· 论著 ·

心电图评分对射血分数降低的心力衰竭患者发生不良结局的预测价值研究

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【摘要】 目的 探讨心电图评分对射血分数降低的心力衰竭(HFrEF)患者发生不良结局的预测价值。方法 选取2021年6—9月郑州大学第一附属医院收治的HFrEF患者169例。将心电图评分>2分的患者作为高风险组($n=93$), 心电图评分 ≤ 2 分的患者作为低风险组($n=76$)。比较两组基线资料、不良结局发生情况。采用Kaplan-Meier法绘制生存曲线, 生存曲线比较采用Log-rank检验。采用单因素、多因素Cox比例风险回归分析探讨HFrEF患者发生不良结局的影响因素; 采用ROC曲线分析心电图评分对HFrEF患者发生不良结局的预测价值。结果 低风险组红细胞计数高于高风险组, N末端脑钠肽前体(NT-proBNP)低于高风险组($P<0.05$)。低风险组累积不良结局发生率低于高风险组($\chi^2=46.390, P<0.001$)。多因素Cox比例风险回归分析结果显示, NT-proBNP升高、心电图评分>2分是HFrEF患者发生不良结局的独立危险因素($P<0.05$)。ROC曲线分析结果显示, 心电图评分预测HFrEF患者发生不良结局的AUC为0.774 [95%CI (0.698, 0.843)], 最佳截断值为2.5分, 灵敏度为72.4%, 特异度为77.4%。结论 心电图评分是HFrEF患者发生不良结局的危险因素, 其对HFrEF患者发生不良结局有一定预测价值。

【关键词】 心力衰竭; 射血分数降低的心力衰竭; 心电图评分; 不良结局

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Predictive Value of ECG Score for Adverse Outcomes in Patients with Heart Failure with Reduced Ejection Fraction

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【Abstract】 Objective To investigate the predictive value of ECG score for adverse outcomes in patients with heart failure with reduced ejection fraction (HFrEF). **Methods** A total of 169 patients with HFrEF admitted to the First Affiliated Hospital of Zhengzhou University from June to September 2021 were selected. Patients with ECG score > 2 were classified as high risk group ($n=93$), and patients with ECG score ≤ 2 were classified as low risk group ($n=76$). Baseline data and adverse outcomes were compared between the two groups. Kaplan-Meier method was used to draw survival curves, and Log-rank test was used to compare survival curves. Univariate and multivariate Cox proportional risk regression analysis was used to investigate the influencing factors of adverse outcomes in HFrEF patients. ROC curve was used to investigate the predictive value of ECG score for adverse outcomes in HFrEF patients. **Results** The red blood cell count in the low risk group was higher than that in the high risk group, and N-terminal pro-brain natriuretic peptide (NT-proBNP) was lower than that in the high risk group ($P < 0.05$). The cumulative incidence of adverse outcomes of low risk group was lower than that of high risk group ($\chi^2=46.390, P < 0.001$). Multivariate Cox proportional risk regression analysis showed that increased NT-proBNP and ECG score > 2 were independent risk factors for adverse outcomes in HFrEF patients ($P < 0.05$). ROC curve analysis results showed that the AUC of ECG score in predicting adverse outcomes in HFrEF patients was 0.774 [95%CI (0.698, 0.843)], the optimal cut-off value was 2.5 points, the sensitivity was 72.4%, and the specificity was 77.4%. **Conclusion** ECG score is a risk factor for adverse outcome in HFrEF patients, and it has certain predictive value for the occurrence of adverse outcomes in HFrEF patients.

【Key words】 Heart failure; Heart failure with reduced ejection fraction; Electrocardiogram score; Adverse outcomes

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射血分数降低的心力衰竭 (heart failure with reduced ejection fraction, HFrEF) 是一种由心室收缩和/或舒张功能受损导致的临床综合征^[1], 是各种心血管疾病的终末阶段。据估计, 成年人HFrEF的发病率高达2.2%^[2]。全世界每年用于治疗心力衰竭的费用约为1 000亿美元^[3]。据报道, 在2.5年的中位随访期间, HFrEF患者的死亡率高达40%, 且大多数死亡发生在出院后的早期, 死亡原因可能是心力衰竭加重或心源性猝死^[4]。在存活的患者中, 近1/3在出院后3个月内因心力衰竭加重再次住院^[5-6]。因此, 评估HFrEF住院患者的短期死亡和再住院风险有助于高风险患者进行强化医疗护理以改善其预后。

心电图是一种方便、经济、高效的检查方法, 现已被广泛用于多种心血管疾病的诊断, 包括急性心肌梗死和心力衰竭。许多心电图参数如QRS波群时限^[7]、QT间期^[8]、JT间期^[9]及左心室肥大(left ventricular hypertrophy, LVH)^[10]、心率变异性^[11]等均可以预测HFrEF患者的不良预后, 但心电图参数的参考范围并不统一; 其次, 无法确定哪种心电图参数能更有效地预测患者预后。2020年, CHATTERJEE等^[12]构建了心电图评分并用于预测冠状动脉疾病患者心律失常猝死(sudden arrhythmic death, SAD)发生率。鉴于上述心电图评分中的参数(QRS波群时限、JT间期延长、LVH和连续性Q波)均与HFrEF患者的不良预后有关, 本研究旨在探究心电图评分对HFrEF患者发生不良结局的预测价值, 以期寻找不良结局风险高的HFrEF患者提供参考。

1 对象与方法

1.1 研究对象 选取2021年6—9月郑州大学第一附属医院收治的HFrEF患者169例。纳入标准: 符合HFrEF的诊断标准, 即有心力衰竭的症状和/或体征以及左心室射血分数 $\leq 40\%$ (左心室射血分数由超声心动图测量)^[13]。排除标准: (1) 年龄 < 18 岁; (2) 急性心肌梗死; (3) 合并慢性肾脏病; (4) 合并肾病综合征; (5) 合并恶性肿瘤; (6) 合并慢性肝功能不全; (7) 合并未受控制的全身性疾病。本研究经郑州大学第一附属医院伦理委员会批准(2020-KY-0185), 所有患者签署知情同意书。

1.2 分组标准 记录所有患者的心电图参数, 并参考CHATTERJEE等^[12]提出的心电图评分方法, 包括4个方面内容, 分别为: (1) QRS波群时限: QRS波群时限 ≤ 80 ms为0分、81~110 ms为1分、 > 110 ms为2分。(2) 连续性Q波: Q波持续时间 > 0.04 s或任意两个连续导联的Q:R振幅比 > 0.25 ^[14]定义为连续性Q波, 计1分。(3) LVH: 采用Sokolow-Lyon指数评估LVH, V_1 S波和 V_5 或 V_6 R波之和 ≥ 3.5 mV定义为LVH, 计1分^[15]。(4) JT间期延长: JT间期=QT间期-QRS波群

时限^[16], JT间期 > 360 ms定义为JT间期延长, 计1分。上述四项内容评分之和即为心电图评分。将心电图评分 > 2 分的患者作为高风险组($n=76$), 心电图评分 ≤ 2 分的患者作为低风险组($n=93$)。

1.3 观察指标 (1) 基线资料。收集患者基线资料, 包括年龄、性别、左心室射血分数、收缩压、舒张压、心率、冠心病史、心肌梗死史、冠状动脉旁路移植术(coronary artery bypass grafting, CABG)/PCI史、高血压史、糖尿病史、慢性阻塞性肺疾病史、脑血管病史、外周血管病史、吸烟史、饮酒史、实验室检查指标〔血钠、血钾、血肌酐、血尿素氮、血尿酸、肾小球滤过率、白细胞计数、红细胞计数、血小板计数、白蛋白、三酰甘油、低密度脂蛋白胆固醇、N末端脑钠肽前体(N-terminal pro-brain natriuretic peptide, NT-proBNP)〕、出院后药物(地高辛、ACEI、ARB、 β -受体阻滞剂、利尿剂、螺内酯、钙通道阻滞剂、抗血小板药、他汀类药物、外周血管扩张剂、华法林、胺碘酮)服用情况。(2) 不良结局发生情况。分别于出院30、60、90 d通过电话或电子邮件联系患者, 记录其不良结局发生情况, 不良结局包括因心力衰竭加重再次住院和全因死亡。

1.4 统计学方法 采用SPSS 25.0统计学软件进行数据分析。符合正态分布的计量资料以 $(\bar{x} \pm s)$ 表示, 组间比较采用两独立样本 t 检验; 不符合正态分布的计量资料以 $[M(QR)]$ 表示, 组间比较采用秩和检验; 计数资料以相对数表示, 组间比较采用 χ^2 检验; 采用Kaplan-Meier法绘制生存曲线, 生存曲线比较采用Log-rank检验; 采用单因素、多因素Cox比例风险回归分析探讨HFrEF患者发生不良结局的影响因素; 采用ROC曲线分析心电图评分对HFrEF患者发生不良结局的预测能力。以 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 基线资料 两组年龄、性别、左心室射血分数、收缩压、舒张压、心率、有冠心病史者占比、有心肌梗死史者占比、有CABG/PCI史者占比、有高血压史者占比、有糖尿病史者占比、有慢性阻塞性肺疾病史者占比、有脑血管病史者占比、有外周血管病史者占比、有吸烟史者占比、有饮酒史者占比、血钠、血钾、血肌酐、血尿素氮、血尿酸、肾小球滤过率、白细胞计数、血小板计数、白蛋白、三酰甘油、低密度脂蛋白胆固醇及服用地高辛、ACEI、ARB、 β -受体阻滞剂、利尿剂、螺内酯、钙通道阻滞剂、抗血小板药、他汀类药物、外周血管扩张剂、华法林、胺碘酮者占比比较, 差异无统计学意义($P > 0.05$); 低风险组红细胞计数高于高风险组, NT-proBNP低于高风险组, 差异有统计学意义($P < 0.05$), 见表1。

表1 两组基线资料比较

Table 1 Comparison of baseline data between the two groups

项目	低风险组 (n=93)	高风险组 (n=76)	检验统计量值	P值
年龄 [M (QR), 岁]	56.0 (20.5)	62.5 (15.0)	-1.864 ^a	0.062
性别 (男/女)	69/24	49/27	1.875 ^b	0.171
左心室射血分数 [M (QR), %]	30.0 (11.0)	31.0 (9.8)	-0.861 ^a	0.389
收缩压 ($\bar{x} \pm s$, mm Hg)	124 ± 19	122 ± 19	0.764 ^c	0.446
舒张压 [M (QR), mm Hg]	76 (15)	75 (8)	-0.468 ^a	0.640
心率 [M (QR), 次/min]	80.0 (25.5)	78.0 (18.2)	-0.838 ^a	0.402
冠心病史 [n (%)]	47 (52.2)	43 (47.8)	0.613 ^b	0.434
心肌梗死史 [n (%)]	24 (25.8)	29 (38.2)	2.964 ^b	0.085
CABG/PCI史 [n (%)]	26 (28.0)	27 (35.5)	1.113 ^b	0.291
高血压史 [n (%)]	35 (37.6)	36 (47.4)	1.627 ^b	0.202
糖尿病史 [n (%)]	21 (22.6)	26 (34.2)	2.818 ^b	0.093
慢性阻塞性肺疾病史 [n (%)]	5 (5.4)	8 (10.5)	1.562 ^b	0.211
脑血管病史 [n (%)]	8 (8.6)	7 (9.2)	0.019 ^b	0.890
外周血管病史 [n (%)]	10 (10.8)	9 (11.8)	0.050 ^b	0.824
吸烟史 [n (%)]	37 (39.8)	21 (27.6)	2.740 ^b	0.098
饮酒史 [n (%)]	19 (20.4)	12 (15.8)	0.601 ^b	0.438
血钠 [M (QR), mmol/L]	141.0 (4.4)	141.0 (4.0)	-1.169 ^a	0.242
血钾 ($\bar{x} \pm s$, mmol/L)	4.4 ± 0.6	4.4 ± 0.6	0.424 ^c	0.672
血肌酐 [M (QR), μmol/L]	87.0 (24.5)	86.4 (50.0)	-0.706 ^a	0.480
血尿素氮 [M (QR), mmol/L]	6.7 (3.1)	7.4 (5.4)	-1.885 ^a	0.059
血尿酸 [M (QR), μmol/L]	384.0 (156.0)	388.0 (213.0)	-0.452 ^a	0.651
肾小球滤过率 [M (QR), ml · min ⁻¹ · (1.73 m ²) ⁻¹]	78.9 (34.6)	78.6 (38.3)	-0.229 ^a	0.819
白细胞计数 [M (QR), ×10 ⁹ /L]	6.6 (2.8)	6.5 (3.0)	-0.119 ^a	0.906
红细胞计数 ($\bar{x} \pm s$, ×10 ¹² /L)	4.4 ± 0.6	4.2 ± 0.7	2.096 ^c	0.038
血小板计数 [M (QR), ×10 ⁹ /L]	187.0 (98.5)	178.0 (71.7)	-0.637 ^a	0.524
白蛋白 [M (QR), g/L]	39.7 (5.3)	39.3 (6.0)	-0.849 ^a	0.396
三酰甘油 [M (QR), mmol/L]	1.1 (0.8)	1.0 (0.6)	-1.354 ^a	0.176
低密度脂蛋白胆固醇 [M (QR), mmol/L]	2.2 (1.2)	2.5 (1.3)	-1.176 ^a	0.240
NT-proBNP [M (QR), ng/L]	1 530 (2 990)	3 220 (5 690)	-4.069 ^a	0.001
服用地高辛 [n (%)]	41 (44.1)	36 (47.4)	0.182 ^b	0.670
服用ACEI [n (%)]	58 (62.4)	43 (56.6)	0.582 ^b	0.445
服用ARB [n (%)]	18 (19.4)	14 (18.4)	0.024 ^b	0.878
服用β-受体阻滞剂 [n (%)]	79 (55.6)	63 (44.4)	0.131 ^b	0.717
服用利尿剂 [n (%)]	83 (89.2)	69 (90.8)	0.110 ^b	0.740
服用螺内酯 [n (%)]	85 (91.4)	62 (81.6)	3.561 ^b	0.059
服用钙通道阻滞剂 [n (%)]	5 (5.4)	6 (7.9)	0.120 ^b	0.729
服用抗血小板药 [n (%)]	45 (52.9)	40 (47.1)	0.301 ^b	0.583
服用他汀类药物 [n (%)]	57 (61.3)	53 (69.7)	1.313 ^b	0.252
服用外周血管扩张剂 [n (%)]	26 (28.6)	26 (23.4)	0.768 ^b	0.381
服用华法林 [n (%)]	20 (21.5)	14 (18.4)	0.248 ^b	0.619
服用胺碘酮 [n (%)]	5 (5.4)	2 (2.6)	0.253 ^b	0.615

注: ^a表示Z值, ^b表示χ²值, ^c表示t值; CABG=冠状动脉旁路移植术, NT-proBNP=N末端脑钠肽前体

2.2 不同心电图评分HFrEF患者生存曲线 生存曲线分析结果显示, 低风险组累积不良结局发生率低于高风险组, 差异有统计学意义 (χ²=46.390, P<0.001), 见图1。

2.3 HFrEF患者发生不良结局影响因素的单因素、多因素Cox比例风险回归分析 以年龄、性别、收缩压、舒张压、左心室射血分数、肾小球滤过率、NT-proBNP、心电图评分为自变量, 以HFrEF患者是否发生不良结局(赋值: 是=1, 否=0)为因变量, 进行单因素、多因素Cox比例风险回归分析, 结果显示, NT-proBNP升高、心电图评分>2分是HFrEF患者发生不良结局的独立危险因素 (P<0.05), 见表2。

2.4 心电图评分对HFrEF患者发生不良结局的预测价值 ROC曲线分析结果显示, 心电图评分预测HFrEF患者发生不良结局的AUC为0.774 [95%CI (0.698, 0.843)], 最佳截断值为2.5分, 灵敏度为72.4%, 特异度为77.4%, 见图2。

图1 不同心电图评分HFrEF患者不良结局发生情况生存曲线
Figure 1 Survival curve of adverse outcomes in HFrEF patients with different ECG scores

图2 心电图评分预测HFrEF患者发生不良结局的ROC曲线
Figure 2 ROC curve of ECG score in predicting adverse outcomes in HFrEF patients

表2 HFrEF患者发生不良结局影响因素的单因素、多因素Cox比例风险回归分析

Table 2 Univariate and multivariate Cox proportional risk regression analysis of influencing factors of adverse outcomes in HFrEF patients

变量	赋值	单因素						多因素					
		β	SE	Wald χ^2 值	P值	HR值	95%CI	β	SE	Wald χ^2 值	P值	HR值	95%CI
年龄	实测值	0.026	0.009	7.416	0.006	1.026	(1.007, 1.045)	0.019	0.011	2.923	0.087	1.019	(0.997, 1.042)
性别	男性=1, 女性=0	0.247	0.242	1.039	0.308	1.280	(0.796, 2.056)	-	-	-	-	-	-
左心室射血分数	实测值	0.005	0.018	0.071	0.790	1.005	(0.970, 1.042)	-	-	-	-	-	-
收缩压	实测值	-0.219	0.064	11.882	0.001	0.803	(0.709, 0.910)	-0.106	0.090	1.376	0.241	0.900	(0.754, 1.073)
舒张压	实测值	-0.330	0.096	11.718	0.001	0.719	(0.595, 0.868)	-0.131	0.139	0.890	0.346	0.877	(0.667, 1.152)
肾小球滤过率	实测值	-0.011	0.004	6.013	0.014	0.989	(0.980, 0.998)	-0.004	0.005	0.656	0.418	0.996	(0.985, 1.006)
NT-proBNP	实测值	0.009	0.001	45.571	<0.001	1.010	(1.007, 1.012)	0.007	0.002	16.797	0.001	1.007	(1.003, 1.010)
心电图评分	>2分=1, ≤2分=0	1.597	0.259	38.004	<0.001	4.937	(2.972, 8.203)	1.455	0.265	30.178	<0.001	4.285	(2.550, 7.202)

注：-表示无相关数据

3 讨论

本研究首次评估了心电图评分对HFrEF患者不良结局发生情况的预测价值，多因素Cox比例风险回归分析结果显示，心电图评分>2分是HFrEF患者发生不良结局的独立危险因素。相关研究证实，QRS波群时限延长与HFrEF患者短期再住院、心源性死亡和长期不良结局有关^[17]。对于HFrEF患者，QRS波群时限延长与潜在的左心室收缩不同步有关^[18-19]。左心室收缩不同步降低了心脏的射血能力和效率，最终导致心脏功能恶化。连续性Q波是心脏异常的标志，表明患者有心肌梗死史^[20]。有Q波的心肌梗死比无Q波的心肌梗死更严重，Q波的出现与左心室功能障碍密切相关^[21]。故连续性Q波可以预测不良结局的发生风险。既往研究表明，LVH可以预测心力衰竭患者的预后^[22-23]。JT间期延长提示心室去极化时间延长，这与舒张功能障碍有关。既往研究表明，心脏舒张功能越差，心力衰竭患者的全因死亡风险越高^[9]。本研究ROC曲线分析结果显示，心电图评分预测HFrEF患者发生不良结局的AUC为0.774。心电图评分结合了心室去极化（QRS波群时限）、心室复极化（JT间期）和心脏异常（连续性Q波和LVH），可以更充分地反映心脏电活动的整体状态。

尽管许多实验室检查指标如NT-proBNP可以评估HFrEF患者的预后，但其检测耗时长、费用高。此外，许多针对心力衰竭患者的风险评分，如healthy ABC心力衰竭风险评分，但这些风险评分常需要许多指标，并不实用^[24]。心电图不仅方便、无创，而且比实验室检查更客观，不易受到其他因素影响。既往有研究将心力衰竭患者的心电图异常情况分为主要心电图异常和次要心电图异常，并用于心力衰竭的风险评估，但该分类方法未结合心电图参数进行综合评估^[25]。根据心电图评分，临床医生可以对心力衰竭患者进行分层，找出高危患者并进行更多的医疗照护，这对心力衰竭患者的预后改善具有重要意义。本研究结果显示，心电图评分预测HFrEF患者发生不良结局的AUC为0.774〔95%CI

(0.698, 0.843)〕，提示心电图评分对HFrEF患者发生不良结局具有一定预测价值。

综上所述，心电图评分是HFrEF患者发生不良结局的危险因素，其对HFrEF患者发生不良结局有一定预测价值，这有利于临床医生发现高风险患者并制定更积极的治疗方案。但本研究样本量较小，未来需要更大样本量的研究进一步验证本研究结论。此外，心电图评分最初是为了预测冠状动脉疾病患者发生SAD的风险，并不是专门为HFrEF患者设计的，所以没有包括其他对HFrEF患者有统计学意义的心电图参数，如PR间期^[26]。

作者贡献：王富行进行文章的构思与设计，撰写、修订论文；韩东建进行研究的实施与可行性分析；张义进行资料收集；代珊进行资料整理；庄沅松进行统计学处理；刘苗苗负责文章的质量控制及审校；沈德良对文章整体负责，监督管理。

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