

临床-影像特征联合 DCE-MRI 影像组学列线图预测 Her-2 低表达乳腺癌激素受体状态

侯唯姝¹, 潘红利¹, 汪群¹, 李小虎¹, 颜蕴文², 余永强¹

(安徽医科大学第一附属医院¹ 医学影像科、² 乳腺外科, 合肥 230022)

摘要 目的 探讨临床-影像特征联合基于动态对比增强磁共振成像(DCE-MRI)影像组学列线图预测人表皮生长因子受体2(Her-2)低表达乳腺癌激素受体(HR)状态的价值。方法 回顾性分析2019年1月—2025年2月行标准化乳腺MRI检查的Her-2低表达乳腺癌患者共198例,分为HR(+)组($n=137$),HR(-)组($n=61$)。将病例按7:3的比例分为训练集($n=138$)和测试集($n=60$),分别构建基于临床和传统影像学特征的临床-影像模型、基于DCE-MRI的影像组学模型以及联合模型,并绘制列线图,采用受试者工作曲线比较不同模型对HR状态的预测效能。结果 HR(+)组和HR(-)组的DEC-MRI影像组学评分(Radscore)在训练集和测试集差异均具有统计学差异(均 $P<0.001$)。基于病灶活动度、Ki67表达、TIC曲线类型、强化特征和病灶长径等预测因子构建的临床-影像模型在训练集和测试集预测HR状态的AUC分别为0.643和0.616,DEC-MRI影像组学模型在训练集和测试集的AUC分别为0.897和0.860,联合临床-影像特征和Radscore绘制的列线图在训练集(AUC=0.913)和测试集(AUC=0.898)的预测效能均优于临床-影像模型和影像组学模型(均 $P<0.05$)。结论 DCE-MRI影像组学联合临床-影像特征的列线图能有效预测Her-2低表达乳腺癌的HR状态,有助于乳腺癌患者个体化治疗方案的制定。

关键词 乳腺癌; 动态增强磁共振成像; 影像组学; 人表皮生长因子受体2; 激素受体; 列线图

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人表皮生长因子受体2(human epidermal growth

factor receptor-2, Her-2)低表达乳腺癌是免疫组织化学(immunohistochemistry, IHC)1+或2+且免疫荧光杂交(fluorescence in situ hybridization, FISH)阴性的乳腺癌^[1],因能够从新型抗体药物偶联物(anti-body-drug conjugate, ADC)治疗中获益,已成为近年来逐渐被重视的乳腺癌治疗新分型^[2]。激素受体(hormone receptor, HR)表达是影响Her-2低表达乳腺癌预后评估的重要因素,HR(+)与较低的病理

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作者简介: 侯唯姝,女,副主任医师;

余永强,男,主任医师,博士生导师,通信作者, E-mail: ay-fyyongqiang@163.com

and the history of statin use. The area under the ROC curve in the training set was 0.897, 0.885, and 0.909 at 1, 2, and 3 years, respectively; The area under the ROC curve in the validation set was 0.885, 0.881, and 0.923 at 1, 2, and 3 years, respectively. These results demonstrated that the model had excellent discriminatory power. The calibration curves and decision curves demonstrated that the model had high clinical practicality in predicting the occurrence of MACE in CHD patients. **Conclusion** The nomogram prediction model based on LP-PLA2, LP(a) and other risk factors provides an effective tool for the prognosis assessment of CHD patients, facilitating the early identification of high-risk patients and enabling individualized intervention.

Key words lipoprotein-associated phospholipase A2; lipoprotein (a); coronary heart disease; nomogram; prognostic prediction model; risk factor

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Corresponding author Hu Zeping, E-mail: 141318679@qq.com

学完全缓解、较好的预后指标密切相关^[3],因此,通过影像学无创评估 HR 状态有助于该类乳腺癌患者个体化治疗方案的选择和预后评估。

乳腺磁共振(magnetic resonance imaging, MRI)影像组学已广泛应用于乳腺癌分子亚型预测的研究中,动态对比增强 MRI(dynamic contrast enhanced MRI, DCE-MRI) 具有高度的空间分辨率和观察者间一致性,是应用最多、诊断效能最高的模式^[4-5]。该研究分别建立 Her-2 低表达乳腺癌的 DCE-MRI 影像组学模型、临床影像模型和联合模型,并通过列线图直观展示临床、传统影像和影像组学特征对 HR 状态的影响程度,探讨不同模型预测 HR 状态的价值。

1 材料与方法

1.1 病例资料 本研究经安徽医科大学第一附属医院伦理委员会批准(批号:安医一附院伦审 PJ 2024-08-93),回顾性研究免除受试者知情同意书。回顾性收集 2019 年 1 月—2025 年 2 月在安徽医科大学第一附属医院接受标准化乳腺 MRI 检查、病理资料完整的新确诊乳腺癌患者的资料。纳入标准:①病理学及 IHC 符合 Her-2 低表达乳腺癌诊断标准;②术前或穿刺前 2 周内行标准化多参数 MRI 扫描;③MRI 扫描前患者未接受穿刺、放化疗或手术治疗。排除标准:①临床或病理资料不完整;②病变最大径小于 10 mm,部分容积效应影响组学分析;③图像质量不佳。最终纳入 198 例入组患者,均为女性,年龄 58(25,85)岁,根据 IHC 结果分为 HR(+)组($n=137$)和 HR(-)组($n=61$)。按 7:3 的比例以分层抽样法分为训练集($n=138$)和测试集($n=60$)。

1.2 HR(+)定义 依据美国临床肿瘤学会/美国病理学家协会指南,Her-2 低表达定义为:IHC 检测 Her-2(+)或 IHC 检测 Her-2(++)且 FISH 检测(-)。雌激素受体(estrogen receptor, ER)/孕激素受体(progesterone receptor, PR)阳性的判读标准为细胞核着色阳性率>1%。ER(+)或 PR(+)均定义为 HR(+)。

1.3 乳腺 MRI 扫描方案 所有患者均采用美国 GE 公司 Discovery MR 750w 3.0T 磁共振扫描仪进行扫描,配备 8 通道相控阵乳腺线圈。患者取俯卧位,双侧乳腺自然悬垂于线圈凹形孔内。MRI 扫描序列包括:①横轴位快速自旋回波序列 FSE T1WI: TR 480.0 ms, TE 7.61 ms;②横轴位翻转恢复序列

STIR T2WI, TR 8 200.0 ms, TE 170.0 ms。③横轴位 DWI: TR 7 000.0 ms, TE, b 值 = 0 ms 和 1 000 ms。上述序列层厚 5.0 mm,层间距 1.0 mm。④DCE-T1WI:横轴位 3D 容积内插快速扰相梯度回波序列 Vibrant: TR 3.6 ms, TE 2.1 ms, FOV 350 mm × 350 mm,层厚 1.2 mm,层间距 0 mm。采集 1 个时相蒙片之后,经高压注射器团注造影剂钆双胺注射液欧乃影(速率 3 mL/s,剂量 0.1 mmol/kg),然后分别于造影剂注射后第 60、120、180、240、300 和 360 s 进行数据采集,扫描时间共 6 min 17 s。

1.4 影像组学分析 本研究中影像组学分析流程包括图像分割、特征提取、特征筛选、模型构建和应用(图 1)。

1.4.1 图像分割与特征提取 基于乳腺磁共振成像报告与数据系统(breast imaging reporting and data system, BI-RADS)的诊断原则,将轴位 DCE-T1WI 第 2 期(注射对比剂后 60 s)原始 DICOM 数据导入开源软件 3D-Slicer (www.slicer.org),沿肿瘤边缘逐层手动进行感兴趣区(region of interest, ROI)图像分割,生成三维感兴趣区(3D volume of interest, VOI)。对于多灶性病变选择最大病变进行图像分割。图像分割由 2 名分别具有 10 年和 14 年乳腺 MRI 诊断经验的诊断医生手动完成。1 个月后,上述 2 名医生从训练集中随机选择 10% 的病例重新进行图像分割,使用双因素随机组内相关系数(intraclass correlation coefficient, ICC)评估观察者间信度和复测信度。ICC < 0.50 定义为较差、0.50 ~ 0.75 为中等、0.76 ~ 0.90 为良好和 0.91 ~ 1.00 为优秀。

使用内置 PyRadiomics 特征库的数坤科技平台(北京数坤网络科技有限公司)提取乳腺癌 3D-VOI 图像的高通量特征。基于 DCE-T1WI 序列提取了 1 874 个影像组学特征,包括形态特征、一阶直方图特征、纹理特征和滤波变换特征。

1.4.2 DCE-MRI 特征预处理、特征降维和模型构建 为防止对单个特征的依赖,对所有提取特征进行 Z-score 归一化预处理。特征降维:当自变量之间 Pearson 相关系数绝对值 ≥ 0.9 时,仅保留与因变量线性相关系数较高的特征以减少冗余;使用“Select K Best”算法保留方差分析 F 值在前 50% 的特征;最后使用最小绝对收缩和选择算子(least absolute shrinkage and selection operator, LASSO)筛选出最小冗余、最大相关的最佳特征集。模型构建:采用 10 折交叉验证法充分优化模型。在使用逻辑回归(Logistic regression, LR)、支持向量机(support vector

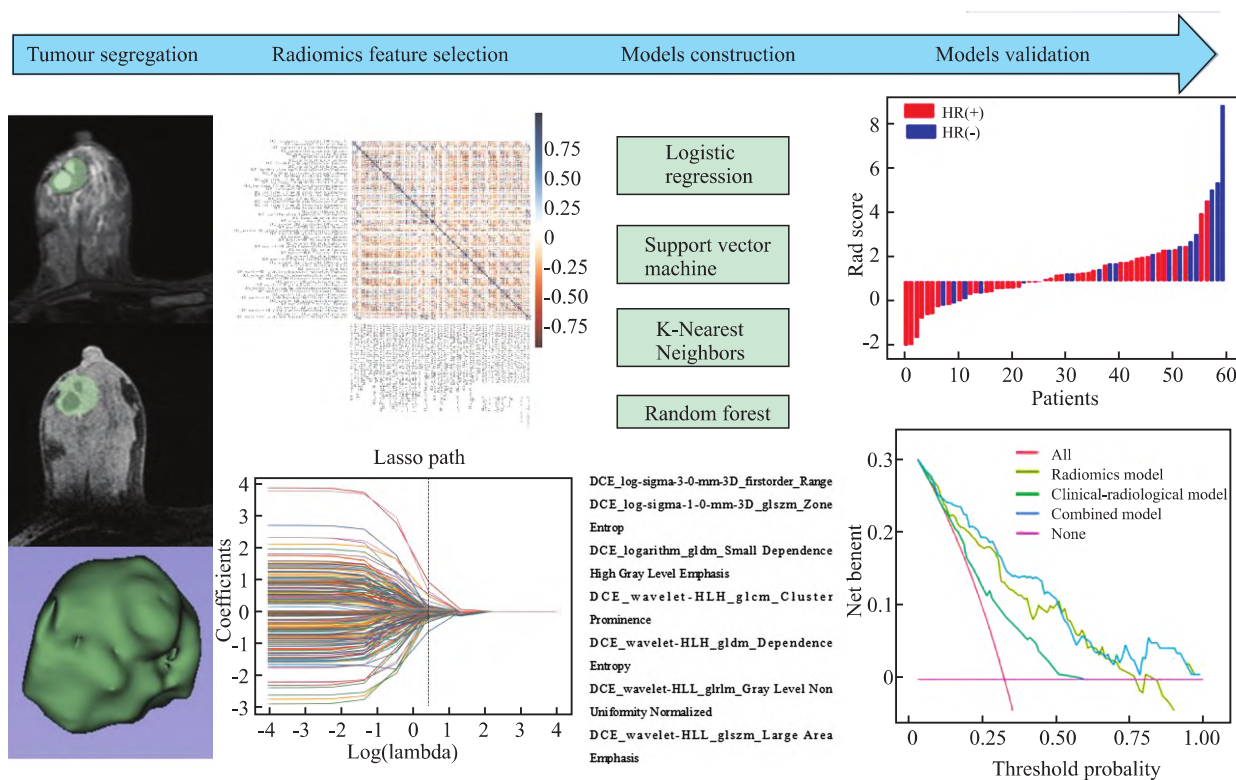


图1 影像组学工作流程图

Fig. 1 Radiomics workflow

machine, SVM)、随机森林(random forest, RF)、K最近邻(k-nearest neighbors, KNN) 4种算法进行预实验后,筛选出诊断效能最佳的RF构建基于DCE-T1WI的影像组学模型。影像组学分析流程见图1。通过影像组学特征及其系数计算患者的影像组学评分(Radscore): $\text{Radscore} = \text{截距} + \beta_i \times X_i$, β 为系数, X 为特征, i 为序数。

1.5 临床特征、常规影像学特征收集与临床-影像特征模型建立

1.5.1 特征收集 从医院管理信息系统查阅并记录患者的年龄、月经状态、乳腺癌家族史、病灶活动度和病灶质地(质韧/质软)等临床特征。根据DCE-MRI图像记录病灶位置、腺体类型(a:脂肪型, b:少量腺体型, c:不均匀致密型, d:极度致密型)、病理类型(浸润性导管癌/其他类型)、Ki67表达($< 20\%$ / $\geq 20\%$)、病灶最长径(mm)、病灶数量(单发/多发)、病灶边界(光整/有毛刺)、病灶形状(结节、肿块型/非肿块型)、强化特征(均匀/不均匀)和时间-信号强度曲线(time-signal intensity curve, TIC)(I流入型/II平台型/III流出型)等DCE-MRI常规影像学特征。在影像学特征的评估中,由上述2名诊断医生独立阅片,意见分歧时通过讨论达成共识。

1.5.2 特征筛选与模型建立 单因素Logistic分析筛选出鉴别HR(-/+)有统计学意义的临床特征和常规影像学特征,使用多因素Logistic回归分析进一步筛选能够预测HR状态的独立预测因子,构建临床影像特征模型。

1.6 列线图构建 联合Radscore和临床影像学特征构建影像组学-临床-影像特征联合模型并绘制列线图。利用校准曲线检验联合模型的校准度,借助临床决策曲线(decision curve analysis, DCA)在不同阈值概率下计算净收益。

1.7 统计学处理 应用SPSS 22.0软件进行数据分析。使用Kolmogorov-Smirnov检验分析计量资料的正态性,符合正态分布以 $\bar{x} \pm s$ 表示,两组间比较采用独立样本 t 检验;不符合正态分布者以 $M(Q_1, Q_3)$ 表示,两组间比较采用Mann-Whitney U 检验。分类资料用 $n(\%)$ 表示,采用 χ^2 检验或Fisher确切概率法比较组间差异。采用受试者工作特征曲线(receiver operating characteristic curve, ROC)评价模型的预测性能,并计算曲线下面积(area under curve, AUC)、灵敏度和特异度。采用DeLong检验比较不同模型间预测性能的差异。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 患者的一般资料 训练集和测试集患者的临床特征和常规影像学特征均无统计学差异(P 均 >0.05)。见表1。

表1 训练集与测试集患者临床及常规影像学特征比较 [n (%) , $\bar{x} \pm s$, $M(Q_1, Q_3)$]

Tab.1 Comparison of clinical and radiological features between patients of the training and testing sets [n (%) , $\bar{x} \pm s$, $M(Q_1, Q_3)$]				
Clinical and radiographic features	Training set ($n=138$)	Testing set ($n=60$)	$t/Z/\chi^2$ value	P value
Age (years)	61.4 $\pm$ 10.6	63.2 $\pm$ 12.8	-0.915	0.360
Menstrual status			0.972	0.324
Premenopausal	70 (50.72)	35 (58.33)		
Postmenopausal	68 (49.28)	25 (41.67)		
Breast cancer history			0.690	0.406
Yes	2 (1.45)	2 (3.33)		
No	136 (98.55)	58 (96.67)		
Lesion mobility			0.009	0.925
Freely	68 (49.28)	30 (50.00)		
Poor	70 (50.72)	30 (50.00)		
Lesion quality			2.213	0.137
Soft	13 (9.42)	2 (3.33)		
Stiff	125 (90.58)	58 (96.67)		
Lesion location			1.218	0.270
Central region	67 (48.55)	37 (61.67)		
Surrounding quadrant	71 (51.45)	23 (38.33)		
No. of lesions			1.915	0.166
Single	103 (74.64)	39 (65.00)		
Multiple	35 (25.36)	21 (35.00)		
Maximum diameter (mm)	21.50 (16.05, 29.08)	19.80 (14.47, 29.23)	1.134	0.258
Glandular density			0.667	0.414
a or b type	30 (21.74)	10 (16.67)		
c or d type	108 (78.26)	50 (83.33)		
Lesion margin			0.204	0.652
Nonspiculated	104 (75.36)	47 (78.33)		
Spiculated	34 (24.64)	13 (21.67)		
Lesion shape			0.154	0.695
Nodular or mass	50 (47.62)	24 (51.06)		
Non-mass	55 (52.38)	23 (48.94)		
Enhancement pattern			2.745	0.098
Homogeneous	24 (17.39)	5 (8.33)		
Heterogeneous	114 (82.61)	55 (91.67)		
TIC type			1.980	0.159
I / II type	92 (66.66)	46 (76.67)		
III type	46 (33.33)	14 (23.33)		
Ki67			<0.001	0.983
$\geq 20\%$	101 (73.19)	44 (73.33)		
<20%	37 (26.81)	16 (26.67)		

2.2 HR (+) 组和 HR (-) 组临床特征和 DCE-MRI 影像学特征比较 训练集中,HR (-) 组比 HR

(+) 乳腺癌更倾向于表现为质地坚硬($P=0.003$)、Ki67 $\geq 20\%$ ($P<0.001$)、TIC III型曲线($P=0.007$)和不均匀的强化特征($P=0.003$),且HR (-) 组的病灶长径长于HR (+) 组($P=0.007$),其余特征无统计学差异(均 $P>0.05$) (表2)。测试集中,HR (+) 组的病灶边界比HR (-) 组更易表现出毛刺征($P=0.015$),其余特征无统计学差异(均 $P>0.05$) (表2)。DCE-MRI 图像显示,HR (+) 乳腺癌表现为均匀强化和TIC II型曲线,HR (-) 乳腺癌表现为不均匀强化和TIC III型曲线(图2)。

2.3 基于 DCE-T1WI 影像组学特征提取和 Rad-score 计算 图像分割与影像组学特征提取的观察者间信度 ICC 中位数为0.898(0.855~0.925),具有显著的可靠性。经预处理、Pearson 相关性分析、Select K Best 单变量筛选和Lasso 回归,最终剩余9个关键影像组学特征,分别为1个一阶特征(DCE_log-sigma-3-0-mm-3D_firstorder_Range)、2个二阶特征(DCE_log-sigma-1-0-mm-3D_glszm_Zone Entropy、DCE_logarithm_gldm_Small Dependence High Gray Level Emphasis)和6个高阶特征(DCE_wavelet-HLH_gldm_Cluster Prominence、DCE_wavelet-HLH_gldm_Dependence Entropy、DCE_wavelet-HLL_gldm_Gray Level Non Uniformity Normalized、DCE_wavelet-HLL_glszm_Large Area Emphasis、DCE_wavelet-LLH_firstorder_Mean、DCE_wavelet-LLH_gldm_Large Dependence Low Gray Level Emphasis)。

计算每个患者的 Radscore,HR (+) 组和 HR (-) 组的 Radscore 在训练集和测试集均呈现出明显的分布差异(图3)。在训练集中,HR (+) 组和 HR (-) 组的 Radscore 分别为-0.08 (-1.02, 0.71) 和 1.35 (0.41, 2.07),Mann-Whitney U 检验显示差异具有统计学意义($Z=-0.329$, $P<0.001$);在测试集中,Radscore 分别为-0.44 (-1.65, 0.80) 和 1.46 (0.58, 1.93),差异具有统计学意义($Z=-0.336$, $P<0.001$)。

2.4 临床及常规影像特征 Logistic 回归结果 对临床及常规影像学特征进行单因素 Logistic 回归分析,以 $P<0.05$ 为标准,筛选出临床特征中的病灶活动度($P=0.007$)、Ki67 表达($P=0.001$)和常规影像学特征中的TIC曲线类型($P=0.014$)、强化特征($P=0.005$)、病灶长径($P=0.046$)为有意义特征。联合上述特征,使用多因素 Logistic 回归进一步筛选出病灶活动度($P=0.046$)、Ki67 表达($P=0.002$)、TIC曲线类型($P=0.008$)、强化特征($P=$

0.012)、病灶长径($P=0.049$)为预测 HR 表达状态的独立预测因子(表3)。

2.5 临床-影像-影像组学联合模型列线图构建及各模型诊断效能比较 基于最优影像组学特征构建的影像组学模型在训练集预测 HR 状态的 AUC 为 0.897(灵敏度为 62.8%,特异度为 98.5%),在测试集的 AUC 为 0.860(灵敏度为 66.7%,特异度为 83.3%)。构建的临床-影像特征模型在训练集

预测 HR 状态的 AUC 为 0.643,灵敏度为 72.6%,特异度为 63.6%,在测试集的 AUC 为 0.616,灵敏度为 66.7%,特异度为 76.7%(表4)。

联合 Radscore、临床-影像特征独立预测因子建立联合模型并绘制列线图,列线图总分对应于对 HR(-) 乳腺癌的诊断概率(图4)。列线图在训练集中 AUC 为 0.913,灵敏度为 82.7%,特异度为 90.4%,在测试集的 AUC 为 0.898,灵敏度为 86.4%,

表2 训练集与测试集内部 HR(+) 与 HR(-) 患者临床及常规影像学特征比较 [$n(\%)$, $\bar{x} \pm s$, $M(Q_1, Q_3)$]

Tab.2 Comparison of clinical and radiological features between HR(+) and HR(-) group in the training and testing sets [$n(\%)$, $\bar{x} \pm s$, $M(Q_1, Q_3)$]

Clinical and radiographic features	Training set				Testing set			
	HR(+) ($n=62$)	HR(-) ($n=71$)	$t/Z/\chi^2$ value	P value	HR(+) ($n=27$)	HR(-) ($n=30$)	$t/Z/\chi^2$ value	P value
Age (years)	59.4 $\pm$ 12.6	60.2 $\pm$ 10.5	1.731	0.085	57.8 $\pm$ 9.5	61.7 $\pm$ 13.3	1.903	0.065
Menstrual status			0.207	0.649			0.623	0.430
Premenopausal	52 (55.91)	27 (60.00)			27 (61.36)	8 (50.00)		
Postmenopausal	41 (44.09)	18 (40.00)			17 (38.64)	8 (50.00)		
Breast cancer history			3.747	0.053			0.576	0.448
Yes	0 (0)	2 (4.44)			1 (2.27)	1 (6.25)		
No	93 (100.00)	43 (95.56)			43 (97.73)	15 (93.75)		
Lesion mobility			3.073	0.080			0.341	0.559
Freely	41 (44.09)	27 (60.00)			23 (52.27)	7 (43.75)		
Poor	52 (55.91)	18 (40.00)			21 (47.73)	9 (56.25)		
Lesion quality			8.759	0.003			0.752	0.386
Soft	89 (95.70)	36 (80.00)			42 (95.45)	16 (100.00)		
Stiff	4 (4.30)	9 (20.00)			2 (4.55)	0 (0)		
Lesion location			0.095	0.758			2.963	0.085
Central region	46 (49.46)	21 (46.67)			30 (68.18)	7 (43.75)		
Surrounding quadrant	47 (50.54)	24 (53.33)			14 (31.82)	9 (56.25)		
No. of lesions			1.166	0.280			0.959	0.327
Single	72 (77.42)	31 (68.89)			27 (61.36)	12 (75.00)		
Multiple	21 (22.58)	14 (31.11)			17 (38.64)	4 (25.00)		
Maximum diameter (mm)	20.00 (15.20, 26.50)	25.6 (18.50, 41.00)	2.710	0.007	20.20 (14.47, 29.45)	19.00 (14.30, 24.20)	0.676	0.501
Glandular density			0.287	0.592			1.705	0.192
a or b type	19 (20.43)	11 (24.44)			9 (20.45)	1 (6.25)		
c or d type	74 (79.57)	34 (75.56)			35 (79.55)	15 (93.75)		
Lesion margin			0.757	0.384			5.952	0.015
Nonspiculated	17 (24.64)	6 (17.14)			6 (17.14)	8 (50.00)		
Spiculated	52 (75.36)	29 (82.86)			29 (82.86)	8 (50.00)		
Lesion shape			2.310	0.129			2.946	0.086
Nodular or mass	37 (52.86)	13 (37.14)			20 (57.14)	5 (31.25)		
Non-mass	33 (47.14)	22 (62.86)			15 (42.86)	11 (68.75)		
Enhancement pattern			8.920	0.003			1.983	0.159
Homogeneous	30 (32.26)	4 (8.89)			5 (11.36)	0 (0)		
Heterogeneous	63 (67.74)	41 (91.11)			39 (88.64)	16 (100.00)		
TIC type			7.271	0.007			0.256	0.613
I / II type	69 (74.19)	23 (51.11)			33 (75.00)	13 (81.25)		
III type	24 (25.81)	22 (48.89)			11 (25.00)	3 (18.75)		
Ki67			20.575	<0.001			2.239	0.135
$\geq 20\%$	57 (61.29)	44 (97.78)			30 (68.18)	14 (87.50)		
<20%	36 (38.71)	1 (2.22)			14 (31.82)	2 (12.50)		

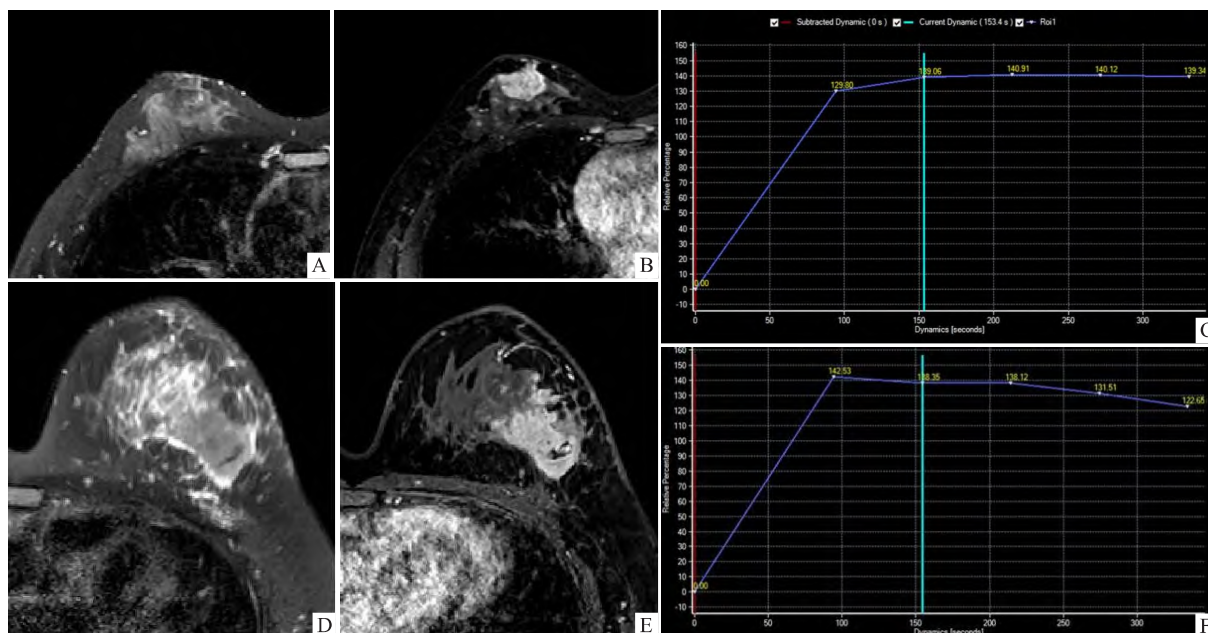


图2 不同HR状态的Her-2低表达乳腺

Fig.2 Her-2 low expression breast cancer with different HR status

A - C: Female patient, 50 year old, Her-2 low expression breast cancer of HR (+) in the central region of the right breast, the longest diameter is 2.7 cm, and it shows homogeneous and type II TIC curve; D - F: Female patient, 56 year old, Her-2 low expression breast cancer of HR (-) in the left lateral breast quadrant, the longest diameter is 5.4 cm, and it early shows heterogeneous enhancement and type III TIC curve.

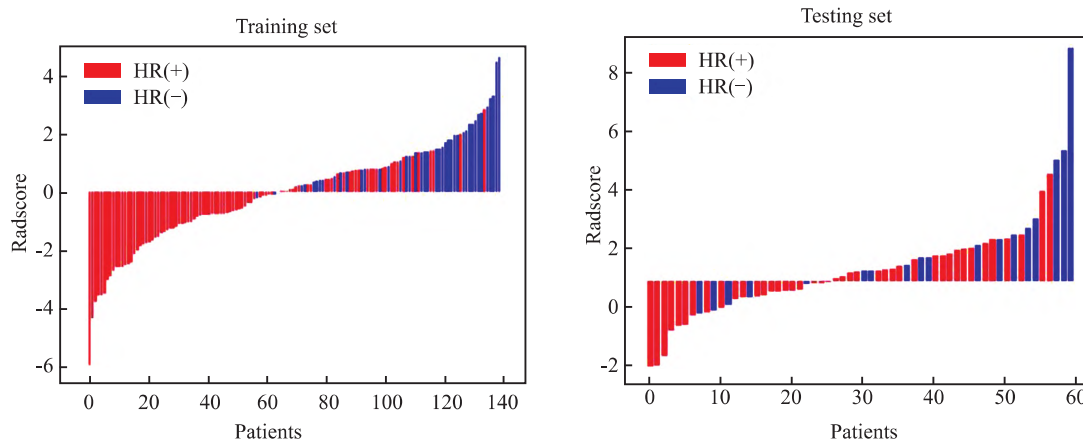


图3 训练集和验证集 radscore 区分乳腺癌HR状态的瀑布图

Fig.3 Waterfall diagram of radscore in distinguishing HR status of breast cancer in training set and testing set

特异度为89.6%。Delong 检验显示,在测试集中,联合模型预测HR状态的价值优于临床-影像模型和影像组学模型($P < 0.001$, $P = 0.036$) (表4)。校准曲线显示(图5A、5B),影像组学模型和联合模型对HR状态的概率预测结果与实际结果一致性较高(影像组学模型:训练集和测试集的 Hosmer-Lemeshow 检验 $P = 0.899$ 、 0.753 ; 联合模型:训练集和测试集的 Hosmer-Lemeshow 检验 $P = 0.764$ 、 0.349),而临床-影像模型的校准度不足(训练集和测试集

的 Hosmer-Lemeshow 检验 $P = 0.034$ 、 0.039)。DCA 曲线提示,在阈值概率0.2~1.0范围内使用联合模型的列线图预测HR表达状态收益高于其他模型(图5C、5D)。

3 讨论

本研究构建并验证了联合DCE-MRI影像组学和临床-影像特征的列线图,用于无创预测Her-2低表达乳腺癌患者HR状态,并证实联合模型在区

表3 训练集病例临床及常规影像学特征的单因素和多因素 Logistic 回归分析结果

Tab.3 Result of univariate and multivariate eregression analysis for clinical and radiological features in training set

Clinical and radiographic features	Univariate analysis		Multivariate analysis	
	OR (95% CI)	P value	OR (95% CI)	P value
TIC type (III type)	2.456 (1.211 – 5.086)	0.014	3.677 (1.464 – 10.130)	0.008
Enhancement pattern (heterogeneous)	4.881 (1.764 – 17.330)	0.005	5.786 (1.625 – 26.300)	0.012
Lesion margin (spiculated)	1.582 (0.584 – 4.780)	0.387		
Lesion shape (non-mass)	1.897 (0.835 – 4.439)	0.131		
Maximum diameter (mm)	1.019 (0.997 – 1.042)	0.046	1.013 (0.985 – 1.040)	0.049
No. of lesions (multiple)	1.548 (0.689 – 3.423)	0.282		
Lesion location(surrounding quadrant)	1.119 (0.548 – 2.293)	0.758		
Glandular density (c/d type)	0.794 (0.344 – 1.894)	0.592		
Axillary lymph node metastasis (yes)	0.859 (0.42 – 1.753)	0.676		
Histology type (NST)	0 (NA – 7.081)	0.987		
Ki67 (≥20%)	0.036 (0.002 – 0.177)	0.001	0.036 (0.001 – 0.201)	0.002
Lesion quality (stiff)	0.180 (0.046 – 0.589)	0.081		
Lesion mobility (freely)	0.635 (0.252 – 0.897)	0.007	0.237 (0.188 – 0.762)	0.046
Breast cancer history (yes)	0 (NA – 1.124)	0.987		
Menstrual status (postmenopausal)	0.526 (0.252 – 1.077)	0.081		
Age	0.768 (0.278 – 1.931)	0.588		

表4 影像组学模型、临床-影像模型及联合模型对 HR 状态的诊断效能

Tab.4 Diagnostic efficacy of radiomics models, clinical-radiological models, and combined models for HR status

Model	Training set				Testing set			
	AUC (95% CI)	Sensitivity (%)	Specificity (%)	P value	AUC (95% CI)	Sensitivity (%)	Specificity (%)	P value
Radiomics	0.897 (0.799 – 0.955)	62.8	98.5	0.080*	0.860 (0.892 – 0.927)	66.7	83.3	0.036*
Clinical-radiological	0.643 (0.596 – 0.758)	72.6	63.6	<0.001#	0.616 (0.595 – 0.706)	66.7	76.7	<0.001#
Combined	0.913 (0.806 – 0.980)	82.7	90.4	–	0.898 (0.832 – 0.945)	86.4	89.6	–

* Delong test between radiomics model and combined model; # Delong test between clinical-radiomics model and combined model.

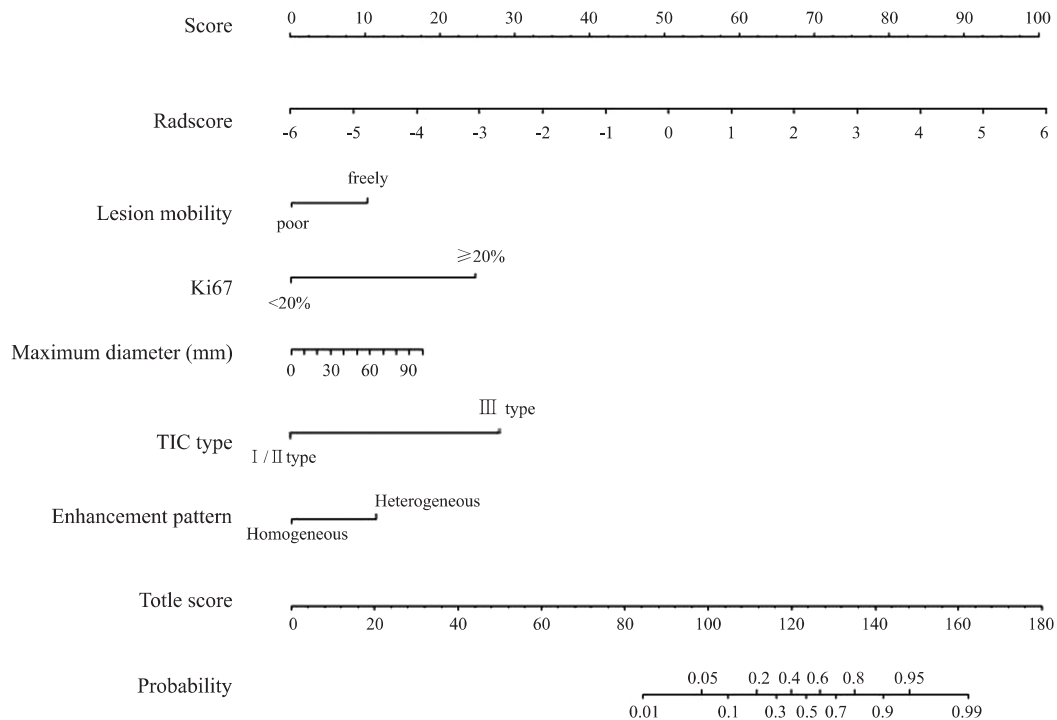


图4 不同模型预测 HR 状态的列线图

Fig. 4 Nomogram for predicting HR status using different models

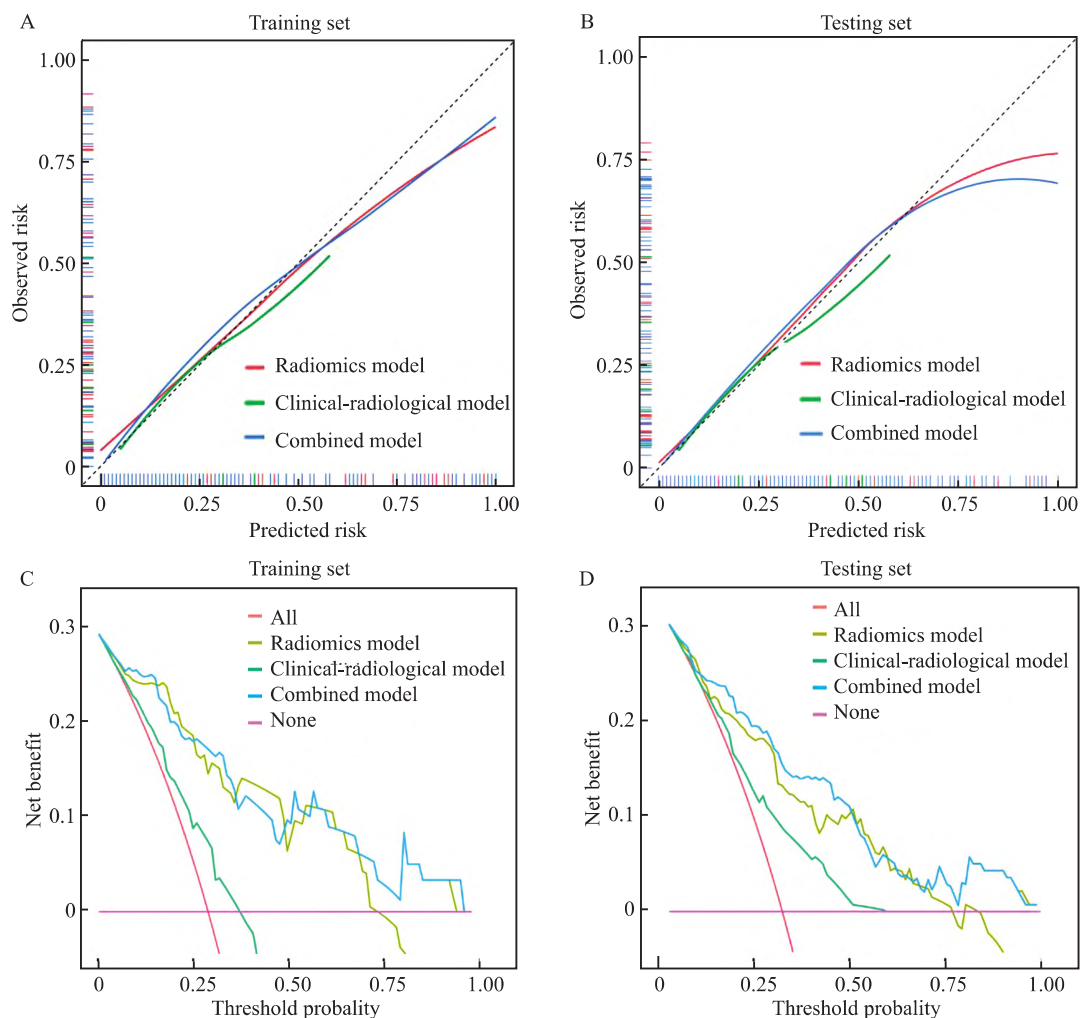


图5 不同模型预测HR状态的校准曲线(A,B)和DCA曲线(C,D)

Fig. 5 The calibration curves (A, B) and DCE curves (C, D) for predicting HR status using different models

分HR状态中具有最优效能,Radscore联合临床-影像特征能够作为HR表达状态的重要预测指标。

本研究共筛选出9个关键组学特征。firstorder_Range为一阶灰度值特征,反映了分割图像中体素信号强度值的分布范围。灰度级带矩阵(gray level size zone matrix, glszm)和灰度共生矩阵(gray-level co-occurrence matrix, glcm)是描述体素空间分布强度等级的二阶纹理特征,High Gray Level Emphasis是高通滤波强调,具有更快灰度变化和更多异质信号的纹理特征,分别映射DCE-MRI图像中肿瘤组织的异质性和灰度区域的分布情况,能够精确反映乳腺癌的高度异质性和增强扫描后的信号强度变化^[6-7]。此外,还有6个关键特征通过滤波变换提取,这是由于滤波变换具有多尺度分析的性能优势,能够同时捕获图像信号的多时域和多频域信息,从而揭示肉眼无法识别的肿瘤高度异质性^[8-10]。

Radscore是通过特定公式和系数整合多个影像

组学特征得到的定量指标,能够使复杂的影像组学信息更容易被理解和应用^[11-12]。本研究显示,HR(-)的Her-2低表达组的Radscore值明显高于HR(+)组,提示HR(-)肿瘤组织的特征更复杂、异质性更明显。

多因素Logistic回归分析显示,临床特征中的病灶活动度和Ki67表达,以及影像学特征中的TIC曲线类型、强化特征和病灶长径是HR状态的独立预测因子。多项研究^[13-14]证实,HR表达状态是Her-2低表达乳腺癌新辅助化疗病理完全缓解的独立预测因素,HR(+)Her-2低表达乳腺癌患者的预后优于HR(-)患者。训练集显示,HR(-)组比HR(+)组更易表现为不均匀的强化方式和TICⅢ型曲线,这一结果与既往研究证实的HR(-)乳腺癌恶性程度更高、侵袭性更强和预后更差的特征一致^[15-16]。恶性肿瘤的迅速生长与肿瘤新生血管密切相关,新生血管密度越高、管壁通透性越强,造影

剂进入血管后更可能表现出早期迅速强化、后期廓清的强化特征^[17]。另一方面,Chen et al^[18]认为,ER(+)肿瘤分泌较少的血供内皮生长因子,从而使肿瘤新生血管被抑制,表现为Ⅱ型TIC曲线。当瘤体较大时,血供和氧供无法满足肿瘤迅速生长的需求,进一步发生了瘤内出血、坏死,导致不均匀的强化。在临床特征中,本研究HR(-)组Ki67表达水平高于HR(+)组,这与Yoon et al^[19]的一项纳入2 162例乳腺癌患者的研究结果类似。然而,临床因素易受样本纳入标准、年龄、种族等多方面的影响,这也是本研究中临床-影像模型的诊断效能较低的原因。

总之,本研究构建的基于DCE-MRI影像组学模型具有预测HR状态的价值,结合临床-影像特征建立的临床-影像-影像组学列线图预测效能进一步提高,为评估Her-2低表达乳腺癌的HR状态提供了无创的新方法,为乳腺癌的精准治疗提供了客观依据。本研究存在一定局限性。首先,作为单中心、回顾性研究,选择偏倚是其主要的局限性,需要多中心、前瞻性研究以进行验证模型的泛化性。其次,本研究仅提取单一序列的MRI影像组学特征进行分析,多模态MRI影像组学将更全面地反映肿瘤的异质性并提高预测性能,因此本研究未来将构建大样本、多模态MRI影像组学模型进一步验证本研究结果。

参考文献

- [1] Choong G M, Cullen G D, O'Sullivan C C. Evolving standards of care and new challenges in the management of HER2-positive breast cancer[J]. CA Cancer J Clin, 2020, 70(5): 355-74. doi: 10.3322/caac.21634.
- [2] Modi S, Jacot W, Yamashita T, et al. Trastuzumab deruxtecan in previously treated HER2-low advanced breast cancer[J]. N Engl J Med, 2022, 387(1): 9-20. doi: 10.1056/NEJMoa2203690.
- [3] Baez-Navarro X, van Bockstal M R, Jager A, et al. HER2-low breast cancer and response to neoadjuvant chemotherapy: a population-based cohort study[J]. Pathology, 2024, 56(3): 334-42. doi: 10.1016/j.pathol.2023.10.022.
- [4] Witowski J, Heacock L, Reig B, et al. Improving breast cancer diagnostics with deep learning for MRI[J]. Sci Transl Med, 2022, 14(664): eabo4802. doi: 10.1126/scitranslmed.abo4802.
- [5] Lafci O, Celepli P, Seher Öztekin P, et al. DCE-MRI radiomics analysis in differentiating luminal A and luminal B breast cancer molecular subtypes[J]. Acad Radiol, 2023, 30(1): 22-9. doi: 10.1016/j.acra.2022.04.004.
- [6] 侯秋阳,叶成坤,刘畅,等.基于多参数磁共振瘤周区域的影像组学模型在脑胶质瘤预后评估中的应用价值[J].安徽医科大学学报,2024,59(1): 154-61. doi: 10.19405/j.cnki.issn1000-1492.2024.01.025.
- [6] Hou Q Y, Ye C K, Liu C, et al. Application value of radiomics model based on multiparametric MRI glioma peritumoral region in glioma prognosis evaluation[J]. Acta Univ Med Anhui, 2024, 59(1): 154-61. doi: 10.19405/j.cnki.issn1000-1492.2024.01.025.
- [7] Corrias G, Micheletti G, Barberini L, et al. Texture analysis imaging "what a clinical radiologist needs to know" [J]. Eur J Radiol, 2022, 146: 110055. doi: 10.1016/j.ejrad.2021.110055.
- [8] 杨守鑫,张丽,吴宁.图像获取与重建中影像组学特征可重复性的研究进展[J].国际医学放射学杂志,2020,43(3): 326-30. doi: 10.19300/j.2020.Z17615.
- [8] Yang S X, Zhang L, Wu N. Research progress on the reproducibility of radiomic features in image acquisition and reconstruction [J]. Int J Med Radiol, 2020, 43(3): 326-30. doi: 10.19300/j.2020.Z17615.
- [9] Bian X, Du S, Yue Z, et al. Potential antihuman epidermal growth factor receptor 2 target therapy beneficiaries: the role of MRI-based radiomics in distinguishing human epidermal growth factor receptor 2-low status of breast cancer [J]. J Magn Reson Imaging, 2023, 58(5): 1603-14. doi: 10.1002/jmri.28628.
- [10] Zheng S, Yang Z, Du G, et al. Discrimination between HER2-overexpressing, low-expressing, and zero-expressing statuses in breast cancer using multiparametric MRI-based radiomics [J]. Eur Radiol, 2024, 34(9): 6132-44. doi: 10.1007/s00330-024-10641-7.
- [11] Li W, Wu X, Wang J, et al. A novel clinical-radscore nomogram for predicting ruptured intracranial aneurysm [J]. Heliyon, 2023, 9(10): e20718. doi: 10.1016/j.heliyon.2023.e20718.
- [12] He H, Liu J, Li C, et al. Predicting hematoma expansion and prognosis in cerebral contusions: a radiomics-clinical approach [J]. J Neurotrauma, 2024, 41(11-12): 1337-52. doi: 10.1089/neu.2023.0410.
- [13] Tarantino P, Niman S M, Erick T K, et al. HER2-low inflammatory breast cancer: clinicopathologic features and prognostic implications [J]. Eur J Cancer, 2022, 174: 277-86. doi: 10.1016/j.ejca.2022.07.001.
- [14] Zhou S, Liu T, Kuang X, et al. Comparison of clinicopathological characteristics and response to neoadjuvant chemotherapy between HER2-low and HER2-zero breast cancer [J]. Breast, 2023, 67: 1-7. doi: 10.1016/j.breast.2022.12.006.
- [15] 任玉琳,张丽,佟仲生.不同激素状态的HER2阳性晚期乳腺癌复发转移特征及生存分析[J].肿瘤防治研究,2019,46(1): 37-44. doi: 10.3971/j.issn.1000-8578.2019.18.0962.
- [15] Ren Y L, Zhang L, Tong Z S. Recurrent and metastatic characteristics and prognosis of advanced HER2-positive breast cancer patients with different HR status [J]. Cancer Res Prev Treat, 2019, 46(1): 37-44. doi: 10.3971/j.issn.1000-8578.2019.18.0962.

- [16] Agostinetti E, Rediti M, Fimereli D, et al. HER2-low breast cancer: molecular characteristics and prognosis [J]. *Cancers (Basel)*, 2021, 13(11): 2824. doi: 10.3390/cancers13112824.
- [17] Tuan Linh L, Minh Duc N, Tra My T T, et al. Correlations between dynamic contrast-enhanced magnetic resonance imaging parameters and histopathologic factors in breast cancer [J]. *Clin Ter*, 2021, 172(5): 453–60. doi: 10.7417/CT.2021.2358.
- [18] Chen P, Zhao S, Guo W, et al. Dynamic contrast-enhanced magnetic resonance imaging features and apparent diffusion coefficient value of HER2-positive/HR-negative breast carcinoma [J]. *Quant Imaging Med Surg*, 2023, 13(8): 4816–25. doi: 10.21037/qims-22-1318.
- [19] Yoon K H, Park Y, Kang E, et al. Effect of estrogen receptor expression level and hormonal therapy on prognosis of early breast cancer [J]. *Cancer Res Treat*, 2022, 54(4): 1081–90. doi: 10.4143/crt.2021.890.

Nomogram based on DCE-MRI radiomics combined with clinical-radiological features in predicting hormone receptor status in breast cancer with low Her-2 expression

Hou Weishu¹, Pan Hongli¹, Wang Qun¹, Li Xiaohu¹, Yan Yunwen², Yu Yongqiang¹

(¹Dept of Medical Imaging, ²Dept of Breast Surgery, The First Affiliated Hospital of Anhui Medical University, Hefei 230022)

Abstract Objective To explore the value of nomogram based on DCE-MRI radiomics combined with clinical-radiological features in predicting HR status in breast cancer with Her-2 low expression. **Methods** A total of 198 patients of Her-2 low expression breast cancer who underwent standardized breast MRI in our hospital from January 2019 to February 2025 were retrospectively analyzed. Patients were divided into HR (+) group ($n = 137$) and HR (-) group ($n = 61$). The cases were divided into a training set (138 cases) and a testing set (60 cases) in a 7 : 3 ratio. Clinical-radiological model was based on clinical and traditional radiological features, radiomics model was based on DCE-MRI, and combined model was constructed, respectively. The nomogram was drawn, and receiver operating characteristic curve was used to compare the performance of different models in predicting HR status. **Results** The DCE-MRI radiomics score (Radscore) between the HR (+) group and the HR (-) group showed statistical differences in both the training and testing sets (both $P < 0.001$). The AUC of the clinical-radiological model based on lesion mobility, Ki67, TIC type, enhancement pattern and maximum diameter for predicting HR status in the training set and testing set were 0.643 and 0.616, respectively. The AUC of the DEC-MRI radiomics model in the training set and testing set were 0.897 and 0.860, respectively. The nomogram drawn by combining clinical-radiological features and Radscore showed better predictive performance in both the training set ($AUC = 0.913$) and testing set ($AUC = 0.898$) than the clinical-radiological model (all $P < 0.05$). **Conclusion**

The nomogram combined by DCE-MRI radiomics and clinical-radiological features can effectively predict HR status of breast cancer with low Her-2 expression, which is helpful to the building of individualized treatment plan for breast cancer patients.

Key words breast cancer; dynamic enhanced magnetic resonance imaging; radiomics; human epidermal growth factor receptor 2; hormone receptor; nomogram

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Corresponding author Yu Yongqiang, E-mail: ayfyyongqiang@163.com