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房颤射频消融术后复发风险预测评分系统的建立及评价*

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摘要 目的:探讨心房颤动(房颤)患者射频消融术后复发的风险因素,并依此构建个性化的风险评分系统。**方法:**选取2017年1~8月行射频消融术的房颤患者154例作为研究对象,依据术后3个月的随访结果将患者分为复发组及未复发组,采用单因素分析和 Logistic 回归分析对各风险因素进行分析,构建其评分系统,采用 Hosmer-Lemeshow 拟合优度检验和 ROC 曲线下面积评价评分系统的准确度及区分度。**结果:**术后随访3个月的结果显示共37例(24.03%)房颤患者出现复发,房颤类型、病程、体质量指数(BMI)、左房前后径(LAD)、左房容积(LAV)及超敏C反应蛋白(hs-CRP)水平均是房颤复发的独立风险因素($P < 0.05$)。构建的风险评分系统得分为0~26分, Hosmer-Lemeshow 拟合优度检验: $\chi^2 = 7.520, P = 0.482$; ROC 曲线下面积为0.864(95%CI:0.837~0.891), 预测评分值为15分时,约登指数最大(0.605),此时的敏感度和特异度分别为77.3%和83.2%。**结论:**房颤患者射频消融术后的复发率较高,依据风险因素构建的风险评分系统具有较高的预测效率和区分能力,可作为房颤患者射频消融术后复发风险评估的参考工具。

关键词:心房颤动;射频消融术;复发风险;预测评分

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Establishment and Evaluation of Recurrence Risk Prediction and Scoring System for Patients with Atrial Fibrillation after Radiofrequency Ablation*

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ABSTRACT Objective: To investigate the risk factors of recurrence after radiofrequency ablation in patients with atrial fibrillation (AF), and construct a personalized risk scoring system. **Methods:** 154 cases of patients with atrial fibrillation who underwent radiofrequency ablation from January to August 2017 were divided into the recurrence group and the non-recurrence group according to the follow-up results at 3 months after operation. Univariate analysis and Logistic regression analysis were used to analyze the risk factors, and the scoring system was constructed. The accuracy and discrimination of the scoring system were evaluated by Hosmer-Lemeshow goodness of fit test and area under ROC curve. **Results:** The results of follow-up for 3 months showed that 37 patients (24.03%) with atrial fibrillation had recurrence. Atrial fibrillation type, course of disease, body mass index (BMI), left atrial anteroposterior diameter (LAD), left atrial volume (LAV) and hypersensitive C-reactive protein (hs-CRP) level were independent risk factors for recurrence of atrial fibrillation. The score of the constructed risk scoring system was $0 \leq 26$, and Hosmer-Lemeshow goodness of fit test: $\chi^2 = 7.520, P = 0.482$; When the area under the ROC curve was 0.864 (95%CI:0.837~0.891) and the predicted score was 15, the Youden index was the largest (0.605), and the sensitivity and specificity were 77.3% and 83.2%, respectively. **Conclusion:** The recurrence rate of patients with atrial fibrillation after radiofrequency ablation is high. the risk scoring system based on risk factors has high predictive efficiency and discrimination ability, and can be used as reference to evaluate the risk of recurrence after radiofrequency ablation in patients with atrial fibrillation.

Key words: Atrial fibrillation; Radiofrequency ablation; Recurrence risk; Predictive score

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前言

心房颤动(Atrial Fibrillation, AF)简称房颤,是临床最常见的心律失常之一,也是患者高住院率、致残率及病死率的主要

原因^[1]。房颤射频消融术目前临床治疗房颤的主要方式^[2],但消融后复发率仍较高,约为20%~61%^[3,4]。如何早期筛查房颤射频消融术后复发风险,并根据风险因素预防管理,以规避其复发风险是医护人员关注的焦点。目前,国内外已经就房颤患者

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射频消融术后复发风险开展了大量的研究,但多数偏重于分析复发的风险因素^[5-9],整合风险因素并依此构建风险筛查工具的相关报道较少。本研究通过探讨房颤患者射频消融术后复发的现状及风险因素,并构建个性化的风险评分系统,旨在为房颤患者射频消融术后复发的风险进行科学有效地管理。

1 资料与方法

1.1 一般资料

选择2017年1~8月在安徽省立医院南区行射频消融术的房颤患者154例作为研究对象,纳入标准:①符合美国心脏病协会(AHA)2014年发布的房颤管理指南中的诊断标准^[10],且经心电图、检查确诊为心房颤动;②进行导管射频消融术,符合手术指征的要求;③首次行导管射频消融术;④签署知情同意书。排除标准:①合并严重的肺部疾病、心肝肾功能不全、凝血功能障碍患者;②临床资料和影像学资料不完整者;③合并有严重的缓慢型心律失常,如病态窦房结综合征、III度房室传导阻滞。房颤复发的标准^[11]:随访记录患者术后的症状变化并进行心电图及24h动态心电图检查,若出现房性心动过速、房颤持续时间>30s则判断为复发。根据术后复发结果将患者分为复发组(37例)和非复发组(117例)。本研究经医院医学伦理委员会批准通过。

1.2 研究方法

主要包括:①一般资料。收集并汇总患者性别、年龄、文化程度、房颤类型、病程、合并症、心功能分级等一般资料,同时计算患者的BMI水平及CHA2DS2-VASc评分。②超声检查结果。依据患者术前超声心动图检查结果获取左房前后径(LAD)、左心室射血分数(LVEF)、左心房容积(LAVI)、左心室舒张末期直径(LVEDd)等心脏超声参数。③化验室检查结果。依据患者术前静脉血检查获取血浆hs-CRP、心肌肌酐、N-末端脑钠肽前体(NT-proBNP)等相关化验室检查结果。

1.3 统计学方法

采用SPSS20.0软件进行数据分析,采用单因素分析及Logistic回归分析对各风险因素进行分析,根据回归分析中各危险因素的 β 值及其变量类型建立房颤患者射频消融术后复发的评分系统,即将风险因素的 β 值最低者设为2分,其他危险因素的评分=(其 β 值/最低 β 值) \times 2,将各风险因素所得评分四舍五入取整后计算评分系统总分。采用Hosmer-Lemeshow拟合优度检验评价预测评分系统的预测准确度,采用ROC曲线评价预测评分系统的区分度并分析评分系统的高风险临界值,检验水准 $\alpha=0.05$ 。

2 结果

2.1 研究对象的一般资料描述

包括:(1)一般资料。男性115(74.68%)例;年龄42~76岁(58.22 \pm 12.12)岁,高中及以上48(31.17%)例;房颤病程0.8~9年,中位病程4(1.25,6.75)年;持续性房颤64(41.56%)例;合并有高血压42(27.27%)例,合并有糖尿病31(20.13%)例,NYHA心功能分级为III或IV级的患者26(16.88%)例,BMI平均水平为(24.11 \pm 3.41)kg/m²,CHA2DS2-VASc平均评分为(1.67 \pm 0.69)分。(2)心脏超声参数。LVEF/LVEDd的平均水平分别为

(57.15 \pm 5.20)%、(49.10 \pm 3.14)mm,LAD、LAV中位水平分别为42(30,54)mm、103(87,119)mm³。(3)化验室检查结果。心肌肌酐平均值为(76.80 \pm 15.29) μ mol/L,hs-CRP及NT-proBNP的中位水平分别为2.10(1.32,2.88) μ mol/L、725(640,810)ng/mL。

2.2 不同特征房颤患者射频消融术后复发情况及单因素分析结果

154例房颤患者中共有37例(24.03%)出现术后复发,单因素结果表明,两组患者在年龄、病程、BMI值、房颤类型、LAD、LAV、hs-CRP、NT-proBNP及是否合并高血压这9个变量上的分布差异有统计学意义($P<0.05$),详见表1。

2.3 房颤患者射频消融术后复发风险因素的 Logistic 回归分析结果

以术后早期情况作为应变变量(赋值:复发=1,未复发=0),将单因素分析中差异有统计学意义的变量作为自变量进行Logistic回归分析,变量筛选采用逐步法(α 入=0.05, α 出=0.1)。自变量赋值情况:①年龄:原值录入;②病程:4年及以上=1,4年以下=0;③房颤类型:持续性房颤=1,阵发性房颤=0;④高血压:有=1,无=0;⑤BMI:23.9 kg/m²及以上=1,23.9 kg/m²以下=0;⑥LAD:42 mm及以上=1,42 mm以下=0;⑦LAV:103 mm³及以上=1,103 mm³以下=0;⑧hs-CRP:2.10 mg/L及以上=1,2.10 mg/L以下=0;⑨NT-proBNP:725 ng/mL及以上=1,725 ng/mL以下=0。房颤患者射频消融术后复发风险因素的Logistic回归分析结果详见表2。

2.4 房颤患者射频消融术后复发风险评分系统的构建及评价

依据回归分析结果建立个性化的风险预测评分系统(总分0~26分),详见表2。在原有研究人群的基础上采用Bootstrap法重采样500次获得内部验证人群,将建立的风险预测评分系统对内部验证人群患者进行风险评估,结果提示,Hosmer-Lemeshow拟合优度检验 $\chi^2=7.520$, $P=0.482$;ROC曲线下面积为0.864(95%CI:0.837~0.891),预测评分为15分时,约登指数最大(0.605),此时的敏感度和特异度分别为77.3%和83.2%,即风险评分系统的高风险临界值为15分,ROC曲线图详见图1。

3 讨论

3.1 房颤患者射频消融术后复发的临床表现

本研究结果显示154例患者中,共有37例(24.03%)出现术后复发,高于郭飞等^[12]报道的14.68%的射频消融治疗的房颤患者出现复发的结果,提示房颤患者射频消融术后复发的风险较高。射频消融手术作为阵发性房颤和药物治疗无效的持续性房颤的一线治疗手段^[13-15],目前各临床中心报道的房颤消融术的成功率在60%~90%^[16]。然而,消融术后相对较高的复发率在一定程度上影响了其临床应用和治疗效果^[17]。因此,早期识别房颤消融术后复发的风险因素,并及时有效地干预,对于保证手术的治疗效果和患者的预后具有重要意义。

3.2 房颤射频消融术后复发风险因素的分析

本研究筛选出房颤患者射频消融术后复发的6项风险因素。①房颤类型:研究显示^[18]射频消融术对不同房颤患者的影响是不同的,阵发性房颤患者术后6个月的LAD较术前明显缩小,而持续性房颤患者较术前略有增加,这种差异的出

表 1 不同特征房颤患者术后复发情况的比较[例(%)]

Table 1 Comparison of postoperative recurrence in patients with different characteristics of atrial fibrillation [(case)%]

Variable	Grouping of recurrence of atrial fibrillation		χ^2/t	P
	Recurring group(n=37)	Non-recurrent group(n=117)		
Male	24(64.86)	91(77.78)	2.479 ^a	0.115
Age(years)	61.23± 11.26	56.34± 12.39	2.137 ^b	0.034
Culutre	8(21.62)	40(34.19)	2.069 ^a	0.150
Course of AF≥ 4 years	25(67.57)	54(46.15)	5.159 ^a	0.023
Persistent AF	22(59.46)	42(35.90)	6.426 ^a	0.011
HTN	15(40.54)	27(23.08)	4.322 ^a	0.038
DM	10(27.03)	21(17.95)	1.441 ^a	0.230
CHF NYHA Level III or IV	7(18.92)	19(16.24)	0.144 ^a	0.704
BMI≥ 23.9 kg/m ²	26(70.27)	59(50.43)	4.476 ^a	0.034
CHA2DS2-VASc score	1.79± 0.96	1.63± 0.75	1.054 ^b	0.294
LAD≥ 42 mm	27(72.97)	53(45.30)	8.624 ^b	0.003
LVEF(%)	57.45± 6.43	56.88± 5.79	0.508 ^b	0.612
LAV≥ 103 mm ³	26(70.27)	56(47.86)	5.669 ^a	0.017
LVEDd(mm)	48.75± 3.48	49.22± 2.69	-0.753	0.455
hs-CRP≥ 2.10 mg/L	23(62.16)	48(41.03)	5.054 ^a	0.025
Cr(μmol/L)	77.85± 15.67	76.24± 16.20	0.531 ^b	0.596
NT-proBNP≥ 725 ng/mL	29(78.38)	57(48.72)	10.029 ^a	0.002

Notes: a. 2 value ,b,t value. Culutre= high school education, HTN= hypertension, DM= diabetes, CHF= heart failure with NYHA class III or IV, LAD= left atrial diastolic inner diameter, LAV= left atrial volume, Cr= serum creatinine concentration.

表 2 房颤患者射频消融术后复发风险因素的 Logistic 回归分析(n=114)

Table 2 Logistic regression analysis of recurrence risk factors after radiofrequency ablation in patients with atrial fibrillation (n=114)

Variable	β	SE	Wald χ^2	P	OR	95%CI	风险评分
Persistent AF	0.549	0.237	5.365	0.041	1.732	1.088~2.755	3
Course of AF≥ 4 years	1.112	0.438	6.446	0.022	3.040	1.289~7.174	6
BMI≥ 23.9 kg/m ²	0.374	0.149	6.300	0.024	1.453	1.085~1.947	2
LAD≥ 42 mm	1.232	0.386	10.182	0.003	3.427	1.609~7.305	7
LAV≥ 103 mm ³	1.017	0.350	8.444	0.007	2.765	1.392~5.490	5
hs-CRP≥ 2.10 mg/L	0.610	0.224	7.407	0.013	1.841	1.186~2.855	3

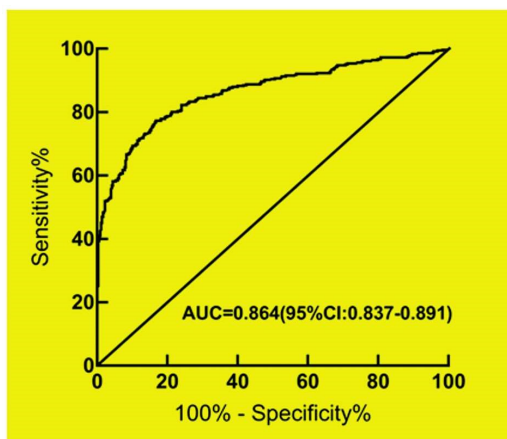


图 1 房颤患者射频消融术后复发风险评分系统的 ROC 曲线图

Fig.1 Roc graph of the recurrence risk scoring system after radiofrequency ablation in patients with atrial fibrillation

现可能与持续性房颤患者术后复发率较高有关^[19]。① 病程:本次研究结果表明房颤病程为术后复发的独立危险因素之一,与赵荣诚^[20-22]等研究结果一致,提示随着病程的延长,左房逐渐扩大,左房越大越利于房颤基质的形成,从而使房颤更容易发生和维持并进展为持续性房颤,且房颤导管消融术后更容易复发。② BMI:本次研究显示超重是房颤患者射频消融术后复发的独立风险因素,与 Deng Hai^[23]、Glover^[24]等的研究结果一致。Cai 等^[25]报道肥胖或超重的房颤患者左心房内径明显大于对照组,提示肥胖或超重患者由于自身 BMI 问题左心房较非肥胖者内径更大,两者协同作用进一步加大了肥胖患者早期复发的风险。③ LAD:本次研究发现 LAD 是房颤射频消融术后复发的独立危险因素,与 An Kang^[26]、Ishii^[27]等的研究结果一致。左房增大可引起心肌间质纤维化、心内膜重塑和心肌细胞肥大,导致离子通道电生理变化,随之提高了心肌的兴奋性、自律性,从

而诱导房颤的发生。^① LAV:一项关于 LAV 与射频消融术后房颤复发的 meta 分析表明^[7],LAV 较 LAD 能更准确地反映不对称的左心房大小。同时与无房颤复发的患者相比,射频消融术后房颤复发的患者具有较高的平均 LAV,并且 LAV 测量值与房颤复发率具有独立的正向相关性。^② hs-CRP:Carballo 等^[28-30]报道 hs-CRP 与房颤射频消融术后复发密切相关。CRP 和其他炎症生物标志物的慢性升高已被证明是全身炎症的标志,而炎症反应的发生也会增加房颤的可诱导性,进而导致房颤的发生和维持^[31,32]。

3.3 房颤射频消融术后复发风险评估系统的构建及验证

对风险预测评分系统进行评价,结果显示 Hosmer-Lemeshow 拟合优度检验的 $\chi^2=7.520, P=0.482$;ROC 曲线下面积为 0.864(95%CI:0.837~0.891),提示模型的准确度和区分度均较好,可用于房颤患者射频消融术后的复发风险因素筛查。且预测评分值达到 15 分时,约登指数最大(0.605),此时的敏感度和特异度分别为 77.3%和 83.2%,可以作为筛查复发风险的判定依据。临床医护人员应注意评分 15 分以上的射频消融术后患者,根据具体风险因素实施针对性的干预,以降低房颤复发风险。

3.4 本次研究的局限性

本研究所收集的病例资料来源较为单一,研究样本的代表性相对不足,其推广应用受到一定限制,拟在将来的临床研究中应采用多中心大样本研究进一步完善。

综上所述,房颤患者射频消融术后具有较高的复发率,分析复发的风险因素并依此构建的风险评分系统具有较好的预测能力,能为房颤患者术后复发风险的筛查提供依据参考。

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