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· 专题研究 ·

Caprini 血栓风险评估量表对脓毒症伴静脉血栓栓塞症高危患者预防性抗凝的指导价值研究

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【摘要】 背景 脓症患者易并发静脉血栓栓塞症(VTE), 而该类患者是否需接受预防性抗凝及其风险、获益目前国内外均无定论, 且针对脓症患者并发VTE的风险评估方法尚缺乏共识且研究较少。目的 探讨Caprini血栓风险评估量表对脓毒症伴VTE高危患者预防性抗凝的指导价值。方法 回顾性选取2017—2019年西安交通大学第二附属医院急诊重症监护室(EICU)收治的脓症患者65例, 均经Caprini血栓风险评估量表评估为VTE高危。根据不同的治疗措施将所有患者分为对照组35例和观察组30例; 另根据VTE发生情况将所有患者分为VTE组10例和无VTE组55例。比较观察组、对照组患者治疗期间VTE、出血发生情况及EICU住院时间、总住院时间; 比较VTE组、无VTE组临床资料。采用多因素Logistic回归分析探讨脓症患者并发VTE的影响因素。结果 观察组患者VTE发生率低于对照组, EICU住院时间、总住院时间短于对照组($P<0.05$); 两组患者出血发生率比较, 差异无统计学意义($P>0.05$)。VTE组患者年龄大于无VTE组, 急性生理学及慢性健康状况评分系统II(APACHE II)评分、序贯器官衰竭估计评分(SOFA)及Caprini血栓风险评估量表评分高于无VTE组, 预防性抗凝治疗率低于无VTE组($P<0.05$)。多因素Logistic回归分析结果显示, Caprini血栓风险评估量表评分 [$OR=16.639$, $95\%CI(2.173, 127.440)$]、预防性抗凝 [$OR=0.005$, $95\%CI(0, 0.380)$] 是脓症患者并发VTE的影响因素($P<0.05$)。结论 Caprini血栓风险评估量表评分越高, 脓症患者VTE发生风险越高; 对于Caprini血栓风险评估量表评估为VTE高危的脓症患者实施预防性抗凝可降低VTE发生率, 并可缩短患者住院时间且不增加出血风险, 故该量表可用于评估并指导脓毒症伴VTE高危患者的预防性抗凝。

【关键词】 脓毒症; 静脉血栓栓塞症; Caprini血栓风险评估量表; 预防性抗凝

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Guidance Value of Caprini Thrombus Risk Assessment Scale for Prophylactic Anticoagulation in Sepsis Patients with High Risk of VTE

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【Abstract】 **Background** Sepsis patients are prone to venous thromboembolism (VTE). Whether to receive prophylactic anticoagulant therapy and its risks and benefits are still uncertain at home and abroad. Moreover, there is a lack of consensus but also only few studies on the risk assessment methods for sepsis patients complicated with VTE. **Objective** To investigate the guidance value of Caprini Thrombus Risk Assessment Scale for prophylactic anticoagulation in sepsis patients with high risk of VTE. **Methods** A total of 65 patients with sepsis admitted to EICU of the Second Affiliated Hospital of Xi'an Jiaotong University from 2017 to 2019 were retrospectively selected, whose VTE risk were assessed as high risk according to Caprini Thrombus Risk Assessment Scale. They were divided into control group (35 cases) and observation group (30 cases) according to different treatment measures, and divided into VTE group (10 cases) and non VTE group (55 cases) according to incidence of VTE. Incidence of VTE and bleeding, EICU hospitalization time and total hospitalization time were compared between the control group and the observation group; clinical data of VTE group and non VTE group were

also compared. Multivariate Logistic regression analysis was used to analyze the influencing factors of VTE in sepsis patients.

Results The incidence of VTE in observation group was lower than that in control group, the EICU hospitalization time and total hospitalization time in observation group were shorter than those in control group ($P < 0.05$); there was no significant difference in incidence of bleeding between the two groups ($P > 0.05$). The age in VTE group was older than that in non VTE group, APACHE II score, SOFA and Caprini Thrombus Risk Assessment Scale score in VTE group were higher than those in non VTE group, prophylactic anticoagulation treatment rate in observation group was lower than that in non VTE group ($P < 0.05$). Multivariate Logistic regression analysis showed that, Caprini Thrombus Risk Assessment Scale score [$OR = 16.639$, 95%CI (2.173, 127.440)] and the prophylactic anticoagulation [$OR = 0.005$, 95%CI (0, 0.380)] were the influencing factors of VTE in patients with sepsis ($P < 0.05$). **Conclusion** The higher of Caprini Thrombus Risk Assessment Scale score, the higher risk of VTE in patients with sepsis. For sepsis patients with high risk of VTE assessed by Caprini Thrombus Risk Assessment Scale, prophylactic anticoagulation can reduce the incidence of VTE, shorten hospitalization time, but do not increase the risk of bleeding. Therefore, Caprini Thrombus Risk Assessment Scale can be used to evaluate and guide the prophylactic anticoagulation for sepsis patients with high risk of VTE.

【Key words】 Sepsis; Venous thromboembolism; Caprini thrombus risk assessment scale; Prophylactic anticoagulation

脓毒症患者血液多呈高凝状态, 易导致静脉血栓栓塞症 (venous thromboembolism, VTE) 或弥散性血管内凝血 (disseminated intravascular coagulation, DIC), 但针对该类患者是否需预防性抗凝及抗凝效果目前尚存在争议^[1-3]。对于 VTE 发生风险的评估, 指南多推荐 Padua 评分用于评估内科疾病患者、Caprini 血栓风险评估量表用于评估外科手术患者^[4-6], 但针对脓毒症患者尚缺乏合适的评估方法。另有研究指出, Caprini 血栓风险评估量表不仅对外科手术患者 VTE 发生风险具有较高的预测价值, 还可评估患者 VTE 风险分级^[7]。本课题组既往研究表明, Caprini 血栓风险评估量表评分与脓毒症患者急性生理学及慢性健康状况评分系统 II (Acute Physiology and Chronic Health Score System II, APACHE II) 评分及序贯器官衰竭估计评分 (Sequential Organ Failure Assessment, SOFA) 相关^[8]; 但 VTE 高危患者在接受抗凝治疗期间亦存在潜在的出血风险^[4-6], 且脓毒症并发 DIC 者也存在出血倾向^[2]。目前临床针对脓毒症伴 VTE 高危患者预防性抗凝评估的研究相对较少。本研究旨在探讨 Caprini 血栓风险评估量表对脓毒症伴 VTE 高危患者预防性抗凝的指导价值, 以为 Caprini 血栓风险评估量表在脓毒症患者中的应用提供参考, 现报道如下。

1 资料与方法

1.1 一般资料 回顾性选取 2017—2019 年西安交通大学第二附属医院急诊重症监护室 (EICU) 收治的脓症患者 65 例, 均符合《中国脓毒症/脓毒性休克急诊治疗指南 (2018)》^[9]

中的脓毒症诊断标准。纳入标准: (1) Caprini 血栓风险评估量表评分 ≥ 5 分, 即 VTE 高危, Caprini 血栓风险评估量表评分参考文献 [4-5, 7]; (2) 依据《肺血栓栓塞症诊治与预防指南》^[4]、《医院内静脉血栓栓塞症防治与管理建议》^[5] 评估患者具有出血危险因素; (3) 年龄 ≥ 18 岁; (4) 入院 48 h 内启动 VTE 预防措施。排除标准: (1) 既往有免疫功能异常、凝血功能异常、血液系统疾病、血栓性疾病或血栓症病史者; (2) 近 2 周内曾接受抗血小板聚集、抗凝、溶栓或使用激素、免疫抑制剂治疗者; (3) 存在活动性出血者; (4) 合并心、肺、肝、肾等脏器功能不全者; (5) 合并肿瘤或结缔组织病者; (6) 妊娠期或哺乳期妇女; (7) 死亡、非医嘱转出 EICU 或非医嘱离院者; (8) 临床资料不全者。根据不同的治疗措施将所有患者分为对照组 35 例和观察组 30 例; 另根据 VTE 发生情况将所有患者分为 VTE 组 10 例和无 VTE 组 55 例。观察组、对照组患者性别、年龄、血小板计数、APACHE II 评分、SOFA、Caprini 血栓风险评估量表评分比较, 差异无统计学意义 ($P > 0.05$, 见表 1)。本研究经西安交通大学第二附属医院医学伦理委员会审核批准, 且患者及家属对本研究知情并签署知情同意书。

1.2 方法 对照组患者采用机械预防, 即给予双下肢气压治疗, 30 min/次, 2 次/d; 观察组患者采用依诺肝素 [商品名: 赛诺菲, 赛诺菲 (北京) 制药有限公司生产, 国药准字 J20180035] 预防性抗凝, 4 000 U, 1 次/d。

1.3 观察指标

表 1 两组患者一般资料比较

Table 1 Comparison of general information between the two groups

组别	例数	性别 (男/女)	年龄 ($\bar{x} \pm s$, 岁)	血小板计数 ($\bar{x} \pm s$, $\times 10^9/L$)	APACHE II 评分 ($\bar{x} \pm s$, 分)	SOFA ($\bar{x} \pm s$, 分)	Caprini 血栓风险评估量表 评分 [$M (P_{25}, P_{75})$, 分]
对照组	35	19/16	53.1 \pm 7.7	187.3 \pm 48.1	19.7 \pm 3.2	11.1 \pm 4.2	5 (5, 6)
观察组	30	16/14	55.1 \pm 7.6	192.3 \pm 47.1	20.3 \pm 3.1	11.0 \pm 4.0	5 (5, 7)
检验统计量值		0.006 ^a	-1.078	-0.423	-0.824	0.056	-0.430 ^b
P 值		0.939	0.285	0.674	0.413	0.955	0.667

注: ^a 为 χ^2 值, ^b 为 Z 值, 余为 t 值; APACHE II = 急性生理学及慢性健康状况评分系统 II, SOFA = 序贯器官衰竭估计评分

1.3.1 观察组、对照组患者治疗情况 比较观察组、对照组患者治疗期间VTE、出血发生情况及EICU住院时间、总住院时间。VTE包括深静脉血栓形成(deep venous thrombosis, DVT)和急性肺栓塞(acute pulmonary embolism, APE),其中DVT通过上下肢静脉加压彩色超声检查并依据《医院内静脉血栓栓塞症防治与管理建议》^[5]进行诊断;APE通过CT肺动脉血管造影并依据《肺血栓栓塞症诊治与预防指南》^[4]进行诊断。出血部位包括皮肤黏膜、口腔黏膜、消化道、呼吸道、泌尿系等。总住院时间指从入院至医嘱出院的时间。

1.3.2 VTE组、无VTE组临床资料 收集两组患者性别、年龄、血小板计数、APACHE II评分、SOFA、Caprini血栓风险评估量表评分、总住院时间及干预方法,以分析脓毒症患者并发VTE的危险因素。

1.4 统计学方法 采用SPSS 21.0统计学软件进行数据处理。符合正态分布的计量资料以($\bar{x} \pm s$)表示,方差齐组间比较采用两独立样本 t 检验,方差不齐组间比较采用 t' 检验;不符合正态分布的计量资料以 $M(P_{25}, P_{75})$ 表示,组间比较采用Mann-Whitney U 检验;计数资料以相对数表示,组间比较采用 χ^2 检验,理论频数 <5 时采用连续性校正;采用多因素Logistic回归分析探讨脓毒症患者并发VTE的危险因素。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 观察组、对照组患者VTE、出血发生情况及EICU住院时间、总住院时间比较 观察组患者VTE发生率低于对照组,EICU住院时间、总住院时间短于对照组,差异有统计学意义($P < 0.05$);两组患者出血发生率比较,差异无统计学意义($P > 0.05$,见表2)。

2.2 VTE组、无VTE组患者临床资料比较 VTE组患者年龄大于无VTE组,APACHE II评分、SOFA及Caprini血栓风险评估量表评分高于无VTE组,预防性抗凝治疗率低于无VTE组,差异有统计学意义($P < 0.05$);两组患者性别、血小板计数、总住院时间比较,差异无统计学意义($P > 0.05$,见表3)。

2.3 脓毒症患者并发VTE危险因素的多因素多因素Logistic回归分析 由于Caprini血栓风险评估量表包含年龄及与APACHE II、SOFA相近的多条项目,故仅选择Caprini血栓风险评估量表评分(赋值:实测值)、干预方法(赋值:机械预防=0,预防性抗凝=1)为自变量,VTE发生情况(赋值:无=0,有=1)为因变量,进行多因素Logistic回归分析,结果显示,Caprini血栓风险评估量表评分、预防性抗凝是脓毒

表2 观察组、对照组患者VTE、出血发生情况及EICU住院时间、总住院时间比较

Table 2 Comparison of incidence of VTE, bleed and EICU hospitalization time, total hospitalization time between observation group and control group

组别	例数	VTE [n(%)]	出血 [n(%)]	EICU住院 时间(d)	总住院 时间(d)
对照组	35	9(25.7)	4(11.4)	8.37 ± 1.35	14.43 ± 2.13
观察组	30	1(3.3)	2(6.7)	7.63 ± 1.40	11.80 ± 2.09
$\chi^2(t)$ 值		4.615	0.054	2.157 ^a	4.999 ^a
P 值		0.032	0.817	0.035	<0.001

注: ^a为 t 值;VTE=静脉血栓栓塞症,EICU=急诊重症监护室

症患者并发VTE的影响因素($P < 0.05$,见表4)。拟合方程为Logit(P) = -17.653 - 5.318 × 干预方法 + 2.812 × Caprini血栓风险评估量表评分。

表4 脓毒症患者并发VTE影响因素的多因素Logistic回归分析

Table 4 Multivariate Logistic regression analysis on influencing factors for VTE in patients with sepsis

变量	B	SE	Wald χ^2 值	P 值	OR(95%CI)
常量	-17.653	6.184	8.149	0.004	0(0, 0.004)
Caprini血栓风险评估量表评分	2.812	1.039	7.327	0.007	16.639(2.173, 127.440)
预防性抗凝	-5.318	2.219	5.741	0.017	0.005(0, 0.380)

3 讨论

脓毒症是因感染诱发全身炎症反应而导致脏器功能损伤的综合征,病情重,临床发病率、病死率均较高,严重者出现休克、多脏器功能衰竭等,因此救治难度大^[10-12]。脓毒症发生时,炎症反应系统被过度激活,进而导致血管内皮损伤并释放大量组织因子,致使机体凝血-纤溶系统失衡,进而致使血液处于高凝状态,可进一步诱发VTE或DIC,加重脏器功能损伤^[13-16]。因此,预防脓毒症患者高凝状态可能诱发的VTE或DIC对于控制疾病进展具有重要意义。然而,关于脓毒症伴VTE高危患者是否需接受预防性抗凝及其风险、获益目前国内外均无定论,且针对脓毒症患者并发VTE的风险评估方法也缺乏共识且研究较少,因此,本研究旨在探索Caprini血栓风险评估量表对脓毒症患者并发VTE的风险评估价值,并分析其可能的应用价值。

Caprini血栓风险评估量表是CAPRINI^[7]于2005年制定并于2009年再次修订的一种量表,量表内容的设计基于临床医学和循证医学,可将VTE风险进行量化并对患者VTE形成

表3 VTE组、无VTE组患者临床资料比较

Table 3 Comparison of clinical data between VTE group and non VTE group

组别	例数	性别 (男/女)	年龄 ($\bar{x} \pm s$, 岁)	血小板计数 ($\bar{x} \pm s$, $\times 10^9/L$)	APACHE II评分 ($\bar{x} \pm s$, 分)	SOFA ($\bar{x} \pm s$, 分)	Caprini血栓风险评估 量表评分 [$M(P_{25}, P_{75})$, 分]	总住院时间 ($\bar{x} \pm s$, d)	干预方法[n(%)]	
									机械预防	预防性抗凝
无VTE组	55	29/26	52.6 ± 7.2	193.0 ± 49.1	19.3 ± 2.9	10.1 ± 3.6	5(5, 6)	13.18 ± 2.65	26(47.3)	29(52.7)
VTE组	10	6/4	62.0 ± 4.2	171.2 ± 31.9	23.6 ± 1.9	16.1 ± 2.5	7(6, 8)	13.40 ± 1.17	9/10	1/10
检验统计量值		0.006 ^a	-3.976	1.344	-4.500	-5.043	-3.596 ^b	-0.257	4.615 ^a	
P 值		0.937	<0.001	0.184	<0.001	<0.001	<0.001	0.799	0.032	

注: ^a为 χ^2 值, ^b为 Z 值, 余为 t 值

风险进行分级（包括低危、中危、高危），每级均具备相应的预防建议^[17-19]。Caprini 血栓风险评估量表在多种疾病中应用的研究较多且其应用价值被肯定^[19-23]。本课题组既往研究表明，根据 Caprini 血栓风险评估量表的评估结果采取相应的预防措施，可有效缩短 EICU 患者住院时间、降低 VTE 发生率^[8]。但目前仍缺少针对脓毒症的专项研究。

本研究结果显示，观察组患者 VTE 发生率低于对照组，但两组患者出血发生率比较差异无统计学意义，可见根据 Caprini 血栓风险评估量表评估结果对脓毒症患者进行预防性抗凝的 VTE 发生率低于机械预防治疗，且并未增加患者出血风险，提示预防性抗凝较机械预防治疗脓毒症可更好地发挥 VTE 的预防作用；另外，Caprini 血栓风险评估量表评分、预防性抗凝是脓毒症患者并发 VTE 的影响因素，分析原因可能为 Caprini 血栓风险评估量表是依据 VTE 的高危因素设计而成，评分越高则表明患者 VTE 的危险因素越多，发生 VTE 的可能性越大，采取预防性抗凝的可能获益也就越大^[4-5]。

既往研究表明，脓毒症患者 DIC 发生率高达 35%^[24-25]。虽然目前临床针对脓毒症伴 DIC 是否需预防性抗凝尚无定论，但已有多项荟萃分析结果显示，预防性抗凝能够降低其病死率且不会增加出血风险^[26-27]。因此，本研究对脓毒症伴 VTE 高危患者进行预防性抗凝的同时是否发挥了预防 DIC 的作用还需进一步深入研究。本研究结果显示，观察组患者 EICU 住院时间、总住院时间短于对照组，可见接受预防性抗凝的脓毒症伴 Caprini 血栓风险评估量表评估为 VTE 高危患者，其 EICU 住院时间和总住院时间均短于接受机械预防者。另外，低分子肝素具有抗炎及缓解氧化应激反应的作用^[28-29]，可有效减轻脓毒症患者的炎症反应、改善微循环、延缓脏器功能损伤^[15]；并且低分子肝素也可改善患者的凝血功能，而凝血功能也与脓毒症患者预后相关^[30-31]，因此，应用低分子肝素预防 VTE 的同时可能通过上述作用改善了脓毒症患者病情并缩短了住院时间，但具体机制还需进一步研究。

综上所述，Caprini 血栓风险评估量表评分越高，脓毒症患者 VTE 发生风险越高，对于 Caprini 血栓风险评估量表评估为 VTE 高危的脓毒症患者实施预防性抗凝可降低 VTE 发生率，并可缩短患者住院时间且不增加出血风险，因此该量表对于脓毒症患者 VTE 风险评估及预防性抗凝具有一定的指导意义。但本研究为回顾性分析的小样本量、单中心研究，结果可能存在偏倚，后续可通过大样本量、多中心的队列研究探讨预防性抗凝是否可能对脓毒症患者 DIC 发生情况产生影响。

作者贡献：党晓燕、潘龙飞进行文章的构思与设计，研究的实施与可行性分析，结果的分析与解释，论文的修订；牛泽群、冯辉、张磊进行数据收集、整理、分析；党晓燕负责撰写论文；潘龙飞负责文章的质量控制及审校，并对文章整体负责、监督管理。

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