脂抗体及血清同型半胱氨酸;女性独有的因素:口服避孕药或激素替代疗法、妊娠或产后状态( $<1$ 个月)及不明原因的习惯性流产史( $\geqslant 3$ 次);其他:卧床 $>72$  h、石膏固定( $<1$ 个月)、中心静脉通路、下肢肿胀及静脉曲张。以及文献报道与VTE发生相关的危险因素,包括机械通气<sup>[11]</sup>、使用糖皮质激素治疗<sup>[12]</sup>、输血<sup>[13]</sup>以及吸烟状态(当前吸烟定义为戒烟时间 $<1$ 个月)<sup>[14]</sup>。收集患者的VTE预防信息,包括机械预防和抗凝药物预防。根据第9版美国胸科医师学会(American College of Chest Physicians, ACCP)推荐的VTE预防指南,Caprini评分为0分的患者为极低危组;1~2分为低危组;3~4分为中危组; $\geqslant 5$ 分为高危组<sup>[15,16]</sup>。

### 1.3 统计学处理

使用SPSS 26.0软件进行统计学处理。符合

正态分布的计量资料采用均数±标准差( $\bar{x} \pm s$ )表述,2组间比较采用t检验,多组间比较采用单因素方差分析;不符合正态分布的计量资料采用中位数(四分位数间距)[ $M(Q_1, Q_3)$ ]表述,组间比较采用Mann-Whitney U检验。计数资料用例数(百分率)表示,组间比较采用 $\chi^2$ 检验或Fisher精确检验。采用单因素及多因素logistic回归分析评估与VTE发生相关的危险因素。 $P < 0.05$ 为差异有统计学意义。

## 2 结果

### 2.1 基线信息

本研究共纳入患者4884例,排除入院时或手术前已确诊为VTE的患者30例;因急性心肌梗死入院给予低分子肝素治疗性抗凝的患者1例;手术时间缺失患者34例,最终纳入分析患者4819例。其中男性1474例,女性3345例,平均年龄( $50.0 \pm 15.3$ )岁。老年组患者925例,中青年组患者3894例。老年组的年龄、BMI、住院时间以及慢性基础疾病患病率均大于中青年组,差异均有统计学意义( $P < 0.001$ ;表1)。

### 2.2 VTE发病情况

老年组有2.59%(24/925)发生症状性VTE,其中19例发生于住院期间(DVT患者16例,DVT合并PTE患者3例),DVT发生于出院后3个月患者5例,发生VTE的中位时间为术后3(2.00,14.75)d。中青年组有0.33%(13/3894)发生症状性VTE,其中11例发生于住院期间(DVT患者10例,PTE患者1例),DVT发生于出院后3个月患者2例,发生VTE的中位时间为术后6(2.5,7.0)d。老年组VTE的发病风险高于中青年组,差异有统计学意义( $RR = 7.952, 95\% CI 4.033 \sim 15.678; P < 0.001$ )。

### 2.3 VTE发病年龄分布

按年龄<45岁、45岁≤年龄<65岁、65岁≤年龄<85岁、年龄≥85岁将患者分为4组,每组VTE

发病率分别为0.22%(4/1856)、0.44%(9/2038)、2.56%(23/897)及3.57%(1/28),可见VTE发病率随年龄增加呈增长趋势,各年龄段VTE发病率比较,差异均有统计学意义(均 $P < 0.001$ )。

### 2.4 各科室老年患者比例及老年VTE发生情况

在纳入研究的11个科室中,神经外科、妇科的老年患者比例较少,但老年患者VTE发病率较高,分别为16.67%(4/24)、6.52%(6/92),其中神经外科的老年患者VTE发病率显著高于其他科室,差异有统计学意义( $P = 0.003$ ;图1)。神经外科老年患者均未接受药物预防,机械预防的比例也低于其他外科手术患者[37.50%(9/24)和45.50%(410/901), $P = 0.437$ ]。

### 2.5 2组患者VTE预防情况

老年组接受预防的比例显著高于中青年组[59.03%(546/925)和23.96%(933/2961), $P < 0.001$ ]。按Caprini评分进行危险分层后,全部高危人群药物预防率为24.62%(547/2222),机械预防率为43.47%(966/2222)。与中青年组高危人群相比,老年组高危人群使用机械预防[51.42%(399/776)和39.21%(567/1446)]及药物预防[31.44%(244/776)和20.95%(303/1446)]的比例均显著增加( $P < 0.001$ )。

37例VTE患者中,72.97%(27/37)发病前未接受药物预防;51.35%(19/37)仅接受机械预防仍发生症状性VTE。老年组24例VTE患者中,70.83%(17/24)在发病前未接受药物预防;58.33%(14/24)仅接受机械预防仍发生症状性VTE。

### 2.6 2组患者VTE相关危险因素比较

老年组有19项危险因素的比例显著高于中青年组,所有危险因素中占比最多的前3项为大手术(>45 min)、恶性肿瘤和肥胖( $BMI > 25 \text{ kg/m}^2$ ),这些危险因素老年组均高于中青年组,差异均有统计学意义(均 $P < 0.01$ ;表2)。

表1 老年组与中青年组患者基线信息

Table 1 Baseline characteristics of patients in two groups

Item	Total( $n = 4819$ )	Elderly group( $n = 925$ )	Young and middle-age group( $n = 3894$ )	$P$ value
Age (years, $\bar{x} \pm s$ )	50.02 ± 15.32	72.09 ± 5.70	44.77 ± 11.80	<0.001
Male[ $n$ (%)]	1474(30.59)	422(45.62)	1052(27.02)	<0.001
BMI( $\text{kg}/\text{m}^2$ , $\bar{x} \pm s$ )	23.85 ± 3.55	24.36 ± 3.26	23.73 ± 3.61	<0.001
Duration of hospitalization[d, $M(Q_1, Q_3)$ ]	7(4,11)	10(6,15)	6(4,10)	<0.001
Chronic underlying diseases[ $n$ (%)]				
Hypertension	1089(22.60)	478(51.68)	611(15.69)	<0.001
Diabetes mellitus	488(10.13)	222(24.00)	266(6.83)	<0.001
Coronary heart disease	218(4.52)	140(15.14)	78(2.00)	<0.001

BMI: body mass index.

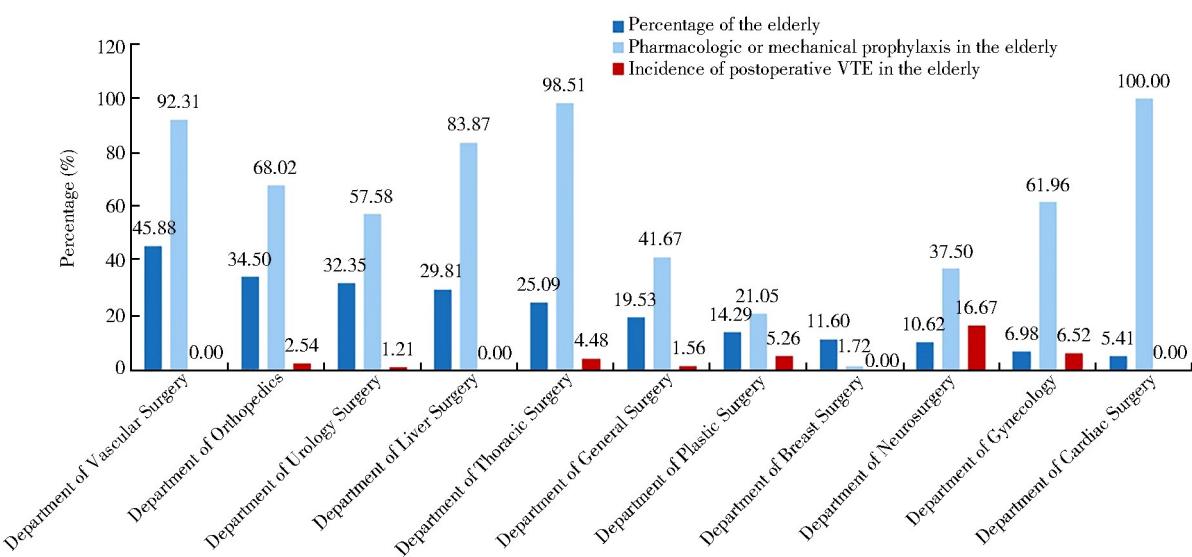


图1 不同科室的老年患者比例以及老年患者预防和发生VTE的情况

Figure 1 Proportion of elderly patients in different departments and prophylaxis and incidence of venous thromboembolism in the elderly group  
VTE: venous thromboembolism.

表2 老年组与中青年组VTE危险因素差异

Table 2 Comparison of factors associated with VTE between two groups

[n (%)]

Item	Total (n = 4 819)	Elderly group (n = 925)	Young and middle-age group (n = 3 894)	P value
Major surgery (>45 min)	3 371 (69.95)	688 (74.38)	2 683 (68.90)	0.001
Malignancy (present or previous)	1 790 (37.14)	454 (49.08)	1 336 (34.31)	<0.001
Obesity (BMI>25 kg/m <sup>2</sup> )	1 631 (33.85)	347 (37.51)	1 284 (32.97)	0.009
Smoking (present or previous)	726 (15.07)	194 (20.97)	532 (13.66)	<0.001
Confined to bed (>72 h)	575 (11.93)	189 (20.43)	386 (9.91)	<0.001
Mechanical ventilation	302 (6.27)	138 (14.92)	164 (4.21)	<0.001
Blood transfusion	344 (7.14)	116 (12.54)	228 (5.86)	<0.001
Current smoking	474 (9.84)	100 (10.81)	374 (9.60)	0.268
Central venous access	249 (5.17)	81 (8.76)	168 (4.31)	<0.001
Elective major lower extremity arthroplasty	125 (2.59)	68 (7.35)	57 (1.46)	<0.001
Glucocorticoid treatment	335 (6.95)	65 (7.03)	270 (6.93)	0.920
Elevated serum homocysteine	91 (1.89)	49 (5.30)	42 (1.08)	<0.001
Swollen legs (current)	78 (1.62)	32 (3.46)	46 (1.18)	<0.001
Serious lung disease (<1 month)	55 (1.14)	28 (3.03)	27 (0.69)	<0.001
Hip, pelvis or leg fracture (<1 month)	42 (0.87)	28 (3.03)	14 (0.36)	<0.001
Congestive heart failure (<1 month)	38 (0.79)	21 (2.27)	17 (0.44)	<0.001
History of prior major surgery (<1 month)	63 (1.31)	18 (1.95)	45 (1.16)	0.057
History of VTE	38 (0.79)	15 (1.62)	23 (0.59)	0.001
Sepsis (<1 month)	31 (0.64)	13 (1.41)	18 (0.46)	0.001
Varicose veins	35 (0.73)	13 (1.41)	22 (0.56)	0.007
Stroke (<1 month)	20 (0.42)	9 (0.97)	11 (0.28)	0.007
Chronic obstructive pulmonary disease	16 (0.33)	8 (0.86)	8 (0.21)	0.005
Immobilizing plaster cast (<1 month)	32 (0.66)	7 (0.76)	25 (0.64)	0.699
Multiple trauma (<1 month)	25 (0.52)	4 (0.43)	21 (0.54)	1.000
Acute myocardial infarction	6 (0.12)	3 (0.32)	3 (0.08)	0.089
Acute spinal cord injury (<1 month)	8 (0.17)	2 (0.22)	6 (0.15)	0.645
History of inflammatory bowel disease	10 (0.21)	2 (0.22)	8 (0.21)	1.000
Heparin-induced thrombocytopenia	1 (0.02)	1 (0.11)	0 (0.00)	0.192
Oral contraceptives or hormone replacement therapy	128 (2.66)	0 (0.00)	128 (3.29)	<0.001
Pregnancy or postpartum (<1 month)	90 (1.87)	0 (0.00)	90 (2.31)	<0.001
Positive lupus anticoagulant	4 (0.08)	0 (0.00)	4 (0.10)	1.000
Recurrent spontaneous abortion (≥ 3)	2 (0.04)	0 (0.00)	2 (0.05)	1.000
Family history of thrombosis	1 (0.02)	0 (0.00)	1 (0.03)	1.000
Elevated anticardiolipin antibodies	1 (0.02)	0 (0.00)	1 (0.03)	1.000

VTE: venous thromboembolism; BMI: body mass index.

## 2.7 老年手术患者发生VTE的危险因素分析

分析老年患者术后发生VTE的危险因素时,将单因素logistic回归中 $P<0.05$ 的因素纳入多因素logistic回归模型中,结果显示下肢肿胀、当前吸烟和手术时间>2 h是老年患者术后发生VTE的独立危险因素( $P<0.05$ ;表3)。

## 3 讨论

本研究结果显示外科患者术后VTE的发病率为0.77%(37/4 189),其中老年患者术后VTE的发病率为2.59%(24/925),高于亚洲最大术后VTE发病率流行病学研究报道(0.71%,7 025/993 459)<sup>[17]</sup>,也高于我国多中心DissolVE-2研究报道的外科患者VTE发病率(0.3%;95%CI 0.2~0.5)<sup>[7]</sup>。

分析老年患者术后VTE发病率较高的原因有以下几方面。首先高龄本身是VTE的危险因素,由于血管退行性改变、肌张力下降等原因,老年患者静脉血液流速下降,因此易导致VTE的发生<sup>[18]</sup>。其次老年患者常合并较多其他VTE的危险因素,本研究老年患者共有19项危险因素比例显著高于中青年患者,并且占比最多的危险因素大手术、恶性肿瘤及肥胖等在老年患者中的比例显著高于中青年患者,因此VTE的发病率较高。

合理预防可以降低VTE的发病率,ACCP指南建议没有高出血风险的情况下所有高危手术患者均应给予药物预防<sup>[15,16]</sup>。本研究中老年高危患者仅31.44%接受药物预防,而国外多中心AVAIL ME研究显示,外科高危患者的药物预防比例为56.9%<sup>[19]</sup>,说明还需加强对围手术期高危老年患者的药物预防。本研究大部分老年VTE患者接受了机械预防,但仍发生症状性VTE,表明单用机械预防对于老年患者VTE的预防效果不佳。机械预防

对于外科手术患者术后VTE的预防效果仍存在争议,有研究表明机械预防的效果不如药物预防,在药物预防的基础上增加机械预防并不能进一步降低VTE的发病率<sup>[20]</sup>。

本研究中神经外科老年患者占比较少但VTE发病率最高,原因可能为预防比例较低。推测神经外科患者由于存在较高的颅内出血风险,导致药物预防率低。美国血液学会2019年VTE管理指南推荐对于接受重大神经外科手术的患者不常规使用药物预防措施,可以使用机械预防,对于大出血风险较低的高风险患者可以考虑进行药物预防<sup>[1]</sup>。一篇meta分析结果显示在接受神经外科手术的患者中,药物预防可有效预防无症状近端DVT的发生( $RR=0.50,95\%CI 0.30\sim0.84$ ;低确定性),而对于患者死亡率、症状性PTE、无症状远端DVT、再次手术和出血风险等重要结局的影响却非常不确定<sup>[21]</sup>。因此神经外科患者特别是老年患者如何平衡术后出血及血栓形成风险,选择何种VTE预防措施,值得进一步探讨。

本研究结果显示,下肢肿胀和当前吸烟是外科老年患者术后发生VTE的独立危险因素。下肢肿胀是VTE的临床表现之一,此外下肢肿胀会阻碍血液循环,造成血液瘀滞而促进VTE形成<sup>[22]</sup>。一项meta分析结果表明与从未吸烟的患者相比,当前吸烟的患者发生VTE的风险比为1.23(95%CI 1.14~1.33),吸烟与血浆纤维蛋白原及纤溶酶原激活物抑制物1升高有关,因此易导致VTE的发生<sup>[14]</sup>。

Caprini风险评估模型将手术时间>45 min定义为大手术,并赋予其2分<sup>[10]</sup>,本研究中多因素分析显示手术时间>2 h是老年患者术后发生VTE的独立危险因素,与一项骨科关节置换术后发生VTE危险因素的meta分析结果一致<sup>[23]</sup>。2010年改良的Caprini风险评估模型将手术时间<1 h、2~3 h和>3 h赋予不同的分

表3 老年组发生VTE的危险因素logistic回归分析

Table 3 Logistic regression analysis of VTE events in elderly patients

Risk factor	VTE group (n=24)	Non-VTE group (n=901)	Univariate analysis		Multivariate analysis	
	[n (%)]	[n (%)]	OR(95%CI)	P value	OR(95%CI)	P value
Swollen legs	6(25.00)	27(3.00)	11.218(4.115~30.582)	<0.001	8.611(2.619~28.316)	<0.001
Current smoking	6(25.00)	94(10.43)	2.862(1.109~7.387)	0.030	3.697(1.300~10.518)	0.014
Duration of surgery >2 h	18(75.00)	353(39.18)	4.793(1.763~13.034)	0.002	3.700(1.289~10.617)	0.015
History of prior major surgery(<1 month)	3(12.50)	15(1.66)	8.438(2.270~31.366)	0.010	5.268(0.908~30.572)	0.064
Blood transfusion	8(33.33)	108(11.99)	3.671(1.535~8.782)	0.003	1.038(0.318~3.394)	0.951
Confined to bed(>72 h)	10(41.67)	179(19.87)	2.881(1.259~6.593)	0.012	1.514(0.564~4.065)	0.411
Mechanical ventilation	9(37.50)	129(14.32)	3.591(1.539~8.377)	0.003	1.532(0.502~4.669)	0.453
Glucocorticoid treatment	5(20.83)	60(6.66)	3.689(1.331~10.223)	0.012	2.750(0.852~8.875)	0.091
Stroke(<1 month)	2(8.33)	7(0.78)	11.610(2.281~59.104)	0.003	2.260(0.253~20.190)	0.465
Multiple trauma(<1 month)	1(4.17)	3(0.33)	13.014(1.304~129.900)	0.029	12.441(0.433~357.128)	0.141
Sepsis(<1 month)	2(8.33)	11(1.22)	7.355(1.538~35.174)	0.012	1.476(0.147~14.825)	0.741
Serious lung disease(<1 month)	3(12.50)	25(2.77)	5.006(1.401~17.885)	0.013	1.358(0.239~7.707)	0.729
Central venous access	5(20.83)	76(8.44)	2.857(1.038~7.865)	0.042	0.800(0.203~3.151)	0.750

VTE: venous thromboembolism.

值<sup>[24]</sup>,但有研究表明与2010年的模型相比,2005年的Caprini风险评估模型能更有效地进行VTE风险分层<sup>[25]</sup>。因此Caprini风险评估模型中手术时间是否需要修订,尚需更大规模临床研究验证。

综上,北京协和医院外科老年患者术后VTE发病率较高,发病率随年龄呈增长趋势。下肢肿胀、当前吸烟和手术时间>2 h是老年患者术后发生VTE的独立危险因素,且高危患者VTE抗凝药物预防率较低,临床仍需加大对VTE的预防措施。

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