·临床研究·

乳腺癌新辅助化疗后肿瘤退缩模式的影响因素分析及其预测模型的构建

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摘　要：【目的】探讨乳腺癌新辅助化疗（NACT）后肿瘤退缩模式的影响因素，构建肿瘤退缩模式的预测模型并进行验证。【方法】选取 2019 年 3 月 1 日至 2024 年 3 月 1 日期间接受 NACT 的 1 314 例乳腺癌患者作为研究对象，随机分为验证队列（n=301）和研究队列（n=603）。研究队列中，根据 NACT 后肿瘤退缩模式将患者进一步分为向心性退缩组（病例组，n=387）与非向心性退缩组（对照组，n=216）。收集两组患者的一般临床病理资料并进行比较，采用非条件 Logistic 回归分析 NACT 后肿瘤退缩模式的影响因素并建立预测模型，使用 Hosmer-Lemeshow 检验和受试者工作特征（ROC）曲线评价模型的拟合优度与预测性能，并进行外部验证。【结果】研究队列中，174 例（28.9%）患者达到病理学完全缓解（pCR），213 例（35.3%）呈单灶退缩，92 例（15.3%）呈多灶退缩，78 例（12.9%）呈主残余病灶伴卫星病灶，43 例（7.1%）为疾病稳定，3 例（0.5%）出现疾病进展。两组间年龄、雌激素受体（ER）、孕激素受体（PR）、Ki-67、人表皮生长因子受体 2（HER2）、组织学分级、预后营养指数（PNI）及化疗方案的差异均有统计学意义（均 $P < 0.05$）。Logistic 回归分析显示，年龄（OR=0.563，95% CI：0.358 ~ 0.885）、ER（OR=0.521，95% CI：0.350 ~ 0.773）、PR（OR=0.552，95% CI：0.379 ~ 0.806）、HER2（OR=3.729，95% CI：2.488 ~ 5.590）、Ki-67（OR=1.804，95% CI：1.071 ~ 3.039）、PNI（OR=2.285，95% CI：1.307 ~ 3.997）和组织学分级（Ⅲ级）（OR=2.194，95% CI：1.283 ~ 3.751）是 NACT 后向心性退缩的独立影响因素（均 $P < 0.05$）。该 logistic 回归模型的 Hosmer-Lemeshow 检验 P 值为 0.927，ROC 曲线下面积为 0.731（95% CI：0.690 ~ 0.772，$P < 0.001$）。外部验证结果显示，该预测模型的 ROC 曲线下面积为 0.764（95% CI：0.709 ~ 0.820，$P < 0.001$），敏感度为 75.0%，特异度为 65.7%，约登指数为 0.407。【结论】该 Logistic 回归模型具有较高的预测价值，可为临床医生预测乳腺癌患者 NACT 后的肿瘤退缩模式提供参考。

关键词：乳腺癌；新辅助化疗；肿瘤退缩模式；预测模型
中图分类号：R737.9　　**文献标志码：**A　　**文章编号：**1672-3554（2026）04-0756-11
DOI：10.11714/jsysu.med.YX20260083

Analysis of Risk Factors for Tumor Regression Patterns After Neoadjuvant Chemotherapy in Breast Cancer and the Construction of Its Predictive Model

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Abstract:【Objective】To explore the influencing factors of tumor regression patterns after neoadjuvant chemotherapy

收稿日期：2026-06-09　　**录用日期：**2026-07-07
基金项目：江西省卫生健康委科技计划项目（SKJP220211021）
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(NACT) in breast cancer, construct and validate a predictive model for tumor regression patterns.【Methods】A total of 1 314 breast cancer patients who received NACT between March 1, 2019, and March 1, 2024, were selected as study subjects and randomly divided into a validation cohort (n=301) and a study cohort (n=603). Within the study cohort, patients were further stratified based on post-NACT tumor regression patterns into a concentric regression group (case group) (n=387) and a non-concentric regression group (control group) (n=216). General clinicopathological data were collected and compared between the two groups. Unconditional logistic regression was used to analyze the influencing factors of tumor regression patterns post-NACT and establish a predictive model. The Hosmer-Lemeshow test and receiver operating characteristic (ROC) curve were employed to evaluate the model's goodness-of-fit and predictive performance, followed by external validation.【Results】Among all subjects in the study cohort, 174 patients (28.9%) achieved pathological complete response (pCR), 213 (35.3%) showed unifocal regression, 92 (15.3%) had multifocal regression, 78 (12.9%) presented main residual lesions with satellite lesions, 43 (7.1%) had stable disease, and 3 (0.5%) experienced disease progression. Significant differences were observed between the two groups in age, estrogen receptor (ER), progesterone receptor (PR), Ki-67, human epidermal growth factor receptor 2 (HER2), histological grade, prognostic nutritional index (PNI), and chemotherapy regimen (all $P < 0.05$). Logistic regression analysis revealed that age (OR=0.563, 95% CI: 0.358 - 0.885), ER (OR=0.521, 95% CI: 0.350 - 0.773), PR (OR=0.552, 95% CI: 0.379 - 0.806), HER2 (OR=3.729, 95% CI: 2.488 - 5.590), Ki-67 (OR=1.804, 95% CI: 1.071 - 3.039), PNI (OR=2.285, 95% CI: 1.307 - 3.997) and histological grade (Ⅲ) (OR=2.194 95% CI: 1.283 - 3.751) were independent influencing factors for concentric regression post-NACT (all $P < 0.05$). The Hosmer-Lemeshow test for the logistic regression model yielded a P-value of 0.927, and the area under the ROC curve was 0.731 (95%CI: 0.690-0.772, $P < 0.001$). External validation demonstrated that the area under the ROC curve of this prediction model was 0.764 (95% CI: 0.709 - 0.820, P <0.001), with a sensitivity of 75.0% and a specificity of 65.7%. The Youden's index was 0.407.【Conclusion】This logistic regression model exhibits high predictive value and provides a reference for clinicians to predict tumor regression patterns in breast cancer patients after NACT.

Key words: breast cancer; neoadjuvant chemotherapy; tumor regression pattern; predictive model

[J SUN Yat-sen Univ (Med Sci), 2026, 47(4): 756-766]

乳腺癌是女性最常见的恶性肿瘤[1]，严重威胁女性的身心健康。新辅助化疗(neoadjuvant chemotherapy，NACT)已广泛应用于局部晚期乳腺癌患者，可有效降低肿瘤的TNM临床分期，使部分原本不能手术的患者获得手术机会，或使原本不适合保乳手术(breast conservation surgery，BCS)的患者得以接受保乳术[2-3]。通常，乳腺癌肿瘤在NACT后会出现不同程度的体积缩小，但其退缩程度和退缩模式表现出显著的异质性[4]。NACT后肿瘤退缩模式可分为向心性退缩和非向心性退缩[5]。研究表明，NACT后呈非向心性退缩的患者，保乳术后局部复发率显著高于向心性退缩者[6]。美国国家综合癌症网络(National Comprehensive Cancer Network，NCCN)指南强调，NACT后肿瘤的反应程度和退缩模式都是影响手术方案制定的关键因素[7]。对于NACT后呈向心性退缩的肿瘤，建议按退缩后的肿瘤范围进行保乳切除；而对于呈筛状退缩模式的肿瘤，则建议按NACT前的肿瘤范围进行切除[8]。因此，NACT后肿瘤退缩模式对乳腺癌患者的预后和手术决策均有重要影响。本研究旨在建立乳腺癌NACT后肿瘤退缩模式的预测模型，为乳腺癌的预后和临床实践提供有价值的参考。

1　材料与方法

1.1　一般资料

对2019年3月1日至2024年3月1日在南昌大学第二附属医院接受NACT的1 314例乳腺癌患者的临床资料进行回顾性分析。依据预设的纳入与排除标准，最终共纳入603例患者作为研究队列(筛选流程详见图1)。将患者分为对照组(非向心性退缩，n=216)和病例组(向心性退缩，n=387)。纳入标准：①经病理确诊的女性乳腺癌患者；②治疗前为单发病灶的乳腺癌患者；③接受NACT的患

者;④放疗/化疗方案完整规范的患者;⑤签署知情同意书的患者。排除标准:①双侧乳腺癌患者;②临床病理资料不完整者;③合并其他原发肿瘤者;④于外院接受部分化疗后再转入我院者。收集所有入组研究对象的临床病理资料,包括基线特征:肿瘤退缩模式、年龄、病理T分期(pT分期)、病理N分期(pN分期)、病理分期、Ki-67指数、雌激素受体(estrogen receptor, ER)、孕激素受体(progesterone receptor, PR)、人表皮生长因子受体2(human epidermal growth factor receptor 2, HER2)、组织学分级、病理类型、手术方式、预后营养指数(prognostic nutritional index, PNI)、中性粒细胞与淋巴细胞比值(neutrophil-to-lymphocyte ratio, NLR)及化疗方案。本研究为回顾性研究,所有患者均签署了手术及放化疗知情同意书,本研究符合《赫尔辛基宣言》对伦理学的要求,通过了伦理委员会的审批,审批号:2026-102。

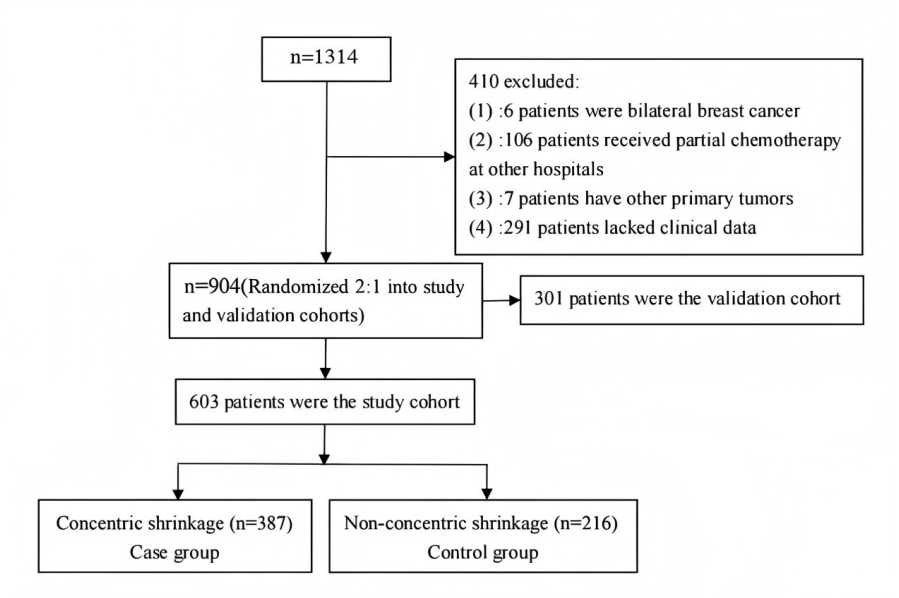


图1 研究人群筛选流程

Fig. 1 Screening process of research population

1.2 HER2状态评估标准及Ki-67的判读标准

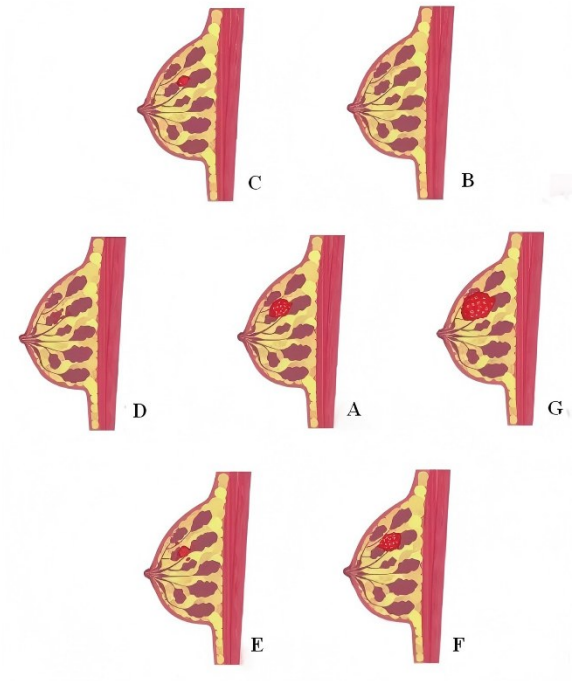
本研究所有患者HER2状态的评估标准及Ki-67的判读标准均根据美国临床肿瘤学会(American Society of Clinical Oncology, ASCO)指南[9]制定,乳腺癌分子分型则根据NCCN指南制定。

1.3 肿瘤退缩模式的评定标准

《实体瘤疗效评价标准(RECIST1.1)》[10]将NACT后肿瘤退缩模式分为以下6种,如图2所示:①乳腺无残留浸润性肿瘤(yp T0/Tis)定义为病理完全缓解(pathological complete response, pCR);②只有一个残余浸润性病灶,且最大直径缩小≥30%定义为单灶性退缩;③≥2个残余浸润性病灶定义为多灶性退缩;④主要残留病灶伴卫星病灶;⑤最大直径减少<30%或增加<20%定义为肿瘤稳定;⑥最大直径增加≥20%定义为肿瘤进展。本研究参照《实体瘤疗效评价标准(RECIST1.1)》由2位工作10年以上的病理科副主任医师对手术大体病理标本进行分析,将pCR和单灶性退缩定义为向心性退缩,多灶性退缩、主要残留病灶伴卫星病灶、肿瘤稳定及肿瘤进展定义为非向心性退缩。

1.4 统计学方法

计量资料采用独立样本 t 检验或Mann-Whitney U非参数检验进行组间比较。计数资料采用Pearson χ^2检验进行组间比较,将单因素分析有意义的因素($P<0.05$)纳入logistic多因素回归分析筛选出有意义的独立影响因素,并根据回归分析结果建立预测模型。采用Hosmer-Lemeshow检验及受试者工作特征(receiver operating characteristic, ROC)曲线评价预测模型的拟合优度及预测效能,最后采用外部研究队列对回归模型进行外部验证。$P<0.05$,表示差异有统计学意义,检验水准$\alpha=0.05$(双尾)。所有数据均采用SPSS 27.0软件进行



A: primary tumor; B: pCR; C: unifocal regression; D: multifocal regression; E: main residual lesions with satellite lesions; F: stable disease; G: progressive disease.

图2　乳腺肿瘤退缩模式示意图

Fig. 2　Schematic illustration of breast tumor regression patterns

统计学分析，所有图形均采用GraphPad Prism 8.0软件制作。

2　结 果

2.1　NACT的退缩模式分析

本研究共纳入603例乳腺癌患者，平均年龄为（48.9±9.8）岁。NACT后，肿瘤退缩模式分布如下：174例（28.86%）达到pCR，213例（35.32%）呈单灶性退缩，92例（15.26%）呈多灶性退缩，78例（12.94%）呈主要残留病灶伴卫星病灶，43例（7.13%）为肿瘤稳定，3例（0.50%）出现肿瘤进展（图3）。

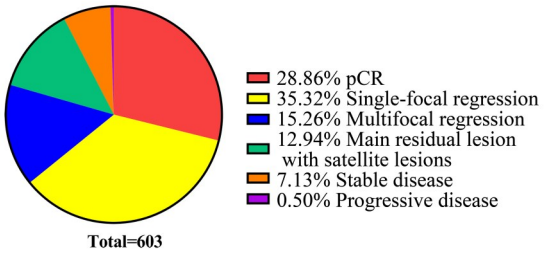


图3　NACT后肿瘤退缩模式分析

Fig. 3　Analysis of tumor regression pattern after NACT

2.2　单因素分析

病例组与对照组临床病理参数的比较显示，年龄、ER、PR、Ki-67、HER2、组织学分级、PNI及化疗方案差异均有统计学意义（均$P<0.05$），其余变量差异均无统计学意义（均$P>0.05$）。

2.3　多因素Logistic回归分析

为明确乳腺癌NACT后发生向心性退缩的独立影响因素，以肿瘤退缩模式（向心性退缩 *vs.* 非向心性退缩）为因变量，将单因素分析中$P<0.05$的协变量作为自变量（变量赋值详见表1），采用向后逐步变量选择法进行非条件logistic回归分析。结果显示，HER2、Ki-67、组织学分级Ⅲ级及PNI是向心性退缩的独立危险因素（$P<0.05$），而年龄、ER和PR是向心性退缩的独立保护因素（$P<0.05$；表2）。

表1　多因素Logistic回归分析的变量赋值表

Table 1　Variable assignment table of multivariate Logistic regression analysis

Variables	Variable assignment		
Dependent variables	–	–	–
tumor regression	Non-concentric=0	Concentric=1	–
Independent variables	–	–	–
Age	≤40=0	>40=1	–
ER	Negative=0	Positive=1	–
PR	Negative=0	Positive=1	–
HER2	Negative=0	Positive=1	–
Ki-67	<14%=0	≥14%=1	–
Histological grading	Ⅰ=0	Ⅱ=1	Ⅲ=2
PNI	<46.175=0	≥46.175=1	–

2.4　预测模型的建立

基于回归结果，建立Logistic回归预测模型如下：

$$\text{Logit}(P)=-0.235-0.575X_1(\text{年龄})-0.653X_2(\text{ER})-0.593X_3(\text{PR})+1.316X_4(\text{HER2})+0.590X_5(\text{Ki-67})+0.274X_6(\text{组织学分级Ⅱ级})+0.786X_7(\text{组织学分级Ⅲ级})+0.826X_8(\text{PNI})$$

对应的预测列线图见图

表2 Logistic回归分析结果

Table 2 Results of Logistic regression analysis

Variables	*b*	S.E.	*Wald* χ^2	*df*	*P* value	OR	95%CI	
							Lower limit	Upper limit
Age(years)(>40 *vs.* ≤40)	−0.575	0.231	6.187	1	0.013	0.563	0.358	0.885
ER(Positive *vs.* Negative)	−0.653	0.202	10.467	1	0.001	0.521	0.350	0.773
PR(Positive *vs.* Negative)	−0.593	0.193	9.466	1	0.001	0.552	0.379	0.806
HER2(Positive *vs.* Negative)	1.316	0.207	40.467	1	<0.001	3.729	2.488	5.590
Ki-67(≥14% *vs.* <14%=0)	0.590	0.266	4.923	1	0.027	1.804	1.071	3.039
Histological grading(Ⅱ *vs.* Ⅰ)	0.274	0.243	1.170	1	0.279	1.315	0.801	2.161
Histological grading(Ⅲ *vs.* Ⅰ)	0.786	0.274	8.240	1	0.004	2.194	1.283	3.751
PNI(≥46.175 *vs.* <46.175)	0.826	0.285	8.396	1	0.004	2.285	1.307	3.997
Constant	−0.235	0.475	0.244	1	0.621	0.791	–	–

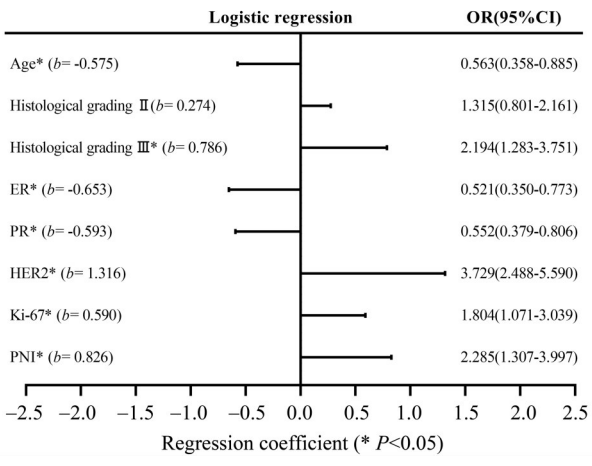


图4 各因素回归系数森林图

Fig. 4 Forest plot of regression coefficients for each factor

4。该模型拟合优度良好(Hosmer-Lemeshow检验:χ^2=3.112,*P*=0.927),预测性能稳健,ROC曲线下面积为0.731(95%CI:0.690-0.772,*P*<0.001;图5)。

2.5 预测模型的外部验证

依据本研究的纳入与排除标准,重新筛选2019年3月1日至2024年3月1日期间接受新辅助化疗的301例乳腺癌患者作为外部验证队列。该队列的基线临床病理特征见表3。将验证队列患者的临床病理资料代入预测模型公式,并将预测结果与实际结果进行比较。外部验证显示,本研究预测模型的ROC曲线下面积为0.764(95% CI:0.709-0.820,*P*<0.001),敏感度为75.0%,特异度为65.7%,约登指数为0.407,见图6,表明该预测模型具有良好的预测价值。

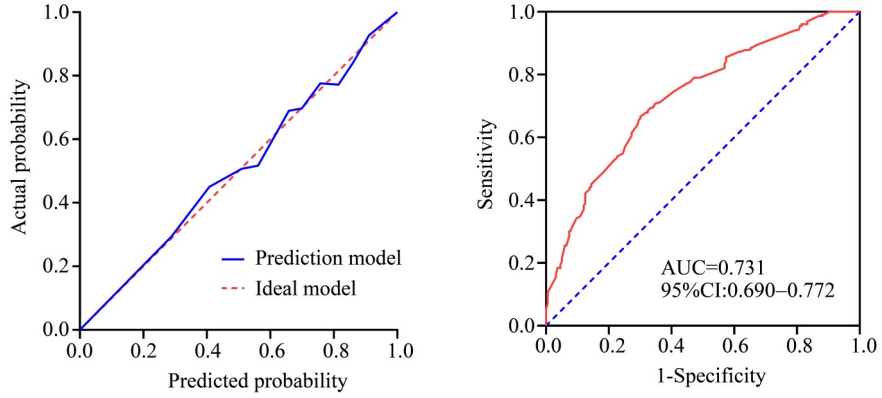


图5 Logistic回归预测模型的校准曲线及ROC曲线

Fig. 5 Calibration curve and ROC curve of Logistic regression prediction model

表3　验证队列的基线临床病理特征

Table 3　Baseline clinicopathological characteristics of the validation cohort

Item	Control group（n=110）	Case group（n=191）	Total（n=301）	χ^2	P
Age /years					
≤40	22(20.0)	60(31.4)	82(27.2)	4.588	0.032
>40	88(80.0)	131(68.6)	219(72.8)		
pT stage					
T2	38(34.5)	76(39.8)	114(37.9)		
T3	55(50.0)	101(52.9)	156(51.8)	5.093	0.078
T4	17(15.5)	14(7.3)	31(10.3)		
pN stage					
N0	25(22.7)	43(22.5)	68(22.6)		
N1	41(37.3)	70(36.6)	111(36.9)	1.210	0.751
N2	34(30.9)	53(27.7)	87(28.9)		
N3	10(9.1)	25(13.1)	35(11.6)		
Pathological stage					
ⅡA	8(7.3)	14(7.3)	22(7.3)		
ⅡB	30(27.3)	57(29.8)	87(28.9)		
ⅢA	53(48.2)	83(43.5)	136(45.2)	1.499	0.827
ⅢB	8(7.3)	11(5.8)	19(6.3)		
ⅢC	11(10.0)	26(13.6)	37(12.3)		
ER					
Negative	27(24.5)	81(42.4)	108(35.9)	9.681	0.002
Positive	83(75.5)	110(57.6)	193(64.1)		
PR					
Negative	37(33.6)	90(47.1)	127(42.2)	5.203	0.023
Positive	73(66.4)	101(52.9)	174(57.8)		
HER2					
Negative	80(72.7)	99(51.8)	179(59.5)	12.643	<0.001
Positive	30(27.3)	92(48.2)	122(40.5)		
Ki-67					
<14%	27(22.5)	20(10.5)	47(15.1)	8.312	0.004
≥14%	93(77.5)	171(89.5)	264(84.9)		
Histological grading					
Ⅰ	25(22.7)	26(13.6)	51(16.9)		
Ⅱ	55(50.0)	84(44.0)	139(46.2)	8.307	0.016
Ⅲ	30(27.3)	81(42.4)	111(36.9)		
Pathological type					
IDC	99(90.0)	171(89.5)	270(89.7)	0.017	0.897
Other	11(10.0)	20(10.5)	31(10.3)		
PNI					
<46.175	21(19.1)	15(7.9)	36(12.0)	8.371	0.004
≥46.175	89(80.9)	176(92.1)	265(88.0)		

续表

Item	Control group (n=110)	Case group (n=191)	Total (n=301)	χ^2	P
NLR					
<4.755	37(33.6)	77(40.3)	114(37.9)	1.323	0.250
≥4.755	73(66.4)	114(59.7)	187(62.1)		
Surgery					
Partial mastectomy	37(33.6)	52(27.2)	89(29.6)	1.378	0.240
Mastectomy	73(66.4)	139(72.8)	212(70.4)		
Chemotherapy					
AT	24(21.8)	73(32.9)	97(29.2)		
TAC	32(29.1)	23(10.4)	55(16.6)		
TP	24(21.8)	34(15.3)	58(17.5)	24.788	<0.001
THP	18(16.4)	61(27.5)	79(23.8)		
TCbHP	12(10.9)	31(14.0)	43(13.0)		

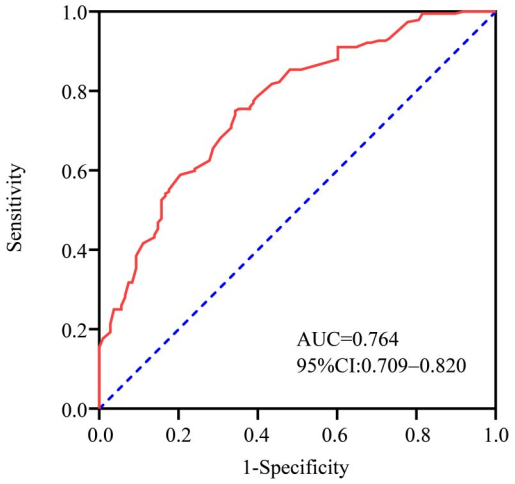


图6 预测模型外部验证的ROC曲线

Fig. 6 ROC curve for external validation of the prediction mode

2.6 亚组分析

为了探究不同亚型乳腺癌新辅助化疗后肿瘤退缩的危险因素,我们基于Luminal A/B、HER2阳性、三阴性乳腺癌进行了亚组分析。结果显示,在Luminal A/B型乳腺癌中,HER2、Ki-67、组织学分级Ⅲ级是向心性退缩的独立危险因素(P<0.05),而年龄、ER和PR是向心性退缩的独立保护因素(P<0.05;表4);在HER2阳性乳腺癌患者中,Ki-67、组织学分级Ⅲ级是向心性退缩的独立危险因素(P<0.05),而年龄是向心性退缩的独立保护因素(P<0.05;表5);在三阴性乳腺癌患者中,Ki-67、组织学分级Ⅲ级及PNI是向心性退缩的独立危险因素(P<0.05),而年龄是向心性退缩的独立保护因素(P<0.05;表6)。

3 讨 论

NACT能够降低乳腺癌的临床分期,使最初被认为无法手术的局部晚期患者或渴望BCS的患者获得手术条件,这推动了其在临床中的广泛应用[11]。鉴于其安全性和有效性,NACT已被指南认定为中晚期乳腺癌的标准治疗方案[12],但NACT并不能保证所有患者都适合保乳手术,因为NACT后出现的非向心性退缩常常导致难以获得阴性切缘,这使得退缩模式成为决定手术策略和切除范围的关键因素[13-14]。在治疗前预测退缩模式,有助于临床医生识别出那些可能实现降期并适合保乳手术的患者,从而推动个体化治疗。Mougalian等[15]针对1 600例接受NACT治疗的患者进行的研究报告,其腋窝pCR率为28.4%,这与我们在603例患者中的研究结果(NACT后pCR率为28.9%)相符。NACT后单灶退缩率在30%至50%之间,其中三阴性乳腺癌(40%~60%)和HER2阳性乳腺癌(50%~70%)的单灶退缩率高于激素受体阳性/HER2阴性肿瘤(20%~40%)[16];我们队列中35.3%的单灶退缩

表4　Luminal A/B型乳腺癌新辅助化疗后肿瘤退缩模式的Logistic回归分析

Table 4　Logistic regression analysis of tumor regression patterns after neoadjuvant chemotherapy in Luminal A/B breast cancer

Variables	*b*	S.E.	*Wald* χ^2	*df*	*P* value	OR	95%CI	
							Lower limit	Upper limit
Age/years(>40 *vs.* ≤40)	−0.717	0.257	7.750	1	0.005	0.488	0.295	0.809
ER(Positive *vs.* Negative)	−1.002	0.247	16.494	1	<0.001	0.367	0.226	0.595
PR(Positive *vs.* Negative)	−1.006	0.219	21.059	1	<0.001	0.366	0.238	0.562
HER2(Positive *vs.* Negative)	1.122	0.250	20.082	1	<0.001	3.072	1.881	5.020
Ki-67(≥14% *vs.* <14%=0)	1.273	0.330	14.910	1	<0.001	3.573	1.872	6.819
Histological grading(Ⅱ *vs.* Ⅰ)	0.295	0.284	1.080	1	0.299	1.343	0.770	2.344
Histological grading(Ⅲ *vs.* Ⅰ)	0.809	0.308	6.919	1	0.009	2.246	1.229	4.104
PNI(≥46.175 *vs.* <46.175)	0.402	0.294	1.870	1	0.171	1.495	0.840	2.660
Constant	0.238	0.536	0.198	1	0.656	1.269	–	–

表5　HER2阳性型乳腺癌新辅助化疗后肿瘤退缩模式的Logistic回归分析

Table 5　Logistic regression analysis of tumor regression patterns after neoadjuvant chemotherapy in HER2-positive breast cancer

Variables	*b*	S.E.	*Wald* χ^2	*df*	*P* value	OR	95%CI	
							Lower limit	Upper limit
Age/years(>40 *vs.* ≤40)	−0.768	0.252	9.323	1	0.002	0.464	0.283	0.759
Ki-67(≥14% *vs.* <14%=0)	1.230	0.318	14.949	1	<0.001	3.422	1.834	6.384
Histological grading(Ⅱ *vs.* Ⅰ)	0.299	0.276	1.167	1	0.280	1.348	0.784	2.317
Histological grading(Ⅲ *vs.* Ⅰ)	0.792	0.300	6.969	1	0.008	2.207	1.226	3.973
PNI(≥46.175 *vs.* <46.175)	0.438	0.286	2.345	1	0.126	1.550	0.885	2.717
Constant	0.874	0.505	2.995	1	0.084	2.396	–	–

表6　三阴性乳腺癌新辅助化疗后肿瘤退缩模式的Logistic回归分析

Table 6　Logistic regression analysis of tumor regression patterns after neoadjuvant chemotherapy in triple-negative breast cancer

Variables	*b*	S.E.	*Wald* χ^2	*df*	*P* value	OR	95%CI	
							Lower limit	Upper limit
Age/years(>40 *vs.* ≤40)	−0.748	0.238	9.883	1	0.002	0.474	0.297	0.755
Ki-67(≥14% *vs.* <14%=0)	0.996	0.290	11.763	1	0.001	2.708	1.532	4.785
Histological grading(Ⅱ *vs.* Ⅰ)	0.383	0.257	2.225	1	0.136	1.466	0.887	2.425
Histological grading(Ⅲ *vs.* Ⅰ)	0.800	0.281	8.113	1	0.004	2.225	1.283	3.875
PNI(≥46.175 *vs.* <46.175)	0.624	0.266	5.494	1	0.019	1.867	1.108	3.146
Constant	−0.686	0.429	2.565	1	0.109	0.503	–	–

率与既往数据一致。单灶/向心性退缩与良好预后相关,而多灶退缩则预示着较差的预后[17-18]。尽管尚无统一的分类标准,但退缩模式通常被大致分为向心性退缩和非向心性退缩[19]。Goorts等[20]提出了一种基于MRI的六型分类法:0型(影像学完全缓解)、1型(向心性退缩>3 mm且无卫星灶)、2型(碎片状退缩伴多结节病灶)、3型(象限弥漫强化)、4型(疾病稳定:变化<3 mm)和5型(疾病进展:增长>3 mm或出现新病灶)。我们的分类基于广泛接受的RECIST1.1标准,确保了科学性。

本研究发现年龄是非向心性退缩的独立危险因素,提示年轻患者更可能出现向心性退缩,这可能是由于年轻乳腺癌患者组织学恶性程度更高、分子分型更不利,从而对化疗更敏感[21]。在我们的分析中,肿瘤pT分期、pN分期和病理分期与退缩模式无相关性,这与先前提示肿瘤直径是关键决定因素的研究[22]有所不同。具有旺盛增殖能力的高度侵袭性肿瘤,因生物学侵袭性与化疗敏感性相关,常在NACT后表现出更高的向心性退缩率[23]。我们认为,pT/pN/病理分期反映的是肿瘤生长时间而非其内在侵袭性[24],这解释了为何晚期疾病并不一定预示着化疗反应。本研究表明,ER、PR和HER2状态显著影响肿瘤退缩模式。ER/PR阳性肿瘤患者更倾向于表现出非向心性退缩,而HER2阳性肿瘤则倾向于向心性退缩,这与国内外研究结果一致[25-27]。这些发现提示,Luminal型乳腺癌在新辅助化疗后行保乳手术时,存在更高的肿瘤残留风险,而三阴性和HER2阳性乳腺癌则更容易通过保乳手术获得阴性切缘。关于组织学分级与退缩模式之间关系的研究有限;我们的多因素分析显示,组织学Ⅲ级是向心性退缩的独立预测因子(OR=2.194,P=0.004)。较高的组织学分级可能因其侵袭性更高、化疗更敏感而与向心性退缩相关,提示组织学分级可作为退缩模式的实用预测指标[28-29]。有关化疗方案对乳腺癌退缩模式影响的研究仍然有限。本研究显示,不同化疗方案间的退缩模式差异有统计学意义。既往研究也表明,不同NACT方案的肿瘤退缩模式存在差异[30]。化疗方案受病理分期和分子分型(ER、PR、HER2、Ki-67状态决定分子分型)的影响,并不是独立存在的变量,本研究多因素回归分析已纳入ER、PR、HER2、Ki-67等变量,为避免共线混杂影响回归分析的结果及效能,故而本研究未将化疗方案纳入多因素分析。预后营养指数(PNI)被认为是一种简单有效的生物标志物,可反映治疗前的营养和炎症状态,并作为乳腺癌和结直肠癌等手术的预后预测因子[31-32]。其在乳腺癌NACT中的作用尚不完全明确。本研究首次提供了PNI与乳腺癌肿瘤退缩模式相关的证据,从而为预测乳腺癌NACT后退缩模式确立了一个新的生物标志物。刘晨以及Huang等[33-34]亦建立了乳腺癌新辅助化疗后肿瘤退缩模式的预测模型,其ROC曲线下面积分别为0.802、0.826,较本研究预测性能更优,但他们的研究均为基于MRI影像组学建立的预测模型,退缩模式的判定标准是根据磁共振图像而定,而本研究则是根据大体病理标本判定,从判定标准的差异来看,本研究仍具有一点的优势。我们建立的NACT后退缩模式预测模型具有临床实用性:①所需变量均可从常规临床记录中便捷获取;②可量化非向心性退缩的概率,有助于术前规划;③可为手术决策提供信息。此外,外部验证已证实该模型具有显著的预测价值(ROC曲线下面积为0.763),表明其具有良好的可用性和稳定性,为临床实践带来实际益处。

本研究存在若干局限性。首先,样本量相对较小(n=603),可能引入统计学偏倚。其次,作为一项单中心研究,研究结果的普适性可能受限。最后,其回顾性设计本身存在选择偏倚和主观影响的风险。

鉴于我们构建的logistic回归模型具有良好的预测性能和一致性,该模型对于帮助临床医生预测乳腺癌患者NACT后的肿瘤退缩模式具有临床应用价值。

综上所述,年轻的三阴性或HER2阳性乳腺癌患者,若Ki-67高表达、组织学分级高、PNI升高,则在NACT后更倾向于向心性退缩,因此,对于此类患者,NACT后接受保乳手术可能是更优选择,而对于年龄较大、Luminal型的乳腺癌患者,NACT后肿瘤更倾向于非向心性退缩,若行保乳手术,切缘应以NACT前为准,避免肿瘤残留。

参考文献

[1] Sung H, Ferlay J, Siegel RL, et al. Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries[J]. CA Cancer J Clin, 2021,71(3):209-249.

[2] Tamirisa N, Hunt KK. Neoadjuvant chemotherapy, endocrine therapy, and targeted therapy for breast cancer: ASCO guideline[J]. Ann Surg Oncol, 2022,29(3):1489-1492.

[3] 杨金喆,李秀凤,次宇婕,等.新辅助化疗联合小剂量阿帕替尼治疗三阴性乳腺癌疗效[J].临床军医杂志,2024,52(10):1053-1055.
Yang JZ, Li XF, Ci YJ, et al. The efficacy of neoadjuvant chemotherapy combined with low-dose apatinib in the treatment of triple-negative breast cancer[J]. Clin J Med Officers,2024,52(10):1053-1055.

[4] Huang X, Xu Z, Zhao Y, et al. Longitudinal MRI-based deep learning model for predicting pathological complete response in breast cancer: a multicenter, retrospective cohort study[J].npj Precision Oncology, 2026, 10(1). doi:10.1038/s41698-025-01256-2.

[5] Zhuang X, Chen C, Liu Z, et al. Multiparametric MRI-based radiomics analysis for the prediction of breast tumor regression patterns after neoadjuvant chemotherapy[J]. Transl Oncol, 2020,13(11):100831.

[6] Fan M, Wang K, Pan D, et al. Radiomic analysis reveals diverse prognostic and molecular insights into the response of breast cancer to neoadjuvant chemotherapy: a multicohort study[J]. J Transl Med, 2024,22(1):637.

[7] Gradishar WJ, Moran MS, Abraham J, et al. Breast cancer, version 3.2022, NCCN clinical practice guidelines in oncology[J]. J Natl Compr Canc Netw, 2022,20(6):691-722.

[8] Dubey S, Krishnanand K, Shukla Y, et al. Factors influencing surgical choices in breast cancer treatment in india: a comparative study of breast-conserving surgery vs mastectomy[J]. Cureus, 2024,16(8):e66825.

[9] Wolff AC, Hammond MEH, Allison KH, et al. Human epidermal growth factor receptor 2 testing in breast cancer: American society of clinical oncology/college of American pathologists clinical practice guideline focused update[J]. J Clin Oncol, 2018,36(20):2105-2122.

[10] Eisenhauer EA, Therasse P, Bogaerts J, et al. New response evaluation criteria in solid tumours: revised RECIST guideline (version 1.1)[J]. J Eur J Cancer, 2009,45(2):228-247.

[11] Harbeck N. Neoadjuvant and adjuvant treatment of patients with HER2-positive early breast cancer[J]. Breast, 2022, 62Suppl 1(Suppl 1):S12-S16.

[12] Gradishar WJ, Moran MS, Abraham J, et al. Breast cancer, version 3.2024, NCCN clinical practice guidelines in oncology[J]. J Natl Compr Canc Netw, 2024,22(5):331-357.

[13] Graeser M, Schrading S, Gluz O, et al. Magnetic resonance imaging and ultrasound for prediction of residual tumor size in early breast cancer within the ADAPT subtrials[J]. Breast Cancer Res, 2021,23(1):36.

[14] Rajan KK, Boersma C, Beek MA, et al. Optimizing surgical strategy in locally advanced breast cancer: a comparative analysis between preoperative MRI and postoperative pathology after neoadjuvant chemotherapy[J]. Breast Cancer Res Treat, 2024,203(3):477-486.

[15] Mougalian SS, Hernandez M, Lei X, et al. Ten-year outcomes of patients with breast cancer with cytologically confirmed axillary lymph node metastases and pathologic complete response after primary systemic chemotherapy[J]. JAMA Oncol, 2016,2(4):508-516.

[16] Li M, Xu B, Shao Y, Liu H, Du B, Yuan J. Magnetic resonance imaging patterns of tumor regression in breast cancer patients after neo-adjuvant chemotherapy, and an analysis of the influencing factors[J]. Breast J, 2017,23(6):656-662.

[17] Mamounas EP, Anderson SJ, Dignam JJ, et al. Predictors of locoregional recurrence after neoadjuvant chemotherapy: results from combined analysis of national surgical adjuvant breast and bowel project B-18 and B-27[J]. J Clin Oncol, 2012,30(32):3960-3966.

[18] Fukada I, Araki K, Kobayashi K, et al. Pattern of tumor shrinkage during neoadjuvant chemotherapy is associated with prognosis in low-grade luminal early breast cancer[J]. Radiology, 2018,286(1):49-57.

[19] Reis J, Thomas O, Lahooti M, et al. Correlation between MRI morphological response patterns and histopathological tumor regression after neoadjuvant endocrine therapy in locally advanced breast cancer: a randomized phase Ⅱ trial[J]. Breast Cancer Res Treat, 2021,189(3):711-723.

[20] Goorts B, Dreuning KMA, Houwers JB, et al. MRI-based response patterns during neoadjuvant chemotherapy can predict pathological (complete) response in patients with breast cancer[J]. Breast Cancer Res, 2018,20(1):34.

[21] Wang W, Tian B, Xu X, et al. Clinical features and prognostic factors of breast cancer in young women: a retrospective single-center study[J]. Arch Gynecol Obstet, 2023,307(3):957-968.

[22] Wang S, Zhang Y, Yang X, et al. Shrink pattern of breast cancer after neoadjuvant chemotherapy and its correlation

with clinical pathological factors [J]. World J Surg Oncol, 2013,11(1):166.

[23] Zhang Y, Liu M, Yang H, et al. PIK3CA mutations are a predictor of docetaxel plus epirubicin neoadjuvant chemotherapy clinical efficacy in breast cancer [J]. Neoplasma, 2014,61(4):461-467.

[24] Dubsky P, Pinker K, Cardoso F, et al. Breast conservation and axillary management after primary systemic therapy in patients with early-stage breast cancer: the Lucerne toolbox [J]. Lancet Oncol, 2021,22(1):e18-e28.

[25] Wang M, Du S, Gao S, et al. MRI-based tumor shrinkage patterns after early neoadjuvant therapy in breast cancer: correlation with molecular subtypes and pathological response after therapy[J]. Breast Cancer Res, 2024,26(1):26.

[26] Cho N. Imaging features of breast cancer molecular subtypes: state of the art[J]. J Pathol Transl Med, 2021,55(1):16-25.

[27] Lee HJ, Song IH, Seo AN, et al. Correlations between molecular subtypes and pathologic response patterns of breast cancers after neoadjuvant chemotherapy[J]. Ann Surg Oncol, 2015,22(2):392-400.

[28] Katayama A, Miligy IM, Shiino S, et al. Predictors of pathological complete response to neoadjuvant treatment and changes to post-neoadjuvant HER2 status in HER2-positive invasive breast cancer[J]. Mod Pathol, 2021,34(7):1271-1281.

[29] Díaz-Redondo T, Lavado-Valenzuela R, Jimenez B, et al. Different pathological complete response rates according to PAM50 subtype in HER2+ breast cancer patients treated with neoadjuvant pertuzumab/trastuzumab vs. trastuzumab plus standard chemotherapy: an analysis of real-world data [J]. Front Oncol, 2019,9:1178.

[30] Gong Y, Zuo H, Zhou Y, et al. Neoadjuvant pseudomonas aeruginosa mannose-sensitive hemagglutinin (PA-MSHA) and chemotherapy versus placebo plus chemotherapy in patients with HER2-negative breast cancer: a randomized, controlled, double-blind trial[J]. Ann Transl Med, 2023,11(6):243.

[31] Xie H, Wei L, Yuan G, et al. Prognostic value of prognostic nutritional index in patients with colorectal cancer undergoing surgical treatment[J]. Front Nutr, 2022,9:794489.

[32] Chen L, Bai P, Kong X, et al. Prognostic nutritional index (PNI) in patients with breast cancer treated with neoadjuvant chemotherapy as a useful prognostic indicator[J]. Front Cell Dev Biol, 2021,9:656741.

[33] 刘晨,陈小波,黄晓媚,等.基于MRI影像组学预测乳腺癌新辅助化疗后肿瘤退缩模式的研究[J].磁共振成像,2023,14(3):28-35.
Liu C, Chen XB, Huang XM, et al. Prediction of tumor regression pattern after neoadjuvant chemotherapy for breast cancer based on MRI radiomics [J]. Chin J Magn Reson Imaging, 2023, 14(3): 28-35.

[34] Huang Y, Chen W, Zhang X, et al. Prediction of tumor shrinkage pattern to neoadjuvant chemotherapy using a multiparametric MRI-based machine learning model in patients with breast cancer [J]. Front Bioeng Biotechnol, 2021,9:662749.

(编辑 孙慧兰)