

◇ 临床医学研究 ◇

非瓣膜性持续性房颤患者合并左心室肥厚的危险因素模型预测及预后分析

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摘要 目的 构建非瓣膜性持续性心房颤动(PeAF)患者合并左心室肥厚(LVH)列线图的预测模型, 随访并进行预后分析。方法 纳入初次诊断且接受住院治疗的非瓣膜性PeAF患者949例(其中合并LVH为403例), 并随机分为训练集(665例)和验证集(284例), 通过二元Logistic回归筛选PeAF合并LVH的独立危险因素, 构建列线图预测模型, 并通过受试者工作特征(ROC)曲线、校准曲线和决策曲线评估模型的预测性能。结果 最终筛选出女性、高血压(HTN)、糖尿病(DM)、红细胞分布宽度-SD值(RDW-SD)、身体质量指数(BMI)、左心房内径(LAD)、左心室射血分数(LVEF)共7项独立危险因素, 并将其纳入预测模型, 训练集中的ROC曲线下面积(AUC)为0.862(95%CI:0.834~0.890), 验证集中的AUC为0.870(95%CI:0.829~0.911), 显示出良好的预测效能。结论 PeAF患者合并LVH的独立危险因素包括女性、HTN、DM、RDW-SD、BMI、LAD、LVEF, 基于此所构建的预测模型有助于早期识别PeAF发生LVH的高危人群。同时, 通过COX回归分析发现房颤合并LVH患者可能从导管消融治疗中获益。

关键词 持续性心房颤动; 左心室肥厚; 危险因素; 列线图; 主要心血管不良事件; 复发; Cox回归分析

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左心室肥厚(left ventricular hypertrophy, LVH)是一种继发于左心室壁厚增加、左心室腔扩大, 或两者同时发生的左室质量增加的病症。临床研究^[1]指出, LVH通常与心脏性猝死的高风险相关, 并且是心血管死亡的预测因子。左心室作为左心房的延续, 两者互相影响, 在持续性心房颤动(persistent atrial fibrillation, PeAF)疾病发展进程中, 心房和心室共同经历了从电重构到结构重构的过程^[2-3], LVH可能为其主要及早期改变之一。PeAF合并LVH患者的病因及预后尚未完全明确。目前研究推测, 这种病理改变可能与房颤(atrial fibrillation, AF)本身的直接影响(如心房重构、心室负荷增加和心输出量降低等)直接相关, 同时也可能受到AF共病如HTN、DM、肾功能不全等协同作用的推动。在这些因素共同作用下, 进一步加重了心肌的重构和功能障碍^[4]。因此, 深入研究AF与共病之间影响的

交互机制, 对于明确病因、优化治疗策略具有重要意义。

本研究旨在探讨PeAF患者合并LVH的危险因素及预后, 通过结合临床经验和统计分析, 筛选最具预测价值的变量, 并构建相应的预测模型, 以期将列线图结果与个体化治疗相结合, 为不同风险水平的患者提供具体的干预措施。

1 材料与方法

1.1 病例资料 本研究纳入2022年1月—2023年10月在该医院首次诊断非瓣膜性PeAF且年龄 ≥ 18 岁的住院患者949例(根据是否合并LVH, 分为LVH组403例, 非LVH组546例; 男性628例, 女性321例; 年龄范围为23~89岁, 年龄中位数为67岁)。将其随机按照7:3的比例纳入训练集($n=665$ 例)和验证集($n=284$ 例)。纳入标准为: 符合2023年心房颤动诊断和治疗中国指南^[5]中PeAF诊断标准的患者。排除标准为: ① 心肌病患者; ② 甲状腺功能异常患者; ③ 恶性肿瘤个人史; ④ 中重度慢性阻塞性肺病患者; ⑤ 安装心脏起搏器/电除颤设备患者; ⑥ 数据缺失严重及失访的患者。本研究经安徽医科大学第一

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1.2 数据收集

1.2.1 一般临床信息 通过东华医为电子病历系统收集患者的一般资料,包括:性别、年龄、身体质量指数(body mass index, BMI)、既往史[高血压(hypertension, HTN)、糖尿病(DM)、脑梗死(cerebral infarction, CI)、冠心病(coronary heart disease, CHD)、慢性心力衰竭(chronic heart failure, CHF)]、用药史[β 受体阻滞剂、血管紧张素转换酶抑制剂(angiotensin-converting enzyme inhibitor, ACEI)/血管紧张素 II 受体拮抗剂(angiotensin II receptor blocker, ARB)/血管紧张素受体-脑啡肽酶抑制剂(angiotensin receptor-neprilysin inhibitor, ARNI)/钠-葡萄糖共转运蛋白 2 抑制剂(sodium-glucose co-transporter 2 inhibitor, SGLT-2)]。

1.2.2 实验室指标 收集患者入院后首次完成的血液检验数据,包括:脑钠肽(brain natriuretic peptide, BNP)、血常规、血生化,共3大类。其中部分指标经计算后可得出:中性粒细胞-淋巴细胞计数比(neutrophil to lymphocyte ratio, NLR)、单核细胞-高密度脂蛋白胆固醇比(monocyte to high density lipoprotein cholesterol ratio, MHR)、尿酸肌酐比(uric acid to creatinine ratio, UACR)。

1.2.3 经胸超声心动图(transsthoracic echocardiography, TTE)、食管超声心动图(transesophageal echocardiography, TEE)和心电图检查 经TTE与TEE检查由高年资心脏超声科医师使用飞利浦EPIQ 7C超声诊断系统完成。TTE检查通过采集胸骨旁左心室长轴切面以及心尖三切面连续3个心动周期动态图像,测量左心房内径(left atrial diameter, LAD)、左心室舒张末期内径(left ventricular end-diastolic diameter, LVEDD)、室间隔厚度(interventricular septum thickness, IVST)、左心室后壁厚度(left ventricular posterior wall thickness, LVPWT)、左心室射血分数(left ventricular ejection fraction, LVEF)、左室壁相对厚度(relative wall thickness, RWT, $RWT=2 \times LVPWT / LVEDD$)。AF患者心电图(electrocardiogram, ECG)中f波振幅测量方法如下:自QRS波群后2~3个f波开始测量,以连续测量10~20个f波为一组,测量从f波峰顶到谷底的垂直距离所代表的AF波电压,随机选择3组f波振幅并求均值,根据f波的粗细可分为粗波型AF(f波振幅 >0.1 mV)、细波型AF(f波振幅 ≤ 0.1 mV)。

1.3 LVH的诊断 LVH的TTE诊断标准为:左心室质量指数(left ventricular mass index, LVMI);男性 >115 g/m²,女性 >95 g/m²,或左室壁厚度(left ventricular wall thickness, LVWT) ≥ 12 mm。LVMI计算公式:LVMI(g/m²)=左心室质量(left ventricular mass, LVM)/体表面积(body surface area, BSA);LVM(g)= $1.04 \times [(LVEDD+IVST+LVPWT)^3-LVEDD^3] \times 0.8+0.6$ (单位均为cm);BSA(m²)= $0.007184 \times$ 身高(cm)^{0.725} \times 体质量(kg)^{0.425}[6]。

1.4 纳入患者治疗措施 PeAF患者入院后,根据病情需要及患者意愿,分别接受药物治疗或导管射频消融术(radiofrequency catheter ablation, RFCA)加药物治疗。所有手术患者均完成环双肺静脉隔离术,此外,基于患者心房基质水平进行额外消融(如上腔静脉隔离、二尖瓣峡部线、左心房顶部线和三尖瓣峡部线等)。完成线性消融的患者应用不同的起搏策略来确认阻滞线的双向阻滞情况。消融术后进行30 min的监测,再次验证是否阻滞;若验证肺静脉隔离及线性消融阻滞后方颤仍然持续存在,则用直流电复律恢复患者的窦性心律。导管消融术后复发定义为:RFCA术3个月后发生持续时间 ≥ 30 s的房颤、房扑、房速。

1.5 终点事件定义与随访 研究终点为主要不良心血管事件(major adverse cardiovascular event, MACE)(包括心力衰竭、脑卒中、急性心肌梗死、严重室性心律失常、死亡)、房颤导管消融术后复发。

该研究由专门人员负责随访工作,研究者对患者出院1个月、3个月、6个月及12个月时通知其门诊随访,进行心电图及动态心电图检查。随访期间,若患者发生心血管症状,可通过随访电话联系随访人员获得就诊建议,并建档记录患者资料。随访时间为1年。

1.6 统计学处理 应用SPSS 26.0软件和R软件(R 4.4.2)进行数据处理。符合正态分布的计量资料采用 $\bar{x} \pm s$ 进行描述,偏态分布的计量资料采用 $M(P_{25}, P_{75})$ 进行描述,组间比较分别采用独立样本 t 检验、Mann-Whitney U 秩和检验;计数资料采用率、例或百分比进行描述,组间比较采用 χ^2 检验。采用单因素及多因素二元Logistic回归分析筛选出独立危险因素,并应用R软件构建列线图预测模型,使用受试者工作特征(receiver operating characteristic, ROC)曲线下面积(area under curve, AUC)、校准曲线、决策曲线(decision curve analysis, DCA)对模型

的区分度、校准度、临床获益性进行验证。最后采用Cox比例风险回归模型探讨PeAF患者预后。检验过程均应用双侧检验, $P < 0.05$ 表示差异有统计学意义。

2 结果

2.1 临床基线特征分析 本研究共纳入1 166例符合标准的患者,其中949例完成出院后随访并获得明确复发或MACE信息,其余217例患者在出院后3个月内失访,无法判断是否发生复发或MACE,未纳入后续生存分析。最终,研究以这949例完成随访的患者为分析对象,将其按7:3随机分为验证集(665例)及训练集(284例),表1总结了患者的临

床基线资料。训练集及验证集患者在性别、年龄、DM、HTN、冠心病、慢性心力衰竭、脑梗死、BMI、BNP、NLR、红细胞计数(red blood cell, RBC)、血红蛋白(hemoglobin, HGB)、红细胞比容(hematocrit, HCT)、RDW-CV、RDW-SD、总胆红素(total bilirubin, TBil)、直接胆红素(direct bilirubin, DBil)、血尿素氮(blood urea nitrogen, BUN)、UACR、eGFR、空腹血糖(fasting plasma glucose, FPG)、三酰甘油(triglyceride, TG)、MHR、LP(a)、LAD、LVEF、心电图f波型、左心耳血栓(left atrial appendage thrombus, LAAT)、 β 受体阻滞剂、ACEI/ARB/ARNI、醛固酮受体阻滞剂、LVH上均无明显差异($P > 0.05$)。两组患者在SGLT-2受体阻滞剂上有差异($P < 0.05$)。

表1 临床资料分析 [$n(\%)$, $\bar{x} \pm s$, $M(P_{25}, P_{75})$]

Tab. 1 Analysis of clinical data [$n(\%)$, $\bar{x} \pm s$, $M(P_{25}, P_{75})$]

Factors	Groups		Z/t/ χ^2 value	P value
	Training set (n=665)	Validation set (n=284)		
Gender			0.03	0.933
Male	439 (66.0)	189 (66.5)		
Female	226 (34.0)	95 (33.5)		
Age (years)	67.0 (59.0, 73.0)	67.0 (57.8, 72.0)	-0.83	0.405
History of DM			2.88	0.107
No	523 (78.6)	209 (73.6)		
Yes	142 (21.4)	75 (26.4)		
History of HTN			0.01	1.000
No	290 (43.6)	124 (43.7)		
Yes	375 (56.4)	160 (56.3)		
History of CI			0.73	0.447
No	537 (80.8)	236 (83.1)		
Yes	128 (19.2)	48 (16.9)		
History of CHD			0.09	0.834
No	551 (82.9)	233 (82.0)		
Yes	114 (17.1)	51 (18.0)		
History of CHF			0.77	0.421
No	380 (57.1)	171 (60.2)		
Yes	285 (42.9)	113 (39.8)		
BMI (kg/m ²)	24.9 (22.7, 27.5)	25.0 (22.7, 27.3)	-0.75	0.454
BNP (pg/mL)	401 (628)	393 (616)	-0.03	0.855
NLR	2.00 (1.53, 2.77)	2.09 (1.64, 2.81)	-1.13	0.259
RBC ($\times 10^{12}/L$)	4.49 (4.11, 4.86)	4.56 (4.14, 4.92)	-0.84	0.399
HGB (g/L)	138 (126, 149)	140 (127, 151)	-0.61	0.543
HCT (%)	41.7 (38.3, 44.7)	42.1 (38.3, 45.3)	-0.91	0.360
RDW-CV (%)	13.2 (12.5, 13.7)	13.2 (12.7, 13.9)	-1.22	0.223
RDW-SD (fL)	44.5 (42.3, 47.3)	44.8 (42.3, 47.4)	-0.36	0.719
TBil ($\mu\text{mol}/L$)	16.8 (13.0, 21.4)	15.9 (12.3, 21.4)	-1.43	0.154
DBil ($\mu\text{mol}/L$)	3.24 (2.43, 4.21)	3.10 (2.20, 4.19)	-1.13	0.258
BUN (mmol/L)	6.03 (5.04, 7.30)	6.12 (4.97, 7.74)	-0.93	0.352
UACR	4.80 (4.01, 5.74)	5.03 (4.14, 5.78)	-1.77	0.077

表 1(续)

Tab.1 (Continued)

Factors	Groups		$Z/t/\chi^2$ value	P value
	Training set (n=665)	Validation set(n=284)		
eGFR [mL/(min·1.73 m ²)]	91.0 (78.0,100.0)	92.0 (77.0,100.0)	-0.26	0.791
FPG (mmol/L)	5.27 (4.81,6.03)	5.29 (4.78,6.26)	-0.82	0.414
TG (mmol/L)	1.20 (0.94,1.73)	1.26 (0.95,1.74)	-0.52	0.605
MHR	0.34 (0.27,0.45)	0.35 (0.26,0.45)	-0.07	0.947
LP (a) (mg/L)	116 (58.0,233.0)	114 (57.1,236.0)	-0.49	0.623
LAD (cm)	4.65 (4.32,5.01)	4.60 (4.28,5.01)	-0.92	0.356
LVEF (%)	57.0 (53.0,60.0)	57.0 (54.0,61.0)	-0.52	0.601
Electrocardiogram f-wave pattern			0.01	0.978
Coarse wave pattern	281 (42.3)	121 (42.6)		
Fine wave pattern	384 (57.7)	163 (57.4)		
LAAT			2.51	0.151
No	619 (93.1)	272 (95.8)		
Yes	46 (6.92)	12 (4.23)		
Clinical medication history				
β -receptor blocker			0.27	0.669
No	536 (80.6)	233 (82.0)		
Yes	129 (19.4)	51 (18.0)		
ACEI/ARB/ARNI			1.50	0.249
No	426 (64.1)	170 (59.9)		
Yes	239 (35.9)	114 (40.1)		
Aldosterone receptor blocker			0.63	0.484
No	555 (83.5)	231 (81.3)		
Yes	110 (16.5)	53 (18.7)		
SGLT-2 inhibitor			4.78	0.039
No	609 (91.6)	247 (87.0)		
Yes	56 (8.42)	37 (13.0)		
LVH			0.65	0.464
No	377 (56.7)	169 (59.5)		
Yes	288 (43.3)	115 (40.5)		

2.2 训练集人群的单因素和多因素 Logistic 回归

分析 训练集人群中单因素 Logistic 回归分析和共线性检验分析结果显示,性别($P<0.001$)、年龄($P<0.001$)、HTN($P<0.001$)、DM($P<0.001$)、BMI($P=0.03$)、BNP($P<0.001$)、红细胞计数($P<0.001$)、HGB($P<0.001$)、红细胞比容($P<0.001$)、RDW-CV($P<0.001$)、RDW-SD($P<0.001$)、总胆红素($P=0.005$)、直接胆红素($P=0.001$)、BUN($P<0.001$)、eGFR($P<0.001$)、LAD($P<0.001$)、LVEF($P<0.001$)、心电图f波型($P=0.06$)与PeAF患者合并LVH有相关性(表2),且无明显共线性(容忍度Tol均 >0.1 、方差膨胀因子VIF均 <10)。将以上变量纳入多因素 Logistic 回归分析,以是否合并LVH(合并=1,未合并=0)为因变量,结果显示,性别、HTN、

DM、LAD、LVEF、BMI、RDW-SD是PeAF患者合并LVH的独立危险因素(表2)。

2.3 列线图构建 基于训练集多因素二元 Logistic 回归分析筛选出的7项独立危险因素构建列线图预测模型。见图1。

2.4 列线图模型的验证与预测精度评价 为评估预测模型的性能,分别绘制了训练集与验证集的ROC曲线(图2A、2B),其AUC值分别为0.862(95%CI: 0.834~0.890)、0.870(95%CI: 0.829~0.911),提示预测模型具有较好的区分度。绘制校准曲线(图3A、3B),训练集和验证集的校准曲线的Hosmer-Lemeshow检验 χ^2 值分别为6.287($P=0.615$)和4.856($P=0.773$),差异无统计学意义,表明列线图模型的预测概率曲线与理想曲线之间均

表 2 训练集单因素和多因素 Logistic 回归分析 [$M(P_{25}, P_{75})$]

Tab. 2 Univariate and multivariate Logistic regression analysis of training set [$M(P_{25}, P_{75})$]

Factors	Univariate logistic regression analysis		Univariate logistic regression analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
Gender				
Male				
Female	3.67 (2.78, 4.88)	<0.001	3.30 (1.07, 7.80)	<0.001
Age (years)	1.03 (1.02, 1.04)	<0.001		
History of DM	4.60 (3.32, 6.42)	<0.001	4.72 (2.94, 6.42)	<0.001
History of HTN	2.23 (1.71, 2.92)	<0.001	1.78 (1.71, 2.92)	0.008
History of CI	1.10 (0.79, 1.53)	0.582		
History of CHD	1.91 (1.37, 2.69)	<0.001		
History of CHF	3.54 (2.70, 4.65)	<0.001		
BMI (kg/m ²)	0.96 (0.93, 1.00)	0.030	0.92 (0.87, 0.97)	0.002
BNP (pg/mL)	1.00 (1.00, 1.00)	<0.001		
NLR	1.02 (0.95, 1.09)	0.566		
RBC (×10 ¹² /L)	0.65 (0.52, 0.81)	<0.001		
HGB (g/L)	0.98 (0.97, 0.99)	<0.001		
HCT (%)	0.95 (0.93, 0.98)	<0.001		
RDW-CV (%)	1.46 (1.30, 1.65)	<0.001		
RDW-SD (fL)	1.08 (1.05, 1.12)	<0.001	1.01 (1.05, 1.10)	0.029
TBil (μmol/L)	1.02 (1.01, 1.04)	0.005		
DBil (μmol/L)	1.14 (1.06, 1.23)	0.001		
BUN (mmol/L)	1.13 (1.07, 1.20)	<0.001		
UACR	0.99 (0.90, 1.08)	0.747		
eGFR [mL/(min·1.73 m ²)]	0.98 (0.98, 0.99)	<0.001		
FPG (mmol/L)	0.98 (0.91, 1.05)	0.516		
TG (mmol/L)	0.91 (0.77, 1.08)	0.263		
MHR	1.01 (0.82, 1.26)	0.900		
LP (a) (mg/L)	1.00 (1.00, 1.00)	0.249		
LAD (cm)	3.52 (2.66, 4.66)	<0.001	3.75 (2.38, 5.90)	<0.001
LVEF (%)	0.89 (0.87, 0.90)	<0.001	0.89 (0.86, 0.92)	<0.001
AF of fine wave pattern	1.44 (1.11, 1.88)	0.006		
LAAT	1.60 (0.94, 2.75)	0.085		
β receptor blocker	1.20 (0.86, 1.66)	0.274		
ACEI/ARB/ARNI	1.06 (0.81, 1.38)	0.674		
Aldosterone receptor blocker	1.09 (0.77, 1.53)	0.628		
SGLT-2 inhibitor	1.50 (0.98, 2.32)	0.063		

具有较好的一致性。DCA 曲线(图 4A、4B)显示,无论是在训练集还是验证集中,列线图都能够较好地预测 PeAF 合并 LVH 的风险,具有较好的净收益。

2.5 预后分析

2.5.1 Cox 回归分析影响 RFCA 术后复发的危险因素 纳入研究患者单因素 Cox 回归分析和共线性检验分析结果显示,年龄、LAD、细波型 AF、RDW-CV、RDW-SD、HGB、HCT、血肌酐 (serum creatinine, CRE)、尿酸(uric acid, UA)等多个变量差异有统计学意义($P<0.05$),且无明显共线性(容忍度 Tol 均>

0.1、方差膨胀因子 VIF 均<10)。进一步多因素 Cox 回归分析并控制其他混杂因素后,显示 LAD 增大和细波型 AF 为 RFAC 术后复发的独立危险因素(表 3)。

2.5.2 Cox 回归分析发生 MACE 事件的危险因素 纳入研究患者单因素 Cox 回归分析和共线性检验分析结果显示,年龄、BNP、LAD、细波型 AF、LVEF、LVH、RFCA 差异有统计学意义($P<0.05$),且无明显共线性(容忍度 Tol 均>0.1、方差膨胀因子 VIF 均<10)。进一步多因素 Cox 回归分析并控制其他混杂

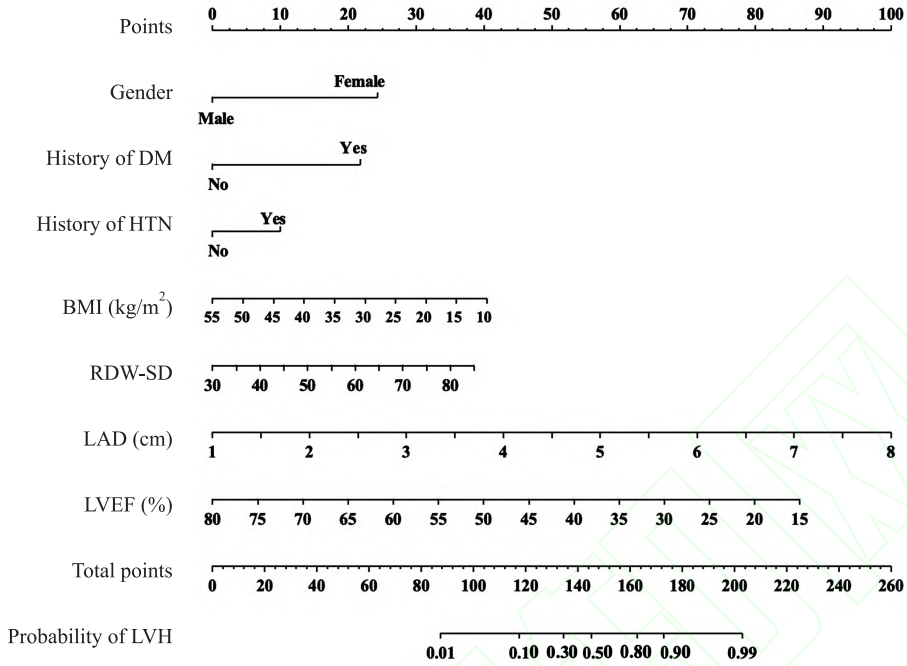


图1 非瓣膜性PeAF患者合并LVH风险列线图

Fig. 1 Nomogram for the risk of LVH in patients with non-valvular PeAF

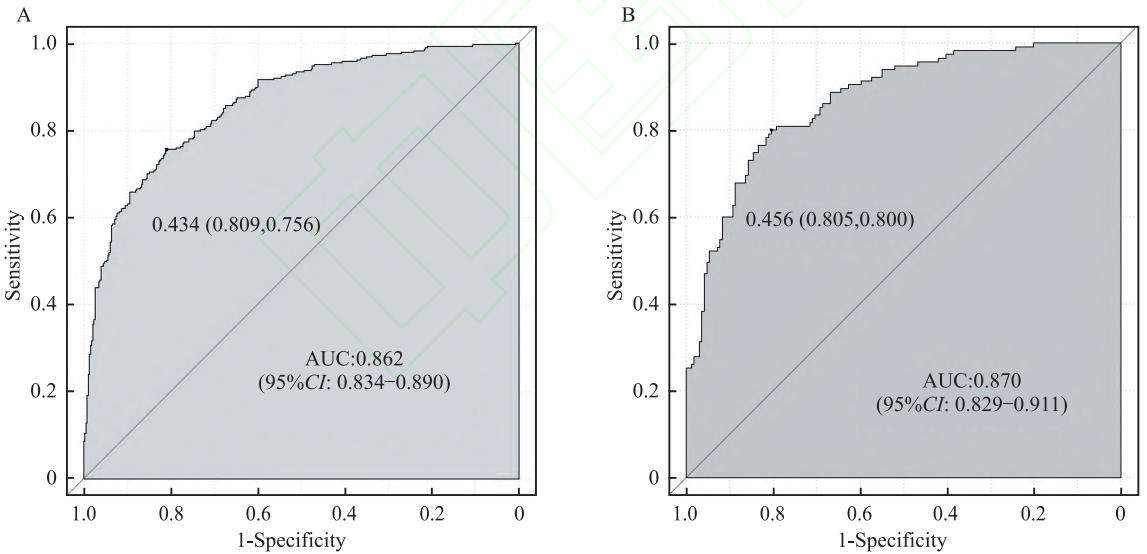


图2 训练集(A)和验证集(B)时间依赖性ROC曲线

Fig. 2 Time-dependent ROC curves of training set (A) and validation set (B)

因素后,年龄增长、LAD增大、细波型AF、LVEF降低、LVH是MACE事件的独立危险因素,而RFCA是MACE事件的保护性因素(表4)。

3 讨论

AF是临床上最常见的快速型心律失常之一,已逐渐成为中国乃至世界范围内严重的健康问题,容易导致缺血性卒中、外周动脉栓塞、心力衰竭、认知功能障碍、病死率增高等并发症,严重影响患者生

存质量^[5]。PeAF患者发生LVH可能是由于PeAF导致了心室的长期负荷增加、心室收缩与舒张功能的异常以及心肌纤维化的进行性改变。而PeAF的患者合并LVH是导致患者高病死率和治疗效果差的一种严重的病态。因此,早期识别并有效管理PeAF患者新发LVH的危险因素具有重要意义。在本研究中,多因素Logistic回归分析结果表明,女性、HTN、DM、LAD、LVEF、BMI、RDW-SD是PeAF合并LVH的重要危险因素。非瓣膜性PeAF患者合并

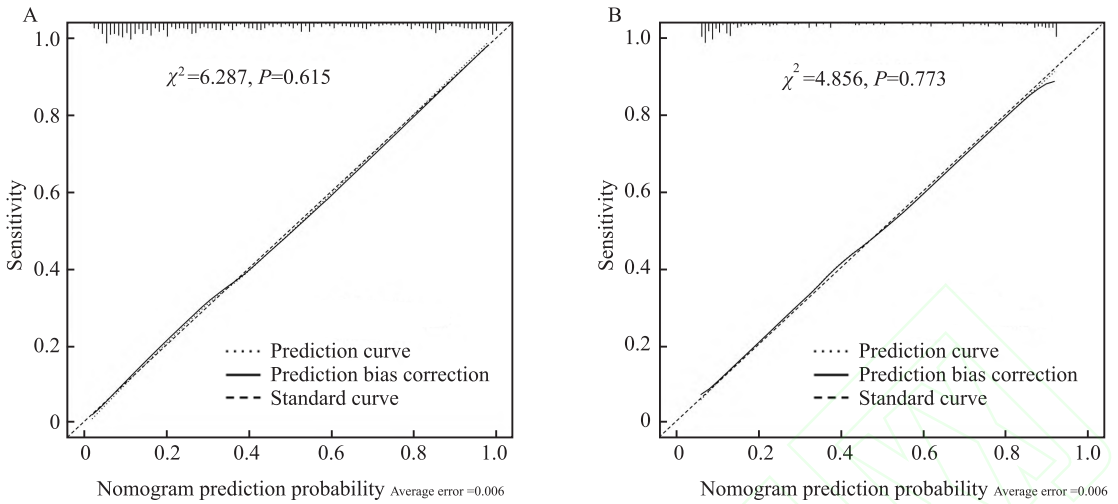


图3 训练集(A)与验证集(B)校准曲线

Fig. 3 Calibration curves of training set (A) and validation set (B)

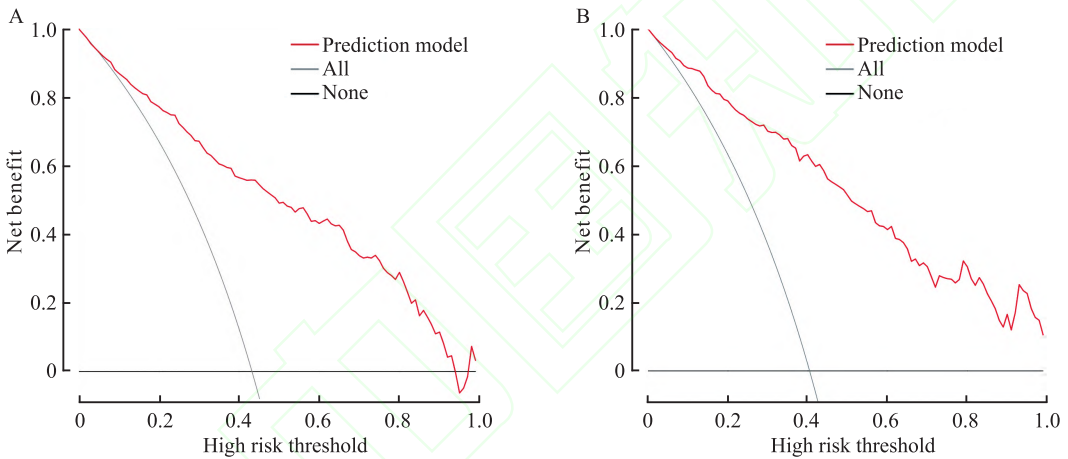


图4 训练集(A)与验证集决策曲线(B)

Fig. 4 Decision curves of training set (A) and validation set (B)

LVH的MACE事件发生率更高,RFCA可能降低MACE事件发生率。

性别对LVH的影响可能与性激素的差异有关。既往研究^[7]表明,男性与女性在心室重构的表现上存在显著差异,这与本研究的结果一致。此外,HTN和DM是已知的LVH重要危险因素,高血压通过长期的压力负荷促进心肌肥厚^[8],而糖尿病则可能通过代谢紊乱和炎症反应影响心肌结构和功能^[9]。

LAD和LVEF作为心脏结构和功能的直接指标,其异常变化可能反映左心室压力或容量负荷增加,从而促进LVH的发生。本研究进一步证实了这两项指标在预测LVH中的重要性。BMI与LVH的关联提示肥胖状态可能通过体循环阻力增加和代谢异常参与LVH的形成。Woodiwiss et al^[10]的研究表明,肥胖促进左心室向心而不是离心几何重塑。本研究中LVH组有55%的超重和肥胖患者,但却有

80%的患者发生的是离心性肥厚,这与上述研究相符。而RDW-SD用于评估红细胞大小的变异程度,有研究表明,RDW-SD还与心血管疾病的发生发展密切相关。Kilicaslan et al^[11]的一项研究显示,RDW是未经诊治的原发性高血压患者LVH的独立危险因素。本研究表明RDW-SD是PeAF患者合并LVH的独立危险因素,其机制可能与RASS激活、氧化应激及慢性炎症有关^[12]。

本研究通过对纳入患者随访观察显示,PeAF合并LVH的患者无论是在RFCA组还是非RFCA组中,MACE事件发生率均高于非LVH组;经RFCA治疗的PeAF患者中,合并LVH的复发率高于非LVH组;在LVH组中,经RFCA治疗的患者MACE事件的发生率低于药物治疗组。一项回顾性研究^[13]表明,心电图诊断LVH是PaAF患者RFCA术后复发的一个强有力的预测因子;一项大型的荟萃分析^[14]也

表3 Cox回归分析影响RFCA术后复发的危险因素

Tab.3 Cox regression analysis of the risk factors influencing the recurrence after RFCA surgery

Variables	Univariate			Multivariate		
	Z value	P value	HR (95%CI)	Z value	P value	HR (95%CI)
Age	2.85	0.004	1.02 (1.01-1.04)	0.21	0.831	1.00 (0.98-1.03)
RBC	-3.48	<0.001	0.68 (0.54-0.84)	-0.22	0.824	0.93 (0.49-1.76)
HGB	-3.72	<0.001	0.99 (0.98-0.99)	-0.03	0.980	1.00 (0.98-1.02)
HCT	-3.66	<0.001	0.96 (0.94-0.98)	-1.44	0.149	0.98 (0.95-1.01)
RDW CV	2.36	0.018	1.12 (1.02-1.23)	0.24	0.808	1.03 (0.82-1.29)
RDW SD	2.71	0.007	1.04 (1.01-1.06)	0.53	0.597	1.02 (0.96-1.08)
CRE	-2.10	0.036	0.99 (0.98-0.99)	-0.58	0.561	1.00 (0.99-1.01)
UA	-2.29	0.022	0.99 (0.99-0.99)	-1.16	0.247	1.00 (1.00-1.00)
LAD	5.59	<0.001	2.10 (1.62-2.72)	4.19	<0.001	2.14 (1.50-3.05)
Gender						
Female			1.00 (Reference)			1.00 (Reference)
Male	-2.57	0.010	0.70 (0.53-0.92)	-0.71	0.475	0.84 (0.52-1.36)
LVH						
No			1.00 (Reference)			1.00 (Reference)
Yes	2.66	0.008	1.43 (1.10-1.87)	-0.05	0.958	0.99 (0.65-1.51)
f-wave pattern						
Coarse wave pattern			1.00 (Reference)			1.00 (Reference)
Fine wave pattern	6.34	<0.001	2.66 (1.97-3.60)	5.09	<0.001	2.44 (1.73-3.44)

表4 Cox回归分析发生MACE事件的危险因素

Tab.4 Cox regression analysis of risk factors for the occurrence of MACE events

Factors	Univariate			Multivariate		
	Z value	P value	HR (95%CI)	Z value	P value	HR (95%CI)
Age	4.14	<0.001	1.03 (1.02-1.05)	2.97	0.003	1.03 (1.01-1.04)
BNP	3.70	<0.001	1.01 (1.01-1.01)	1.11	0.266	1.00 (1.00-1.00)
LAD	5.49	<0.001	1.08 (1.05-1.11)	4.06	<.001	1.07 (1.03-1.10)
LVEF	-5.56	<0.001	0.96 (0.95-0.98)	-3.28	0.001	0.97 (0.96-0.99)
LVH						
No			1.00 (Reference)			1.00 (Reference)
Yes	4.65	<0.001	1.87 (1.44-2.44)	2.06	0.040	1.40 (1.02-1.92)
f-wave pattern						
Coarse wave pattern			1.00 (Reference)			1.00 (Reference)
Fine wave pattern	4.51	<0.001	1.95 (1.46-2.61)	3.27	0.001	1.72 (1.24-2.39)
RFCA						
No			1.00 (Reference)			1.00 (Reference)
Yes	-5.68	<0.001	0.45 (0.34-0.59)	-2.67	0.008	0.64 (0.46-0.89)

表明, LVH是心房颤动患者不良后果风险增加的一个标志。综上所述, PeAF合并LVH导致一系列不良临床事件风险更高, 如进一步加重心功能不全、增加血栓栓塞的风险、使药物及手术治疗效果更差、增加病死率等。因此, 筛选高危人群是必要的, 并给予相应的治疗, 如控制血糖血压、减肥、RFCA治疗、抑制纤维化及氧化应激等新型药物的应用等, 对改善AF有积极作用^[15]。

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Analysis of risk factors in patients with nonvalvular persistent atrial fibrillation complicated with ventricular hypertrophy and construction and validation of prediction model

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Abstract Objective To construct a nomogram prediction model for non-valvular persistent atrial fibrillation (PeAF) patients with left ventricular hypertrophy (LVH), followed by prognostic analysis through follow-up. **Methods** This study retrospectively enrolled 949 patients with newly diagnosed and hospitalized non-valvular PeAF. Among them, 403 patients presented with LVH. The cohort was randomly stratified into a training set ($n=665$) and a validation set ($n=284$). Univariate and multivariate Logistic regression analyses were employed to identify independent risk factors for PeAF complicated by LVH. A nomogram prediction model was subsequently con-

structured and evaluated for discriminative ability, calibration, and clinical utility using receiver operating characteristic (ROC) curve analysis, calibration plots, and decision curve analysis (DCA). **Results** Seven independent risk factors were ultimately identified and included in the prediction model: female sex, hypertension, diabetes, red blood cell distribution width-SD (RDW-SD), body mass index (BMI), left atrial diameter (LAD), and left ventricular ejection fraction (LVEF). The area under the ROC curve (AUC) in the training set was 0.862 (95% CI: 0.834-0.890), and in the validation set, it was 0.870 (95% CI: 0.829-0.911), demonstrating excellent predictive performance. **Conclusion** Independent risk factors for LVH in PeAF patients include female, hypertension, diabetes, RDW-SD, BMI, LAD, and LVEF. The prediction model built based on this can help early identification of PeAF patients with high risk of LVH. At the same time, the incidence of major adverse cardiovascular events (MACE) is higher in PeAF patients with LVH. Patients with atrial fibrillation combined with LVH may benefit from catheter ablation.

Key words persistent atrial fibrillation; left ventricular hypertrophy; risk factor; nomogram; major adverse cardiovascular events; recrudescence; Cox regression analysis

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Preparation and hydrolytic activity analysis of dual-catalytic-triad PETase

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Abstract Objective To prepare a recombinant PETase with a dual-catalytic-triad and to evaluate its efficiency in the biodegradation of polyethylene terephthalate (PET). **Methods** Based on the crystal structure of wild-type PETase, point mutations (T88H/L117D) were introduced *via* site-directed mutagenesis. The recombinant protein was prepared using prokaryotic expression and chromatography purification techniques. The enzymatic hydrolysis of the mutant PETase was assessed by relatively quantifying the products mono (2-hydroxyethyl) terephthalate (MHET) and terephthalic acid (TPA). **Results** Both wild-type and mutant PETases accumulated as inclusion bodies, accounting for approximately 20% of the total bacterial protein. After solubilization in urea, the proteins were eluted at 300 mmol/L imidazole during affinity chromatography purification, with concentrations of 1.824 and 1.833 mg/mL and purities of 83.11% and 84.32%, respectively. Subsequent anion-exchange chromatography yielded highly pure enzymes in the 200 mmol/L NaCl fraction: 2.776 mg/mL (96.86% purity) for the wild type and 1.967 mg/mL (95.13% purity) for the mutant. Following refolding, the final concentrations were 0.484 mg/mL for the wild type and 0.991 mg/mL for the mutant. Hydrolysis assays revealed that the mutant released MHET and TPA at (237.67±17.00)% and (197.33±12.01)% of the wild-type levels, respectively. **Conclusion** The T88H/L117D dual-catalytic-triad PETase is successfully prepared and it significantly enhanced PET-degrading activity, thus, it's a promising biocatalyst for PET bioremediation.

Key words polyethylene terephthalate; hydrolase; dual catalytic triad; site-directed mutagenesis; recombinant protein; biodegradation

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