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· 心房颤动专题研究 ·

急性心肌梗死患者院内新发心房颤动的影响因素及其风险预测列线图模型构建

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【摘要】 背景 急性心肌梗死(AMI)患者并发心房颤动会影响其血流动力学,增加患者死亡风险。而整合AMI患者新发心房颤动的危险因素并构建风险预测列线图模型,有助于识别新发心房颤动高风险人群。目的 探讨AMI患者院内新发心房颤动的影响因素,并构建其风险预测列线图模型。方法 选取2017年1月至2021年3月在青岛市市立医院行急诊经皮冠状动脉介入术(PCI)的513例AMI患者作为研究对象,按照患者院内是否新发心房颤动分为房颤组($n=82$)和非房颤组($n=431$)。通过医院信息系统收集AMI患者人口学特征及入院时临床资料。比较两组患者人口学特征及入院时临床资料,采用多因素Logistic回归模型分析AMI患者院内新发心房颤动的影响因素,采用R 3.4.3软件包绘制列线图模型,绘制受试者工作特征(ROC)曲线以评估列线图模型的预测效能,并采用Bootstrap方法重复抽样1000次验证列线图模型的预测效能。结果 房颤组年龄和左心房内径(LAD)大于非房颤组,有吸烟史者所占比例、糖尿病发生率、Gensini积分、N末端B型利钠肽前体(NT-proBNP)高于非房颤组($P < 0.05$)。多因素Logistic回归分析结果显示,年龄[$OR=1.047, 95\%CI(1.011, 1.085)$]、吸烟史[$OR=1.828, 95\%CI(1.042, 3.206)$]、糖尿病[$OR=3.073, 95\%CI(1.622, 5.819)$]、LAD[$OR=1.138, 95\%CI(1.069, 1.211)$]、Gensini积分[$OR=1.048, 95\%CI(1.032, 4.064)$]、NT-proBNP[$OR=1.114, 95\%CI(1.069, 2.005)$]均是AMI患者院内新发心房颤动的独立影响因素($P < 0.05$)。将上述6个独立影响因素作为预测指标,构建AMI患者院内新发心房颤动风险预测列线图模型。ROC曲线分析结果显示,列线图模型预测AMI患者院内新发心房颤动的曲线下面积(AUC)为0.839[$95\%CI(0.786, 0.892)$],说明列线图模型的区分能力较好。Bootstrap方法结果显示,校准曲线的平均绝对误差(MAE)为0.019,说明校准曲线与理想曲线贴合良好。结论 年龄、吸烟史、糖尿病、LAD、Gensini积分及NT-proBNP是AMI患者院内新发心房颤动的独立影响因素,而基于上述影响因素构建的AMI患者院内新发心房颤动风险预测列线图模型具有较高的预测效能。

【关键词】 心肌梗死;新发心房颤动;影响因素分析;列线图模型;预测

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【Abstract】 **Background** Acute myocardial infarction (AMI) with atrial fibrillation will affect the patients' hemodynamics and increase the risk of death. Integrating the risk factors of new onset atrial fibrillation in patients with AMI and constructing a risk prediction nomogram model will help identify high-risk groups of new onset atrial fibrillation. **Objective** To explore the influencing factors of new onset atrial fibrillation during hospitalization in patients with AMI, and establish a risk prediction nomogram model. **Methods** A total of 513 AMI patients who underwent emergency percutaneous coronary intervention (PCI) in Qingdao Municipal Hospital from January 2017 to March 2021 were selected as the research objects, they were divided into atrial fibrillation group ($n=82$) and non atrial fibrillation group ($n=431$) according to whether occurred new onset atrial fibrillation during hospitalization. The demographic features and clinical data at admission were collected by

hospital information system. The demographic features and clinical data at admission were compared between the two groups. The influencing factors of new onset atrial fibrillation during hospitalization in patients with AMI were analyzed by multivariate Logistic regression model. The nomogram model was drawn by R 3.4.3 software package, and the receiver operating characteristic (ROC) curve was drawn to evaluate the prediction efficiency of the nomogram model, the Bootstrap method (self-sampling 1 000 times) was used to verify the prediction efficiency of the nomogram model. **Results** Age and left atrial diameter (LAD) in atrial fibrillation group were larger than those in non atrial fibrillation group, and the proportion of patients with smoking history, incidence of diabetes, Gensini score and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were higher than those in non atrial fibrillation group ($P < 0.05$). The multivariate Logistic regression analysis results showed that age [$OR=1.047, 95\%CI(1.011, 1.085)$], smoking history [$OR=1.828, 95\%CI(1.042, 3.206)$], diabetes [$OR=3.073, 95\%CI(1.622, 5.819)$], LAD [$OR=1.138, 95\%CI(1.069, 1.211)$], Gensini score [$OR=1.048, 95\%CI(1.032, 4.064)$] and NT-proBNP [$OR=1.114, 95\%CI(1.069, 2.005)$] were independent influencing factors of new onset atrial fibrillation during hospitalization in AMI patients ($P < 0.05$). The above six independent influencing factors were used as predictors to construct a nomogram model for predicting the risk of new onset atrial fibrillation in patients with AMI. ROC curve analysis showed that the area under curve (AUC) of nomogram model in predicting new onset atrial fibrillation during hospitalization in patients with AMI was 0.839 [$95\%CI(0.786, 0.892)$], indicating that the nomogram model has good discrimination ability. Bootstrap method result showed that the MAE of the calibration curve was 0.019, indicating that the correction curve fit well with the ideal curve. **Conclusion** Age, smoking history, diabetes, LAD, Gensini score and NT-proBNP are independent influencing factors of new onset atrial fibrillation during hospitalization in AMI patients. The nomogram model based on the above independent influencing factors in predicting the risk of new onset atrial fibrillation during hospitalization in AMI patients has a higher predictive power.

【 Key words 】 Myocardial infarction; New onset atrial fibrillation; Root cause analysis; Nomogram model; Forecasting

急性心肌梗死 (acute myocardial infarction, AMI) 是临床常见的急危重症, 发病迅速, 据相关数据显示, 中国 2.9 亿心血管疾病患者中有 250 万例 AMI 患者, 且 AMI 死亡率高达 10%^[1]。近年随着循证医学发展, 经皮冠状动脉介入术 (percutaneous coronary intervention, PCI) 在 AMI 患者中得到较好的推广与应用, 其可使患者梗死血管被及时开通并实现再灌注, 进而有效延缓病情发展^[2]。但 AMI 患者 PCI 后并发症仍是当前关注的重点, 尤其是新发心房颤动, 发生率高达 6%~21%^[3]。心房颤动会改变 AMI 患者血流动力学, 使病情恶化, 增加患者死亡风险。但 AMI 患者新发心房颤动的机制尚未明确, 临床缺乏有效的预测指标。基于此, 本研究整合了 AMI 患者院内新发心房颤动的危险因素并构建风险预测列线图模型, 旨在帮助临床医生早期识别伴有新发心房颤动高风险的 AMI 患者并早期采取有针对性的干预措施。

1 对象与方法

1.1 研究对象 选取 2017 年 1 月至 2021 年 3 月在青岛市市立医院行急诊 PCI 的 513 例 AMI 患者作为研究对象。纳入标准: (1) 年龄 ≥ 18 岁; (2) 既往无心房颤动病史; (3) 发病后 24 h 内入院行急诊 PCI; (4) 人口学特征、临床资料完整。排除标准: (1) 合并恶性肿瘤; (2) 伴有非梗阻性冠心病、原发性心肌病; (3) 有临床感染证据; (4) 伴有免疫系统疾病; (5) 合并严重肝、肾功能障碍; (6) 急诊 PCI 前 6 个月内有严重创伤史、输血史、手术史; (7) 伴有贫血。按照患者院内是否新发心房颤动分为房颤组 ($n=82$) 和非房颤组 ($n=431$)。

1.2 研究方法

1.2.1 资料收集 通过医院信息系统 (hospital information system, HIS) 收集 AMI 患者人口学特征及入院时临床资料, 包括年龄、性别、吸烟史、心率、收缩压、合并症 (包括高

血压、糖尿病及血脂异常)、心脏彩超检查结果 [包括左心室射血分数 (left ventricular ejection fraction, LVEF)、左心房内径 (left atrial diameter, LAD) 及左房室瓣反流发生情况]、Gensini 积分、实验室检查指标 [包括白细胞计数、血红蛋白、超敏 C 反应蛋白 (high-sensitivity C-reactive protein, hs-CRP)、心肌肌钙蛋白 I (cardiac troponin I, cTnI)、N 末端 B 型利钠肽前体 (N-terminal pro-B-type natriuretic peptide, NT-proBNP)]。吸烟史定义: 吸烟 ≥ 1 支/d, 连续吸烟时间 > 6 个月。高血压参照《中国高血压防治指南 (2018 年修订版)》^[4] 中的相关诊断标准: 收缩压 ≥ 140 mm Hg (1 mm Hg=0.133 kPa) 和 / 或舒张压 ≥ 90 mm Hg。糖尿病参照《中国 2 型糖尿病防治指南 (2017 年版)》^[5] 中的相关诊断标准, 即空腹血糖 ≥ 7.0 mmol/L 或餐后随机血糖 ≥ 11.1 mmol/L。血脂异常定义: 存在高胆固醇血症、高三酰甘油血症、高低密度脂蛋白胆固醇血症中的任意一项。根据冠状动脉造影检查结果计算 Gensini 积分^[6], 每处病变积分为狭窄程度评分乘以病变部位评分, 所有病变积分总和为 Gensini 积分。冠状动脉狭窄程度及病变部位评分标准如下: (1) 狭窄程度: 100% 记 32 分, 91%~99% 记 16 分, 76%~90% 记 8 分, 51%~75% 记 4 分, 26%~50% 记 2 分, 1%~25% 记 1 分; (2) 病变部位: 小分支记 0.5 分, 左前降支远段记 1.0 分, 右冠状动脉记 1.0 分, 左回旋支中段或远段记 1.0 分, 左前降支中段记 1.5 分, 左前降支或回旋支近段记 2.5 分, 左主干记 5 分。

1.2.2 新发心房颤动诊断标准 患者住院期间行 12 导联心电图或动态心电图检查发现心房颤动或心房扑动, 或在心电图监护下能捕捉到持续 30 s 以上的心房颤动, 则定义为新发心房颤动^[7]。

1.3 统计学方法 采用 SPSS 19.0 统计学软件进行数据处理。计数资料以 n (%) 表示, 组间比较采用 χ^2 检验; 计量资料以

($\bar{x} \pm s$) 表示, 组间比较采用成组 t 检验; 采用多因素 Logistic 回归模型分析 AMI 患者院内新发心房颤动的影响因素; 采用 R 3.4.3 软件包绘制列线图模型, 通过 rms 程序包建立列线图模型及校准曲线, 并进行 Hosmer-Lemeshow 拟合优度检验; 绘制受试者工作特征 (receiver operating characteristic, ROC) 曲线以评估列线图模型的预测效能, 并采用 Bootstrap 方法重复抽样 1 000 次验证列线图模型的预测效能。

2 结果

2.1 两组人口学特征及入院时临床资料比较 房颤组与非房颤组男性占比、心率 > 100 次/min 者所占比例、收缩压 < 100 mm Hg 者所占比例、高血压发生率、血脂异常发生率、LVEF < 50% 者所占比例、左房室瓣反流发生率、白细胞计数、血红蛋白、hs-CRP、cTnI 比较, 差异无统计学意义 ($P > 0.05$); 房颤组年龄和 LAD 大于非房颤组, 有吸烟史者所占比例、糖尿病发生率、Gensini 积分、NT-proBNP 高于非房颤组, 差异有统计学意义 ($P < 0.05$), 见表 1。

2.2 多因素 Logistic 回归分析 以 AMI 患者院内是否新发心房颤动 (赋值: 否 = 0, 是 = 1) 为因变量, 以表 1 中差异有统计学意义的指标为自变量, 进行多因素 Logistic 回归分析, 结果显示, 年龄、吸烟史、糖尿病、LAD、Gensini 积分、NT-proBNP 是 AMI 患者院内新发心房颤动的独立影响因素 ($P < 0.05$), 见表 2。

2.3 列线图模型构建与验证 将多因素 Logistic 回归分析筛选出的 6 个独立影响因素作为预测指标, 构建 AMI 患者院内新发心房颤动风险预测列线图模型, 见图 1。Hosmer-Lemeshow 拟合优度检验结果显示, 列线图模型的风险预测值与实际观察值的偏差比较, 差异无统计学意义 ($\chi^2=10.654, P=0.222$), 说明预测模型不存在过拟合现象。ROC 曲线分析结果显示, 列线图模型预测 AMI 患者院内新发心房颤动的曲线下面积 (area under curve, AUC) 为 0.839 [95%CI (0.786, 0.892)], 见图 2, 说明列线图模型的区分能力较好。采用 Bootstrap 方法重复抽样 1 000 次验证列线图模型发现, 校准曲线的平均绝对误差 (mean absolute error, MAE) 为 0.019, 说明校准曲线与理想曲线贴合良好, 见图 3。

3 讨论

新发心房颤动不仅会引起 AMI 患者心功能进一步恶化, 还会增加缺血性卒中发生风险, 进而影响患者预后。MAAGH 等^[8]研究表明, 心房颤动会增加 AMI 患者院内死亡率并缩短患者院外生存时间。WORE 等^[9]研究表明, 合并新发心房颤动的 AMI 患者总死亡率高于无新发心房颤动的 AMI 患者, 究其原因可能如下: 心房颤动可导致患者心率加快、心室电活动不规则、心室充盈量减少, 心肌耗氧增加, 缺血、缺氧加重, 使患者血管梗死面积扩大、心功能恶化加速, 进而增加死亡风险。因此, 早期有效、鉴别伴有新发心房颤动高风险的 AMI 患者极为重要。

本研究结果显示, 本组患者中院内新发心房颤动 82 例, 发生率为 15.98%, 与国内外报道基本一致^[10-11] 本研究多因素 Logistic 回归分析结果显示, 年龄、吸烟史、糖尿病、LAD、Gensini 积分、NT-proBNP 是 AMI 患者院内新发

表 1 两组人口学特征及入院时临床资料比较

Table 1 Comparison of demographic features and clinical data at admission between the two groups

人口学特征及临床资料	房颤组 (n=82)	非房颤组 (n=431)	$\chi^2 (t)$ 值	P 值
年龄 ($\bar{x} \pm s$, 岁)	67.6 ± 8.6	64.0 ± 8.5	3.593 ^a	< 0.001
男性 [n (%)]	63 (76.8)	344 (79.8)	0.374	0.541
吸烟史 [n (%)]	47 (57.3)	182 (42.2)	6.348	0.012
心率 > 100 次/min [n (%)]	35 (42.7)	154 (35.7)	1.431	0.232
收缩压 < 100 mm Hg [n (%)]	24 (29.3)	96 (22.3)	1.881	0.170
高血压 [n (%)]	31 (37.8)	122 (28.3)	2.970	0.085
糖尿病 [n (%)]	27 (32.9)	64 (14.8)	10.818	0.001
血脂异常 [n (%)]	38 (46.3)	166 (38.5)	1.762	0.184
LVEF < 50% [n (%)]	33 (40.2)	135 (31.3)	2.490	0.115
LAD ($\bar{x} \pm s$, mm)	38.2 ± 4.5	35.9 ± 5.0	3.714 ^a	< 0.001
左房室瓣反流 [n (%)]	7 (8.5)	22 (5.1)	1.522	0.217
Gensini 积分 ($\bar{x} \pm s$, 分)	83.5 ± 19.1	67.3 ± 19.1	7.069 ^a	< 0.001
白细胞计数 ($\bar{x} \pm s$, × 10 ⁹ /L)	8.94 ± 2.05	8.69 ± 2.13	0.979 ^a	0.328
血红蛋白 ($\bar{x} \pm s$, g/L)	131 ± 18	134 ± 19	1.283 ^a	0.199
hs-CRP ($\bar{x} \pm s$, mg/L)	4.17 ± 1.12	3.96 ± 1.05	1.642 ^a	0.101
cTnI ($\bar{x} \pm s$, μg/L)	2.48 ± 0.63	2.37 ± 0.72	1.292 ^a	0.197
NT-proBNP ($\bar{x} \pm s$, ng/L)	979 ± 249	819 ± 198	6.436 ^a	< 0.001

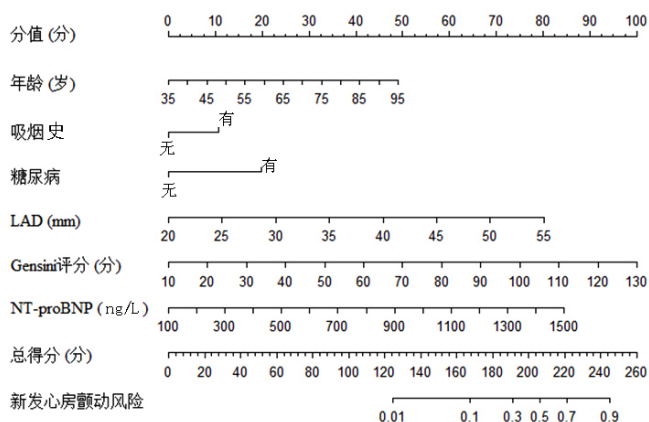
注: LVEF= 左心室射血分数, LAD= 左心房内径, hs-CRP= 超敏 C 反应蛋白, cTnI= 心肌肌钙蛋白 I, NT-proBNP=N 末端 B 型利钠肽前体; ^a 表示 t 值

表 2 AMI 患者院内新发心房颤动影响因素的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis on influencing factors of new onset atrial fibrillation during hospitalization in patients with AMI

变量	赋值	β	SE	Wald χ^2 值	P 值	OR (95%CI)
年龄	实测值	0.046	0.018	6.526	0.011	1.047 (1.011, 1.085)
吸烟史	无 = 0, 有 = 1	0.603	0.287	4.427	0.035	1.828 (1.042, 3.206)
糖尿病	无 = 0, 有 = 1	1.122	0.326	11.867	0.001	3.073 (1.622, 5.819)
LAD	实测值	0.129	0.032	16.452	< 0.001	1.138 (1.069, 1.211)
Gensini 积分	实测值	0.047	0.008	35.581	< 0.001	1.048 (1.032, 4.064)
NT-proBNP	实测值	0.108	0.031	12.137	< 0.001	1.114 (1.069, 2.005)

心房颤动的独立影响因素, 可能原因如下: (1) 随着年龄增长, 心肌出现退化及纤维化, 导致心肌应激性、自律性、兴奋性及传导性下降, 心肌电活动不稳定, 进而增加患者心房颤动发生风险, 与熊丹群等^[12] 研究结果一致。(2) 吸烟产生的烟雾及微粒状物质均可刺激交感神经传递, 引起血浆中儿茶酚胺浓度升高, 致使心率加快; 另外, 香烟中的尼古丁还可作用于心房肌细胞中的离子通道, 导致心肌电活动不稳定, 进而易诱发心房颤动, 与 SUZUKI 等^[13] 报道的吸烟是心房颤动的独立危险因素一致。(3) 糖尿病患者长期处于糖代谢紊乱状态, 可造成心肌收缩力、心输出量降低, 直接导致包括心房颤动在内的心律失常^[14]; 而随着患者体内肾上腺素被激活, 心肌坏死可直接导致应激性高血糖, 进而诱发心房颤动。KORACEVIC 等^[15] 研究报道, 伴有高血糖的 AMI 患者住院期



注: LAD=左心房内径, NT-proBNP=N末端B型利钠肽前体

图1 AMI患者院内新发心房颤动风险预测列线图模型

Figure 1 Nomogram model for predicting the risk of new onset atrial fibrillation during hospitalization in patients with AMI

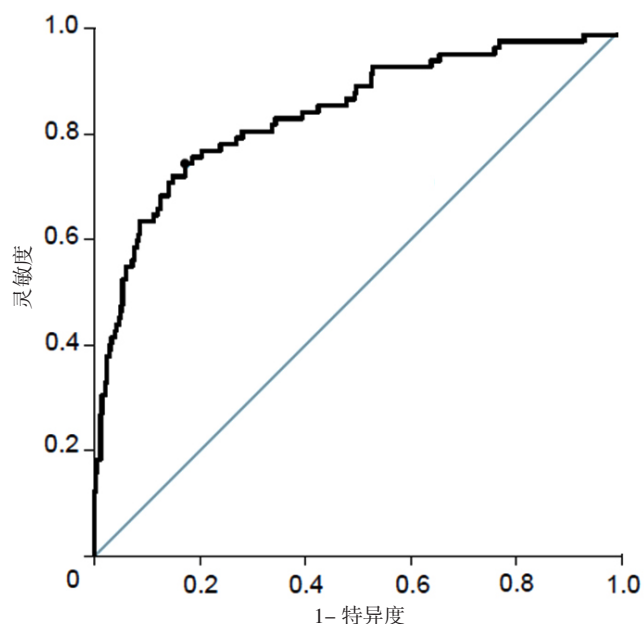


图2 列线图模型预测AMI患者院内新发心房颤动的ROC曲线

Figure 2 ROC curve of nomogram model in predicting the risk of new onset atrial fibrillation during hospitalization in patients with AMI

间新发心房颤动的风险是未伴有高血糖的AMI患者的14.5倍。

(4) AMI患者因部分冠状动脉堵塞导致心肌失去血液供应而坏死,在该过程中患者左心室舒张末期压力明显增高,使左心房负荷增加及LAD增大,引起机械-电反馈和神经改变^[16],使扩张的心房电活动不稳定,进而增加心房颤动发生风险。

(5) Gensini积分是评估冠状动脉病变严重程度的常用工具,积分越高提示患者冠状动脉病变程度越严重,其侧支循环供血越差、心肌缺血越严重,故该类患者心功能更易受损,肾素-血管紧张素-醛固酮系统激活也更明显,这极大地增加了心房颤动的发生风险。(6) NT-proBNP是一种无生物活性的蛋白质,其生物学机制相对稳定^[17]。但在左心室容量增大的情况下NT-proBNP水平会明显升高^[18],NT-proBNP水平与冠心病患者心功能呈负相关^[19]。AMI患者心肌缺血缺氧导致冠

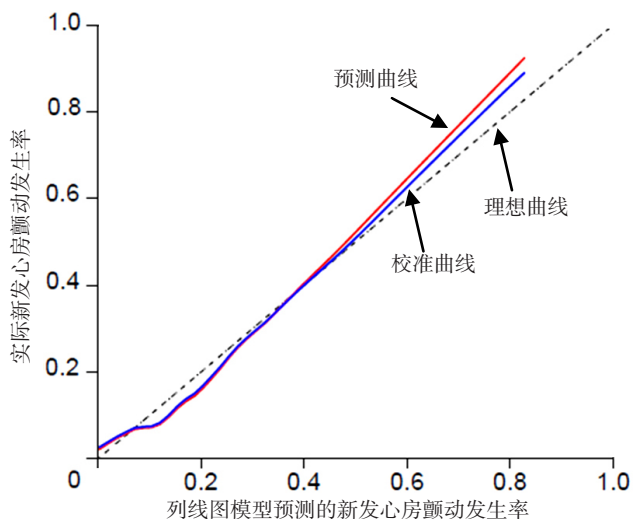


图3 列线图模型预测AMI患者院内新发心房颤动的校准曲线

Figure 3 Calibration curve of nomogram model in predicting the risk of new onset atrial fibrillation during hospital in patients with AMI

状动脉痉挛、血管重塑、血液黏稠度增加、醛固酮水平升高,这一过程可使心房压力增加、心房受到牵拉,致使心肌细胞合成或分泌NT-proBNP并进入血液循环。而心房压力增大与心房牵拉均会导致心房有效不应期缩短,无法保障脏器得到较好的血流灌注,进而增加心房颤动发生风险。

良好的预测模型不仅需要筛选有效的预测指标,还需要临床应用的简化。既往研究表明,列线图模型在预测AMI患者术后院内源性休克风险^[20]、急性肾损伤风险^[21]等方面均具有较好的效果。但国内尚缺乏对AMI患者院内新发心房颤动风险预测列线图模型的探索。本研究将多因素Logistic回归分析筛选出的6个独立影响因素作为预测指标,构建AMI患者院内新发心房颤动风险预测列线图模型,并经过内、外部验证表明,该列线图模型不存在过拟合现象,区分能力较好,且预测AMI患者院内新发心房颤动风险与实际新发心房颤动风险具有良好的一致性。

综上所述,年龄、吸烟、糖尿病、LAD、Gensini积分及NT-proBNP是AMI患者院内新发心房颤动的独立影响因素,而基于上述影响因素构建的AMI患者院内新发心房颤动风险预测列线图模型具有较高的预测效能,临床可根据该列线图模型筛选出伴有新发心房颤动高风险的AMI患者并给予其针对性的预防措施,以降低患者院内新发心房颤动风险。

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本文无利益冲突。

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