

• 专题研究:心脏疾病 •

基于机器学习的心脏术后衰弱预测模型的构建与验证

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[摘要] 目的: 构建并验证一种用于预测心脏术后衰弱风险的个体化预测模型。方法: 纳入2023年1—12月在南京医科大学第一附属医院接受心脏手术的患者, 在术后1个月采用衰弱筛查量表对患者进行衰弱评估。根据评估结果将患者分为衰弱组及非衰弱组。采用最小绝对收缩和选择算子(least absolute shrinkage and selection operator, LASSO)、随机森林(random forest, RF)以及极限梯度提升(extreme gradient boosting, XGBoost)3种机器学习算法筛选共同预测因子, 随后使用Logistic回归构建列线图模型。采用受试者工作特征(receiver operating characteristic, ROC)曲线及其曲线下面积(area under the curve, AUC)评估模型的区分度、校准曲线评估模型的一致性、决策曲线分析(decision curve analysis, DCA)评估该模型的临床价值, 并在内部验证集以及时间分层验证集中予以验证。结果: 共纳入301例患者, 其中235例按7:3比例分为训练集($n=165$)、内部验证集($n=70$), 其余66例患者作为时间分层验证。依据机器学习结果, 纳入4个共同预测因子: 年龄、术前左心室射血分数(left ventricular ejection fraction, LVEF)、术前白蛋白水平和术前左心室舒张末期内径(left ventricular diastolic dimension, LVDd)。以此构建列线图, 在训练集(AUC=0.846, 95%CI: 0.763~0.928)、内部验证集(AUC=0.821, 95%CI: 0.701~0.940)和时间分层验证集(AUC=0.846, 95%CI: 0.740~0.951)中均表现出优异的区分能力。校准曲线显示预测风险与观察风险之间具有高度一致性。DCA进一步证明了其良好的临床实用性。结论: 基于患者年龄、术前白蛋白水平、LVEF以及LVDd构建的心脏术后衰弱预测列线图模型具有良好的预测效能与临床适用性, 有助于早期识别高危患者。

[关键词] 机器学习; 预测模型; 心脏手术; 衰弱; 列线图

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Development and validation of a machine learning-based nomogram model for predicting frailty after cardiac surgery

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[Abstract] **Objective:** To develop and externally validate a patient-level prediction model for postoperative frailty in adults undergoing cardiac surgery. **Methods:** Our study included patients who underwent cardiac surgery at the First Affiliated Hospital of Nanjing Medical University between January and December 2023. Frailty was assessed one month postoperatively using the FRAIL scale, and patients were categorized into frailty and non-frailty groups. Three machine learning algorithms, least absolute shrinkage and selection operator (LASSO), random forest (RF), and extreme gradient boosting (XGBoost), were employed to identify common predictors. A nomogram prediction model was subsequently constructed using Logistic regression. The model's discriminative ability was evaluated using the receiver operating characteristic (ROC) curve and the area under the curve (AUC). Calibration curves assessed consistency, and decision curve analysis (DCA) evaluated clinical utility. The model was validated internally and externally. **Results:** A total of 301 patients were included. Among them, 235 patients were divided into a training set ($n=165$) and an internal validation set ($n=70$) at a ratio of 7:3, while the remaining 66 patients served as temporal validation. Based on the machine learning results, four common predictors were identified: age, preoperative left ventricular ejection fraction (LVEF), preoperative albumin level, and preoperative left ventricular end-diastolic dimension (LVDd). These were used to construct the nomogram. The model

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demonstrated excellent discriminative ability in the training set (AUC=0.846, 95% CI: 0.763–0.928), internal validation set (AUC=0.821, 95% CI: 0.701–0.940), and temporal validation set (AUC=0.846, 95% CI: 0.740–0.951). The calibration curve indicated high consistency between predicted and observed risks. Decision curve analysis further confirmed its good clinical practicality. **Conclusion:** The nomogram prediction model for post-cardiac surgery frailty, based on patient age, preoperative albumin level, LVEF, and LVDD, exhibits good predictive performance and clinical applicability, facilitating the early identification of high-risk patients.

[Key words] machine learning; prediction model; cardiac surgery; frailty; nomogram

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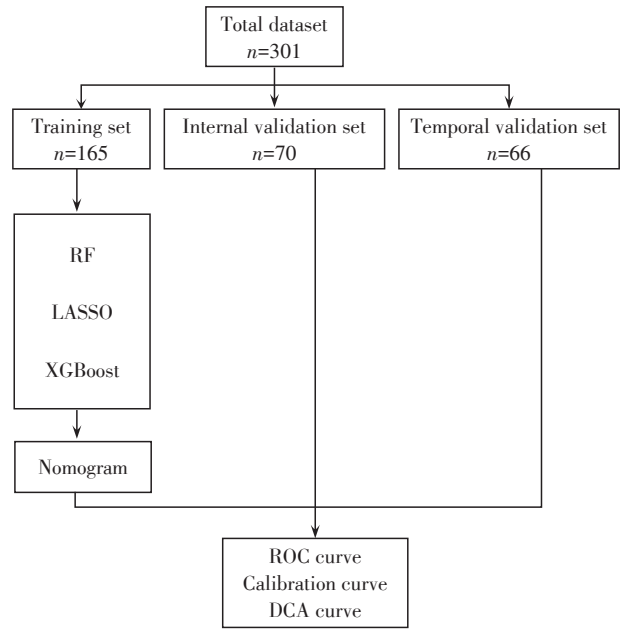
随着人口老龄化进程加速及心脏外科技术的长足进步,接受心脏手术的老年及高风险患者日益增多^[1]。然而,心脏手术作为重大的生理应激源,常引发一系列术后并发症,其中衰弱正逐渐成为一个备受关注的突出问题^[2-3]。衰弱是一种体现生理储备下降、多系统功能受损的临床综合征,大量研究证实,衰弱与心脏术后死亡、主要并发症的发生相关^[4-6]。在心脏术后,手术创伤、炎症反应及长期制动等因素可能诱发或加剧衰弱状态,这种新发或加重的术后衰弱会给患者带来显著影响,因此早期识别和干预心脏术后衰弱状态,对改善患者预后意义重大,但目前缺少相关预测模型^[7-8]。

由于围术期患者的检查指标之间存在复杂的非线性关系,传统统计学方法难以深入挖掘。机器学习作为一种人工智能的核心分支,在医学领域的应用已日益广泛,其善于从高维、非线性数据中提取关键特征和构建预测模型^[9-11]。因此,本研究旨在整合3种主流机器学习算法,系统筛选心脏术后衰弱的关键预测因子,并构建一个直观、易用的列线图预测模型,以便早期识别衰弱的高危患者,改善远期预后。

1 对象和方法

1.1 对象

纳入2023年1—12月在南京医科大学第一附属医院心脏大血管外科接受心脏手术的患者,其中1—8月手术的患者作为训练集以及内部验证集,9—12月手术的患者作为时间分层验证集。纳入标准:①年龄≥60岁;②接受心脏手术;③神志清楚,可配合问卷。排除标准:①既往有心脏手术史;②术前长期使用精神类药物;③病历资料不完整;④合并大血管手术;⑤急诊手术,术前无法进行评分;⑥术后自动出院或死亡。本研究通过南京医科大学第一附属医院医学伦理委员会审批(审批号:2022-SR-357),符合伦理要求。研究流程见图1。



RF: random forest; LASSO: least absolute shrinkage and selection operator; XGBoost: extreme gradient boosting; ROC: receiver operating characteristic; DCA: decision curve analysis.

图1 研究流程图

Figure 1 Research flowchart

1.2 方法

1.2.1 资料收集

通过文献阅读并结合临床经验,最终纳入18个临床相关变量,包括①人口学特征:年龄、性别、体重指数(body mass index, BMI);②合并症:慢性阻塞性肺病(chronic obstructive pulmonary disease, COPD)、高血压、糖尿病、脑梗死、吸烟、饮酒;③手术类型:是否合并冠状动脉旁路移植术(coronary artery bypass grafting, CABG)以及瓣膜手术、手术时长;④术前综合状态:匹兹堡睡眠质量评分(Pittsburgh sleep quality index, PSQI)、左心房内径(left atrial diameter, LAD)、左心室舒张末期内径(left ventricular diastolic dimension, LVDD)、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)及术前白蛋

白水平。

1.2.2 患者术后衰弱的评估与分组

依据《老年心血管疾病合并衰弱评估与管理中国专家共识》推荐,采用FRAIL量表评估心脏疾病患者的衰弱状态。该量表耗时较短、客观且重复性好,目前在许多心血管疾病的研究中表现出优异的评估性能^[12-14]。FRAIL量表共包含5个条目,如果患者有3个及以上的回答为“是”,则可诊断为衰弱。评估选择在术后1个月左右,患者门诊复查时进行。该时间点的选择基于以下考量:①避开了住院期间急性手术应激、疼痛以及麻醉药物影响的急性期,能更真实地反映患者中期的恢复趋势;②此时患者常规进行随访,避免电话随访带来不准确性;③术后1~3个月是评估心脏手术后中期并发症与功能恢复的关键时间窗口,有学者也采用术后1个月设为评估衰弱的第一个正式随访点^[15]。FRAIL评分 ≥ 3 分者纳入衰弱组,FRAIL评分 < 3 分者纳入非衰弱组。

1.2.3 基于机器学习的变量筛选

采用最小绝对收缩和选择算子(least absolute shrinkage and selection operator, LASSO)、随机森林(random forest, RF)以及极限梯度提升(extreme gradient boosting, XGBoost)3种机器学习算法筛选共同预测因子。所有模型均使用10折交叉验证进行评估。RF模型使用500棵决策树训练,通过平均下降Gini指数对变量重要性进行排序,保留前10个最重要变量。对于LASSO回归,通过二项式惩罚将非信息变量压缩至零系数,使用最小准则和1个标准误规则选择最优正则化参数;将 $\lambda.1se$ 准则下系数非零的变量视为显著预测因子。在XGBoost中,计算沙普利加和解释(Shapley additive explanation, SHAP)以量化各变量对模型预测的贡献度,并选择按增益排序的前10个变量。最终通过韦恩图可视化3种方法确定共同变量。

1.2.4 列线图构建

基于3种机器学习方法确定的共同变量,构建Logistic回归模型以开发列线图,作为个体化风险预测的可视化工具。采用受试者工作特征(receiver operating characteristic, ROC)曲线及其曲线下面积(area under the curve, AUC)评估模型的区分度、校准曲线评估模型的一致性、决策曲线分析(decision curve analysis, DCA)评估该模型的临床价值,并在内部验证集以及时间分层验证集中予以验证。

1.3 统计学方法

使用RStudio 4.4.2进行统计分析,符合正态分

布的计量资料采用均数 \pm 标准差($\bar{x} \pm s$)表示,组间比较采用独立样本 t 检验;偏态分布数据以中位数(四分位数) $[M(P_{25}, P_{75})]$ 表示,组间比较采用Mann-Whitney U 检验;计数资料以频数(百分比) $[n(\%)]$ 描述,组间比较采用 χ^2 检验。使用“randomForest”“glmnet”和“xgboostR”等R包进行机器学习分析;“pROC”包计算ROC值,“ggplot2”包绘制图片;“rms”包进行预测模型验证和列线图构建及验证;“ggDCA”包分析临床决策曲线。双侧检验, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者基线特征

训练集及内部验证集纳入235例患者,按照7:3的比例随机分为训练集165例,验证集70例。训练集与验证集的基线特征比较显示,各组间变量分布均衡,无显著差异(表1)。在训练集中,44例患者发生衰弱,发生率为26.7%。单因素分析显示,衰弱组与非衰弱组在年龄、糖尿病、LVDd、LVEF及白蛋白水平上差异均有统计学意义(P 均 < 0.05 ,表2)。

2.2 机器学习结果

LASSO模型(AUC为0.795,95%CI:0.698~0.892)在 $\lambda.1se$ 下选择了7个非零系数变量(图2A~D),XGBoost模型(AUC为0.839,95%CI:0.757~0.921,图2E~G)以及RF模型(AUC=0.838,95%CI=0.756~0.920,图2H~J)则分别根据变量重要性排序选取前10个特征。3种机器学习方法共同筛选出4个关键变量,包括年龄、术前白蛋白、术前LVEF和LVDd值,其方差膨胀系数(variance inflation factor, VIF)均远小于4,表明这些预测因子之间不存在显著的多重共线性,确保了模型估计的稳定性和结果的可靠性(图2K)。

2.3 列线图构建与验证

将上述4个因子纳入Logistic回归,构建列线图模型。每个因素都可以查询到1个分数,通过将4个分数相加并在总评分轴上定位总和来计算总分和(图3)。该列线图在训练集和内部验证数据集中均表现出稳健的预测性能。训练集AUC为0.846(95%CI:0.763~0.928),最大约登指数对应的临界值为0.247,校准曲线Brier值为0.144。将训练集模型置于内部验证集中进行验证,内部验证集AUC为0.821(95%CI:0.701~0.940),最大约登指数对应的临界值为0.315,校准曲线Brier值为0.131。

表1 训练集与内部验证集基线资料

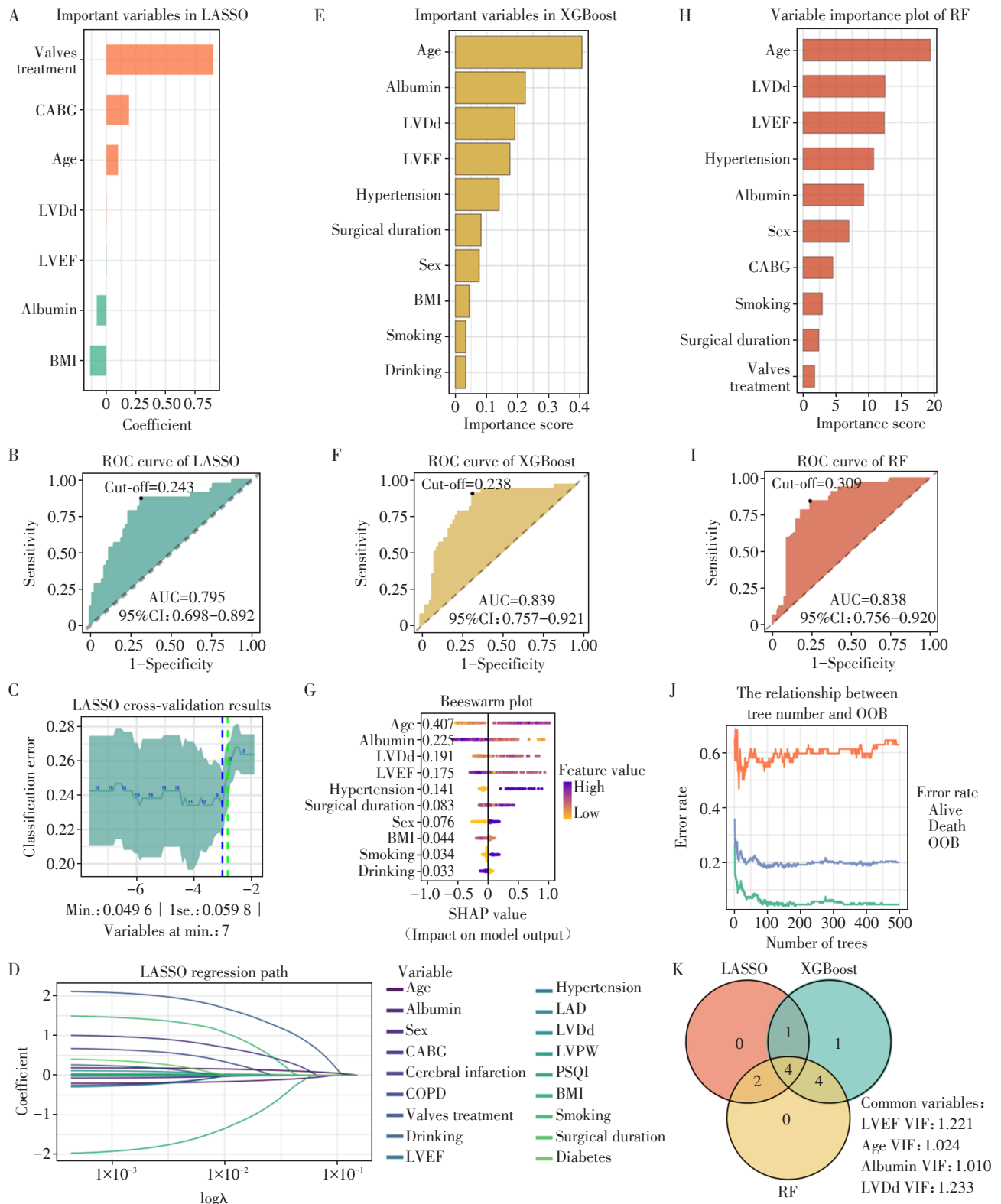
Table 1 Baseline characteristics of the training set and internal validation set

Variable	Training set(n=165)	Internal validation set(n=70)	χ^2/Z	P
Age[years, $M(P_{25}, P_{75})$]	68.00(64.00, 72.00)	68.00(65.00, 71.75)	-0.421	0.674
Sex[n(%)]			0.001	0.981
Female	97(58.8)	41(58.6)		
Male	68(41.2)	29(41.4)		
BMI[kg/m ² , $M(P_{25}, P_{75})$]	22.77(21.09, 24.98)	22.88(21.33, 25.99)	-0.763	0.445
COPD[n(%)]	31(18.8)	13(18.6)	0.002	0.968
Hypertension[n(%)]	53(32.1)	27(38.6)	0.907	0.341
Diabetes[n(%)]	22(13.3)	10(14.3)	0.045	0.832
Cerebral infarction[n(%)]	24(14.5)	10(14.3)	0.003	0.957
Smoking[n(%)]	27(16.4)	10(14.3)	0.172	0.678
Drinking[n(%)]	40(24.2)	19(27.1)	0.237	0.626
CABG[n(%)]	12(7.3)	4(5.7)	0.213	0.645
Valves treatment[n(%)]	131(79.4)	56(80.0)	0.012	0.914
PSQI[$M(P_{25}, P_{75})$]	9.00(7.00, 11.00)	9.00(7.00, 11.00)	-0.508	0.611
LAD[mm, $M(P_{25}, P_{75})$]	44.00(41.00, 47.00)	44.50(41.25, 47.00)	-0.683	0.495
LVDd[mm, $M(P_{25}, P_{75})$]	49.00(46.00, 55.00)	50.00(46.00, 54.00)	-0.100	0.920
LVPWT[mm, $M(P_{25}, P_{75})$]	10.00(9.00, 10.00)	10.00(9.00, 10.00)	-0.651	0.515
LVEF[% , $M(P_{25}, P_{75})$]	61.00(56.60, 63.00)	60.95(58.00, 62.68)	-0.011	0.991
Albumin[g/L, $M(P_{25}, P_{75})$]	37.20(35.20, 40.10)	37.45(35.02, 40.62)	-0.233	0.816
Surgical duration[min, $M(P_{25}, P_{75})$]	235.00(220.00, 250.00)	245.00(225.00, 255.00)	-1.436	0.151
FRAIL ≥ 3 [n(%)]	44(26.7)	19(27.1)	0.006	0.940

表2 训练集衰弱组与非衰弱组基线资料

Table 2 Baseline characteristics of the frail and non-frail groups in the training set

Variable	Non-frail group(n=121)	Frail group(n=44)	χ^2/Z	P
Age[years, $M(P_{25}, P_{75})$]	67.00(64.00, 70.00)	71.50(66.00, 75.25)	-4.324	< 0.001
Sex[n(%)]			3.265	0.071
Female	66(54.5)	31(70.5)		
Male	55(45.5)	13(29.5)		
BMI[kg/m ² , $M(P_{25}, P_{75})$]	22.60(20.96, 24.62)	23.59(21.85, 25.27)	-1.174	0.240
COPD[n(%)]	21(17.4)	10(22.7)	0.602	0.438
Hypertension[n(%)]	36(29.8)	17(38.6)	1.123	0.289
Diabetes[n(%)]	9(7.4)	13(29.5)	13.243	< 0.001
Cerebral infarction[n(%)]	17(14.0)	7(15.9)	0.089	0.765
Smoking[n(%)]	22(18.2)	5(11.4)	1.067	0.302
Drinking[n(%)]	31(25.6)	9(20.5)	0.424	0.515
CABG[n(%)]	6(5.0)	6(13.6)	3.556	0.059
Valves treatment[n(%)]	95(78.5)	36(81.8)	0.217	0.641
PSQI[$M(P_{25}, P_{75})$]	9.00(7.00, 11.00)	9.00(8.00, 11.00)	-0.728	0.467
LAD[mm, $M(P_{25}, P_{75})$]	45.00(41.00, 47.00)	44.00(40.00, 46.25)	-1.146	0.252
LVDd[mm, $M(P_{25}, P_{75})$]	49.00(46.00, 55.00)	51.00(48.00, 57.25)	-2.015	0.044
LVPWT[mm, $M(P_{25}, P_{75})$]	10.00(9.00, 10.00)	10.00(9.00, 10.00)	-0.957	0.339
LVEF[% , $M(P_{25}, P_{75})$]	61.20(57.10, 63.00)	59.95(52.85, 61.47)	-2.153	0.031
Albumin[g/L, $M(P_{25}, P_{75})$]	38.10(35.80, 40.70)	35.45(33.68, 37.23)	-4.239	< 0.001
Surgical duration[min, $M(P_{25}, P_{75})$]	235.00(220.00, 250.00)	240.00(225.00, 252.50)	-0.974	0.330



A-D: The optimal parameter λ selection in the LASSO model employed 10-fold cross-validation using the one-standard-error rule ($\lambda_{1se} = 0.0598$), which resulted in the selection of seven variables. E-G: The XGBoost model selected the top 10 most important variables. Panel G presented the SHAP beeswarm plot, demonstrating feature importance and the directional impact of features on the model's predictions. H-J: The RF model selected the top 10 most important variables, trained with 500 decision trees to ensure stability, and 10-fold cross-validation was applied to optimize hyperparameters and prevent overfitting. Panel J displayed the out-of-bag (OOB) error curve of the RF model, illustrating the relationship between the model's error rate and the number of decision trees. K: A Venn diagram compared the overlap of variables selected by the three different methods.

图2 机器学习分析结果

Figure 2 Machine learning analysis results

在66例患者中进行时间分层验证集,结果也保持了良好的预测准确性,模型AUC为0.846(95%CI: 0.740~0.951),最大约登指数对应的临界值为0.288,

校准曲线Brier值为0.122。此外,各数据集中DCA均表明该模型在较大阈值概率范围内具有良好的净获益(图4)。

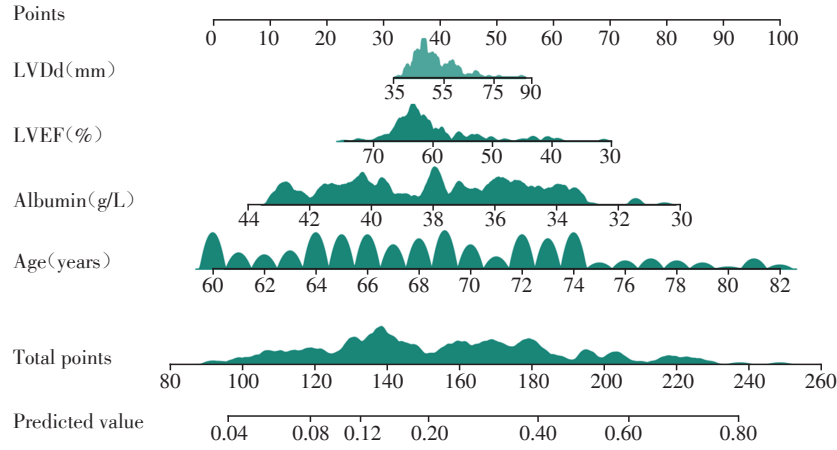
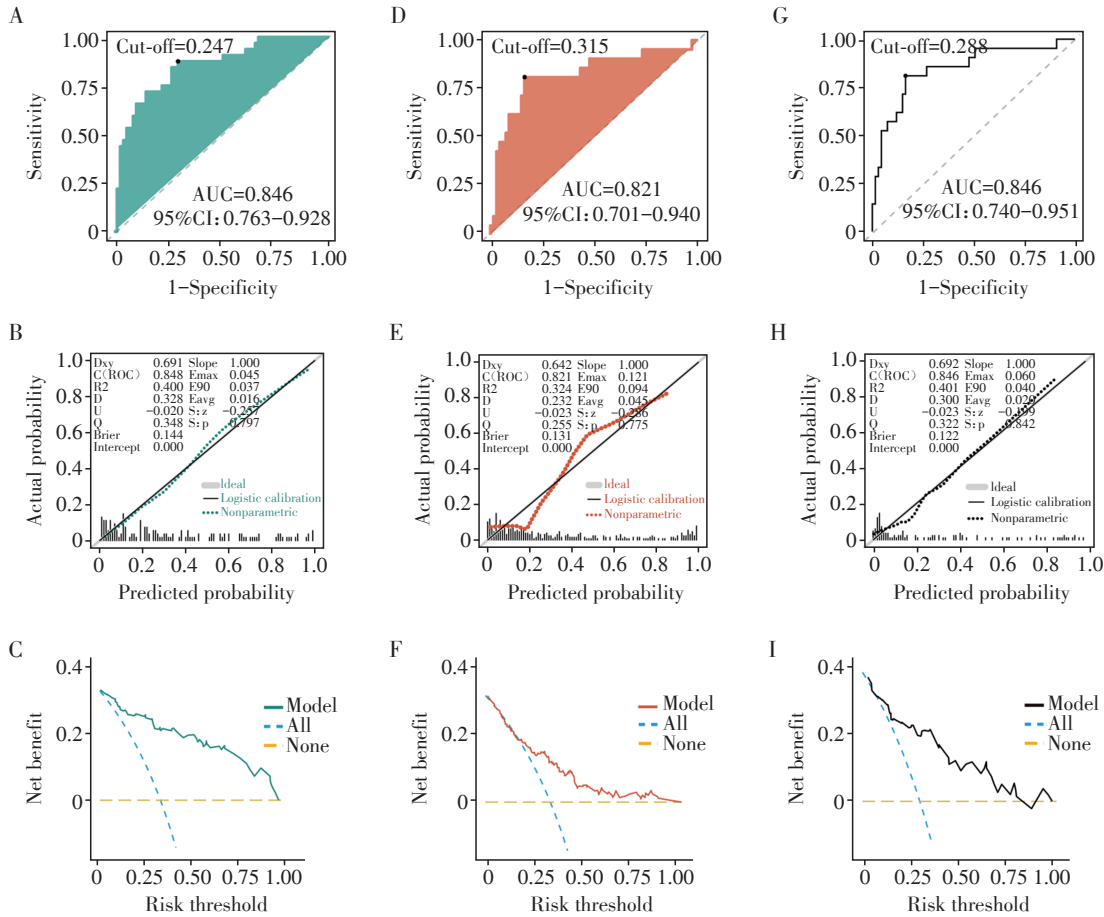


图3 心脏术后衰弱风险的列线图模型

Figure 3 Nomogram for predicting the risk of postoperative frailty after cardiac surgery



A-C: ROC curve(A), calibration curve(B), and DCA(C) curve for the training set. D-F: ROC curve(D), calibration curve(E), and DCA(F) curve for the internal validation set. G-I: ROC curve(G), calibration curve(H), and DCA(I) curve for the temporal validation set.

图4 列线图验证

Figure 4 Nomogram validation

3 讨 论

衰弱是一种表现为生理储备下降、多系统功能受损的临床综合征,可使个体在面对应激时维持自稳态的能力显著降低,已成为手术后的常见并发症^[16]。尤其在心脏外科领域,术后6个月仍有29%的患者评估为衰弱状态,且与患者不良结局显著相关^[17-18]。因此,在术前精准识别衰弱高风险患者,并据此实施针对性干预,对于改善心脏手术患者的整体预后具有至关重要的意义。本研究正是基于这一临床需求,成功构建并验证了一个可用于个体化预测心脏术后1个月衰弱风险的列线图模型。

本研究基于3种机器学习算法,最终纳入4个共识性预测因子:年龄、术前白蛋白水平、术前LVEF和LVDD。该模型在训练集、内部验证集及时间分层验证集中均表现出优异且稳定的区分能力,校准曲线与DCA进一步证实了其预测准确性及潜在临床实用价值。

4个衰弱预测因子均与现有病理生理学认知相符。高龄及低白蛋白水平作为衰弱的重要预测因子,与既往研究结论一致,这反映了生理储备减少是衰弱发生的根本基础^[19-20]。随着年龄增长,细胞内葡萄糖转运功能失调,导致能量供应不足及功能紊乱,这可能是导致衰弱的关键机制^[21]。白蛋白作为评价全身营养状况的关键指标,也与衰弱存在极强的关联性。白蛋白水平降低通常提示营养不良,而营养不良会直接导致肌肉量减少和身体功能下降,进而增加衰弱发生风险^[22]。此外,手术创伤会引发显著的炎症和分解代谢反应,机体需要消耗大量的蛋白质,而术前白蛋白水平较低的患者往往难以满足这种额外的营养需求,即便顺利出院,也会出现后续组织修复延迟、免疫功能下降及对并发症的易感性增加等问题^[23]。

本研究还揭示了心脏自身结构与功能状态对术后衰弱发生的影响。较低的LVEF与较大的LVDD分别从心脏的功能与结构两个维度提示了患者较低的心脏功能储备,目前大量文献结果也证实了二者与衰弱的相关性^[24-25]。较差的心功能可能导致全身血流灌注不足、细胞缺氧,进一步加剧上述细胞能量供应失调的风险;并且心衰患者通常伴随慢性炎症,可能通过“慢性炎症-心肌纤维化-心室重构”促进衰弱发生,而衰弱又会反过来加剧心功能减退,形成恶性循环^[26]。

本研究结果对临床医疗工作具有明确的指导

意义。该模型为临床医生提供了简洁直观的风险评估工具,可在术前快速筛选出衰弱高危人群。对于LVEF值低下、LVDD增大的高龄患者,术前应尽可能提高其心功能储备;对于存在营养不良风险的患者,需实施个性化营养支持护理与指导。

本研究为单中心回顾性研究设计,结论仍需前瞻性、多中心研究进一步验证。受限于纳入病例数,部分术中参数(如体外循环时间、主动脉钳夹时间)及术后相关数据未纳入分析,可能影响模型的全局性。未来前瞻性研究应致力于整合多维度数据,以构建效能更优的预测工具,并且可在术前、出院时及术后多个时间点开展纵向评估,动态描绘衰弱进展轨迹,明确其与手术的因果关联。

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YANG Yue was responsible for data analysis and initial draft preparation; GE Yuan and LI Minghui were responsible for creating charts and graphs; GENG Dandan participated in experiment supervision and manuscript revision.

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