

· 临床研究 ·

心血管植入式电子装置导线相关静脉血栓形成的危险因素分析:112 例报告

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【摘要】 目的 研究心血管植入式电子装置(CIED)导线相关静脉血栓形成的相关危险因素,为临床预防提供理论依据。方法 选取2013年9月至2015年12月解放军总医院心血管内科使用CIED且随访资料完整的住院患者112例,根据术后血管超声检查结果进行分组,血栓组56例,年龄(71.86±8.35)岁;非血栓组56例,年龄(71.23±10.62)岁,运用多因素logistic回归分析对CIED导线相关静脉血栓形成的危险因素进行分析。结果 两组房颤患者数、植入除颤导线患者数、服用抗凝药物患者数和左室射血分数、全糖化血红蛋白水平以及手术中静脉穿刺次数、手术时间、导线数量相比较,差异均有统计学意义($P<0.05$)。多因素logistic回归分析表明,房颤、术中静脉穿刺次数、手术时间及导线数量是CIED导线相关静脉血栓形成的危险因素,服用抗凝药物是保护因素。结论 房颤、静脉穿刺次数、手术时间及导线数量是CIED导线相关静脉血栓形成的独立危险因素。

【关键词】 心血管植入式电子装置;深静脉血栓;危险因素;心血管疾病

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Risk factors for venous thrombosis related to the lead of cardiovascular implantable electronic device: an analysis of 112 cases

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【Abstract】 Objective To analyze the risk factors for venous thrombosis related to the lead of cardiovascular implantable electronic device (CIED) in order to provide the theoretical basis for clinical prevention. **Methods** A total of 112 patients undergoing CIED implantation and with full follow-up data who hospitalized in our department from September 2013 to December 2015 were recruited in this study. According to the results of postoperative vascular ultrasound examination, they were assigned to the thrombosis group [$n=56$, at an age of (71.86±8.35) years] and the non-thrombosis group [$n=56$, at an age of (71.23±10.62) years]. Their clinical data were collected and retrospectively analyzed. Multivariate logistic regression analysis was applied to assess the risk factors of the related venous thrombosis. **Results** There were significant differences in the numbers of patients with atrial fibrillation, those with implanted defibrillator leads and those taking anticoagulant medications, the left ventricular ejection fraction, the serum level of glycosylated hemoglobin, as well as the times of venipuncture, operation time, and lead numbers between the thrombosis and the non-thrombosis groups ($P<0.05$). Multivariate logistic regression analysis showed atrial fibrillation, times of venipuncture, operation time and lead numbers were the risk factors for the related venous thrombosis, and administration of anticoagulant medications was the protective factor. **Conclusion** Atrial fibrillation, times of venipuncture, operation time and lead numbers are the independent risk factors for venous thrombosis related to CIED leads.

【Key words】 cardiovascular implantable electronic device; deep vein thrombosis; risk factors; cardiovascular disease

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流行病学调查研究结果表明,全球每年置入的心血管植入式电子装置(cardiovascular implantable-electronic devices, CIED)约75万台,且呈逐年增加趋势^[1]。主要包括单、双腔植入式永久起搏器(permanent pacemaker, PPM)、埋藏式心脏转复除颤器(implantable cardioverter defibrillator, ICD)、心脏再同步化治疗除颤器(cardiac resynchronization therapy defibrillator, CRT-D)。1962年,经静脉途径植入电极导线开始应用于临床。由于其方法安全、简便,已成为CIED导线植入最常用的方法^[2],但导线植入引起的相关静脉血栓形成可导致肺栓塞及上腔静脉综合征发生^[3],并且使起搏器升级和更换导线时难以植入新的电极导线。导线植入相关静脉血栓的发生率约14.0%~32.9%^[4],其中术后早期发生率>90%^[5]。目前关于CIED并发症的报道仍较少,其危险因素更少提及,本研究探讨了CIED导线相关静脉血栓形成的危险因素,为临床预防和治疗提供理论依据。

1 对象与方法

1.1 研究对象

选取2013年9月至2015年12月解放军总医院心血管内科使用CIED且随访资料完整的住院患者112例,根据术后血管超声检查结果进行分组,血栓组56例,男性32例,女性24例,年龄(71.86±8.35)岁,非血栓组56例,男性32例,女性24例,年龄(71.23±10.62)岁。纳入标准:使用CIED且经锁骨下静脉途径植入导线患者。排除标准:非经锁骨下静脉途径植入导线;术前一明确有锁骨下静脉或上腔静脉血栓形成或狭窄;术前一有导线植入锁骨下静脉患者。

1.2 方法

回顾性分析病例,详细记录患者的性别、年龄、体质指数(body mass index, BMI)、吸烟、高血压病、房颤、脑卒中、慢性阻塞性肺疾病、心肌梗死和有无抗凝药物服用史以及住院期间第1次血常规、血脂、肾功能、全血糖化血红蛋白、超声心动图检查结果和手术时间、锁骨下静脉穿刺次数、是否使用临时起搏器、导线数量、导线种类等一般资料。术前及术后1周、1个月、3个月、1年分别行双侧锁骨下静脉和上腔静脉彩色多普勒血流和频谱多普勒超声检查,以明确有无导线植入相关静脉血栓形成。

1.3 统计学处理

采用SPSS17.0统计软件对数据进行处理。计量资料以均数±标准差($\bar{x} \pm s$)表示,组间比较采用 t

检验。计数资料以百分率表示,组间比较采用 χ^2 检验。多因素logistic回归分析导线相关静脉血栓形成的危险因素。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 两组患者临床资料比较

血栓组服用抗凝药患者数及左室射血分数均显著低于非血栓组,差异具有统计学意义($P < 0.01$)。血栓组房颤患者数、全血糖化血红蛋白水平以及术中静脉穿刺次数、手术时间、导线数量和植入除颤导线患者数均显著高于非血栓组,差异具有统计学意义($P < 0.05$;表1)。

2.2 多因素logistic回归分析

对有统计学差异的临床指标进行多因素logistic回归分析,房颤、静脉穿刺次数、导线数量和手术时间是导线相关静脉血栓形成的危险因素,而服用抗凝药是导线相关静脉血栓形成的保护因素($P < 0.05$;表2)。

3 讨论

由于锁骨下静脉、上腔静脉侧枝循环丰富,大部分静脉血栓患者没有临床症状,因此导线相关静脉血栓形成是CIED并发症中易被忽视的一种,但静脉血栓形成会导致起搏器更换或升级时原导线难以拔出,新导线无法植入以及出现植入侧上肢肿胀、颈静脉充盈或怒张、面部水肿、头痛等上腔静脉综合征,甚至出现肺栓塞而导致患者死亡等,这一并发症已经越来越受到临床医师的重视。

房颤是一种常见的快速型心律失常,易在心房内形成血栓,房颤患者植入CIED易导致导线相关静脉血栓形成的具体机制还不明确,可能与以下因素相关。房颤患者本身存在心房内血流动力学紊乱,导线植入右房、右室或左室后,导线周围的血流也会因导线的存在而产生湍流或瘀滞,血流冲刷和稀释作用减弱,激活的凝血酶局部浓度升高,水解纤维蛋白原的能力提高,进而导致血栓形成。并且房颤患者不规律的心房和心室跳动,带动植入导线对相关静脉血管壁不规律冲击,从而增加血管内皮损伤的可能性,促使静脉血栓形成。研究表明,房颤患者本身还存在凝血系统激活、纤溶系统活性降低、血小板活化以及炎症因子如C-反应蛋白、肿瘤坏死因子- α 、白细胞介素-2、白细胞介素-6、白细胞介素-8等水平升高,这些凝血状态的改变会加剧导线相关静脉血栓的形成^[6-9]。本研究表明,房颤患者导线相关静脉血栓形成的发生率显著高于非房颤患者(OR=110.270)。

表1 两组患者临床资料比较

Table 1 Comparison of clinical data between two groups

(n = 56)

Item	Non-thrombosis group	Thrombosis group	P value
Age (years, $\bar{x} \pm s$)	71.23 $\pm$ 10.62	71.86 $\pm$ 8.35	0.730
Male/female	32/24	32/24	1.000
BMI (kg/m ² , $\bar{x} \pm s$)	24.82 $\pm$ 3.01	23.66 $\pm$ 4.86	0.130
Smoking [n (%)]	17 (30.4)	16 (28.6)	0.836
History of disease [n (%)]			
Hypertension	41 (73.2)	40 (71.4)	0.833
Atrial fibrillation	16 (28.6)	28 (50.0)	0.020
MI	6 (10.7)	8 (14.3)	0.568
COPD	8 (14.3)	8 (14.3)	1.000
Stroke	16 (28.6)	24 (42.9)	0.115
Laboratory indices ($\bar{x} \pm s$)			
HbA1c (%)	6.16 $\pm$ 1.04	6.70 $\pm$ 0.67	0.001
TG (mmol/L)	1.16 $\pm$ 0.62	0.96 $\pm$ 0.46	0.062
TC (mmol/L)	3.87 $\pm$ 1.01	4.07 $\pm$ 1.08	0.328
HDL (mmol/L)	1.26 $\pm$ 0.46	1.30 $\pm$ 0.27	0.496
LDL (mmol/L)	2.30 $\pm$ 0.93	2.58 $\pm$ 0.97	0.121
LVEF (%)	57.30 $\pm$ 14.00	48.43 $\pm$ 14.61	0.001
eGFR (ml/min)	67.15 $\pm$ 24.14	66.28 $\pm$ 23.31	0.847
Hb (g/L)	130.84 $\pm$ 18.94	134.86 $\pm$ 17.88	0.251
PLT ($\times 10^9$ /L)	196.21 $\pm$ 54.75	184.86 $\pm$ 58.29	0.290
TR [n (%)]	13 (23.2)	22 (39.3)	0.067
Anti-coagulant medications [n (%)]	20 (35.7)	8 (14.3)	0.009
Temporary pacemaker implantation [n (%)]	25 (44.6)	24 (42.9)	0.849
Times of venipuncture ($\bar{x} \pm s$)	2.82 $\pm$ 1.15	4.29 $\pm$ 1.04	0.000
Operation time (h, $\bar{x} \pm s$)	1.75 $\pm$ 0.45	2.24 $\pm$ 0.55	0.000
Defibrillation lead [n (%)]	8 (14.3)	26 (46.4)	0.000
Lead number ($\bar{x} \pm s$)	2.02 $\pm$ 0.67	2.71 $\pm$ 0.46	0.000

BMI: body mass index; MI: myocardial infarction; COPD: chronic obstructive pulmonary disease; HbA1c: glycosylated hemoglobin; TG: triglycerides; TC: total cholesterol; HDL: high-density lipoprotein; LDL: low-density lipoprotein; LVEF: left ventricular ejection fraction; eGFR: estimated glomerular filtration rate; Hb: hemoglobin; PLT: platelet; TR: tricuspid regurgitation

表2 静脉血栓形成危险因素的多因素 logistic 回归分析

Table 2 Multivariate logistic regression analysis for risk factors related to venous thrombosis

Risk factor	β	OR	95% CI	P value
Atrial fibrillation	4.703	110.270	5.993 – 2028.941	0.002
HbA1c	0.325	1.384	0.603 – 3.177	0.444
LVEF	-0.021	0.979	0.877 – 1.093	0.707
Anti-coagulant medications	-7.330	0.001	0.000 – 0.031	0.000
Times of venipuncture	1.787	5.969	2.157 – 16.518	0.001
Operation time	3.632	37.802	4.135 – 345.567	0.001
Lead number	1.492	4.445	1.012 – 19.518	0.048
Defibrillation lead	-1.825	0.161	0.003 – 7.827	0.357

HbA1c: glycosylated hemoglobin; LVEF: left ventricular ejection fraction

静脉穿刺植入电极导线已成为 CIED 导线植入的最常用方法。由于静脉穿刺可导致血管内皮细胞受损、凝血系统激活,进而导致静脉血栓形成。静脉穿刺次数与导线相关静脉血栓形成有密切关系。术中尽量减少静脉穿刺次数可减轻相关静脉的损伤,对预防导线相关静脉血栓形成有积极作用。本研究表明,血栓组和非血栓组的静脉穿刺次数差异有明显的统计学意义($P < 0.001$)。

手术时间的长短与患者接受的手术类型、患者自身因素及术者的操作经验密切相关。通常情况下,单腔起搏器手术时间最短,双腔起搏器次之,ICD 耗时较长,CRTD 最长。患者锁骨下静脉走行变异、心脏结构改变以及导线固定位置测试参数不满意等自身因素也会延长手术时间,而术者的操作手法与手术经验对手术时间长短的影响也是肯定的。手术时间的延长会增加患者应激状态的时间,

也会增加手术操作步骤,这些都会导致血管内皮损伤、血液瘀滞及血液处于高凝状态,进而增加静脉血栓风险。虽然目前对手术时间延长是否是静脉血栓形成的一个独立危险因素尚未完全被证实^[10],但本研究表明手术时间延长会增加患者导线相关静脉血栓形成的风险。

已有研究表明,植入多根电极导线的患者导线相关静脉血栓的发生风险高于单根电极导线患者^[11,12]。其病理生理机制可能为多根导线缩窄了静脉管腔,使血液通过导线时流速减慢,湍流增加,血液瘀滞;从而增加导线与血液接触面积,激活凝血途径,使活化血小板黏附点增多,使得静脉血栓风险升高。本研究表明导线数量是导线相关静脉血栓形成的危险因素(OR = 4.445)。目前抗凝治疗对CIED导线相关静脉血栓形成有无预防作用文献报道不一致,尚无定论,但近期有文献报道其有一定的预防作用^[12]。本研究表明服用抗凝药物是导线相关静脉血栓形成的保护因素(OR = 0.001),可降低静脉血栓形成的发生率。因此,对于导线相关静脉血栓形成的高危患者,服用抗凝药有积极作用。另部分文献报道糖尿病^[13]、心功能不全^[2]、植入除颤电极^[14,15]等是导线相关静脉血栓形成的危险因素,本研究两组患者确有差异,但是否是危险因素仍需更进一步研究。病理研究已证实导线在血管内和心腔内可形成广泛的纤维结缔组织包裹和粘连,导线及血管、心腔内壁的血栓较常见^[16]。导线相关静脉血栓形成的发生率可能远高于预期,但由于检测方法的局限性以及临床医师的忽视,对其认识仍不足。

血管超声检查由于诊断准确率较高、无创、经济、方便以及不使用造影剂、放射线等特点,已作为临床评价深静脉血栓形成的首选方法。但由于气体对超声影响很大,加之超声检查在清晰度、分辨率等方面仍有不足,在评价导线相关静脉特别是上腔静脉时,准确率不如静脉造影检查高。本研究的局限性在于血栓组病例数偏少以及未考虑术后随访时间对静脉血栓形成的影响,在以后的研究中会做进一步的补充。

综上所述,房颤、静脉穿刺次数、手术时间及导线数量是导线相关静脉血栓形成的独立危险因素。对导线相关静脉血栓形成高危患者,应及时采取干预措施,给予抗凝治疗。

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