DOI:10.16016/j.2097-0927.202504075

全身炎症反应指数联合临床病理参数预测宫颈癌复发的模型建立与验证

管停宏[1],龚春霞[2],涂 袁[1],田晨帆[1],余佳欣[1],蒋 鹏[1] [1]重庆医科大学附属第一医院妇产科,重庆;[2]重庆医科大学附属妇女儿童医院妇产科,重庆

[摘要] **目的** 探讨术前全身炎症反应指数(systemic inflammatory response index, SIRI)联合临床病理参数预测宫颈癌术后复发的价值,并构建预后模型优化复发风险评估。**方法** 本研究通过纳入、排除标准纳入了2017年1月至2022年1月期间于重庆医科大学附属第一医院(训练队列,n=996)及重庆医科大学附属妇女儿童医院(验证队列,n=496)接受标准手术治疗的宫颈癌患者。通过单因素、多因素Cox回归分析筛选影响患者无复发生存期(recurrence-free survival,RFS)的危险因素并构建列线图,通过曲线下面积(area under curve,AUC)和校准曲线评估其预测效能。基于列线图进行风险分层,采用Kaplan-Meier曲线评估模型的临床效能。**结果** Cox回归分析显示国际妇产科联合会(international federation of gynecology and obstetrics, FIGO)分期(P<0.001)、肿瘤直径(P<0.001)、病理类型(P<0.001)、分级(P=0.007)、宫旁浸润(P<0.001)、肌层浸润深度(P=0.019)、淋巴脉管间隙浸润(P=0.019)、阴道切缘受累(P=0.010)、辅助治疗(P=0.012)以及SIRI(P<0.001)是宫颈癌患者RFS的独立预后因素。基于以上预后因素构建的综合预测模型在预测宫颈癌患者1年、3年和5年RFS方面表现优异,其预测效能显著优于单一指标模型(AUC=0.886)。**结论** 基于SIRI联合临床病理参数的列线图模型在预测宫颈癌患者的RFS方面展现了足够的准确性,能够为未来的临床实践提供个性化的临床决策支持。

[关键词] 宫颈癌;全身炎症反应指数;预后;预测模型
[中图法分类号] R181.23;R730.7;R737.33 [文献标志码] A

Construction and validation of prediction model for cervical cancer recurrence based on systemic inflammation response index and clinicopathological parameters

GUAN Tinghong[1], GONG Chunxia[2], TU Yuan[1], TIAN Chenfan[1], YU Jiaxin[1], JIANG Peng[1] [1]Department of Gynecology and Obstetrics, the First Affiliated Hospital of Chongqing Medical University, Chongqing; [2]Department of Gynecology and Obstetrics, Women and Children's Hospital Affiliated to Chongqing Medical University, Chongqing, China

[**Abstract**] **Objective** To investigate the predictive value of preoperative systemic inflammatory response index (SIRI) combined with clinicopathological parameters for postoperative recurrence in cervical cancer and to construct a prognostic model in order to optimize recurrence risk assessment. **Methods** Patients with cervical cancer who underwent standard surgical treatment at the First Affiliated Hospital of Chongqing Medical University (training cohort, n=996) and Chongqing Maternal and Child Health Hospital (validation cohort, n=496) between January 2017 and January 2022 were retrospectively enrolled based on our strict inclusion and exclusion criteria. Univariate and multivariate Cox regression analyses were performed to identify independent prognostic factors for recurrence-free survival (RFS), and then a nomogram

[通信作者] 蒋 鹏,E-mail:1094496466@qq.com

2097-0927/Copyright © 2025, 陆军军医大学(第三军医大学)。这篇开放获取文章遵循CC BY许可协议(https://creativecommons.org/licenses/by/4.0/)
引用格式:管停宏,龚春霞,涂袁,等. 全身炎症反应指数联合临床病理参数预测宫颈癌复发的模型建立与验证[J]. 陆军军医大学学报,2025,47(16):1950-1961. DOI:10.16016/j.2097-0927.202504075.
Citation:GUAN T H, GONG C X, TU Y, *et al*. Construction and validation of prediction model for cervical cancer recurrence based on systemic inflammation response index and clinicopathological parameters[J]. J Army Med Univ, 2025, 47(16): 1950-1961. DOI:10.16016/j.2097-0927.202504075.

was constructed. Receiver operating characteristic (ROC) curve was plotted to assess the predictive performance of the model, and the area under the curve (AUC) and calibration curve were employed to evaluate the model. Kaplan-Meier survival analysis was performed to determine the clinical application. **Results** Cox regression analysis demonstrated that International Federation of Gynecology and Obstetrics (FIGO) stage (P<0.001), tumor size (P<0.001), pathological type (P<0.001), tumor grade (P=0.007), parametrial invasion (P<0.001), depth of myometrial invasion (P=0.019), lymphovascular space invasion (P=0.019), vaginal margin involvement (P=0.010), adjuvant therapy (P=0.012), and SIRI (P<0.001) were independent prognostic factors for RFS. Our nomogram model based on above prognostic factors exhibited superior predictive performance for 1-, 3-, and 5-year RFS, with a significantly higher AUC value (0.886) than those of single-parameter models. **Conclusion** Our nomogram model demonstrated good accuracy in predicting RFS in cervical cancer patients, providing a potential tool for personalized clinical decision-making in recurrence risk management.

[**Key words**] cervical cancer; systemic inflammatory response index; prognosis; prediction model

Corresponding author: JIANG Peng, E-mail: 1094496466@qq.com

宫颈癌是全球女性癌症相关死亡的主要负担之一。据2020年全球癌症统计数据显示,该病新发病例约60.4万例,死亡病例约34.2万例[1],其中约48.3万例新发病例和27.4万例的死亡病例发生在低收入和中等收入国家[2]。尽管人乳头瘤病毒疫苗接种和规范化筛查项目的实施使发达国家宫颈癌发病率显著下降超过80%[3],该疾病仍构成重大的全球公共卫生挑战。对于早期宫颈癌(ⅠA-ⅡA期),治疗选择包括多种手术方式,盆腔外照射放疗联合近距离放疗和化疗的综合治疗方案;而对于局部晚期宫颈癌(ⅡB-ⅣA期),标准治疗策略为以顺铂为基础的同步放化疗,酌情结合近距离放疗[4]。值得注意的是,尽管近年来宫颈癌诊疗技术取得了显著进步,但术后复发和转移的风险依然存在,且不同患者的预后差异显著,对于复发或转移的患者,治疗选择有限,这通常导致疾病预后不良。即便经过有效治疗,复发或转移患者的中位总生存期仅为17个月[5]。目前,一项基于美国癌症监测数据库(surveillance, epidemiology, and end results program;SEER)的研究表明,预测宫颈癌患者复发的指标或模型仍主要依赖于传统的临床病理参数,如国际妇产科联合会(international federation of gynecology and obstetrics,FIGO)分期、肿瘤大小、组织学分级、淋巴结状态、浸润深度等[6-7]。且有研究报道,部分早期患者术后复发较早,预后差,而一些晚期患者的生存期很长,这提示仅凭FIGO分期等临床病理参数可能无法准确评估患者的预后[8]。这一临床现状凸显了探索新型预后预测指标的必要性,以期建立更加完善的风险评估体系,为宫颈癌患者个体化治疗方案的制定提供新的科学依据。

近年来多项研究证实,癌症本质上是以局部病灶为特征的全身性疾病[9]。长期以来,炎症一直被认为是癌症的标志,深入解析肿瘤微环境与全身性免疫炎症反应间的动态交互,对准确评估肿瘤复发风险及预后具有重要科学意义。在实体肿瘤预后预测领域,多项外周血炎症标志物展现出重要临床价值,包括血小板-淋巴细胞比值[10]、淋巴细胞-单核细胞比值[11]、C反应蛋白-白蛋白比值[12]、预后营养指数[13]和全身炎症反应指数(systemic inflammatory response index, SIRI)[14]。其中,SIRI作为新型预后生物标志物备受关注,其通过中性粒细胞计数、单核细胞计数与淋巴细胞计数的乘积比值(SIRI=中性粒细胞×单核细胞/淋巴细胞)反映机体炎症-免疫平衡状态。自2016年QI等[15]开创性将SIRI引入胰腺癌预后评估以来,该指标已在鼻咽癌[16]、结直肠癌[17]、卵巢癌[18]等多种实体瘤的生存结局评估中展现出普适性价值。然而,SIRI在宫颈癌预后分层中的临床应用尚未形成系统证据。基于此,本研究立足宫颈癌精准诊疗需求,重点探讨术前SIRI水平与患者复发的相关性。通过整合SIRI与FIGO分期、肿瘤分化程度等临床病理特征,拟构建多维度预后预测模型,实现宫颈癌复发的个体化动态预测,为临床提供兼具科学性与实用性的预后评估工具。

1 材料与方法

1.1 患者队列

本研究为双中心回顾性队列研究,根据纳入排除标准,最终纳入2017年1月至2022年1月期间于重庆医科大学附属第一医院(训练队列,n=996)及重庆医

科大学附属妇女儿童医院(外部验证队列,n=496)接受初次手术治疗的1 492例宫颈癌患者。

纳入标准包括:①行宫颈癌根治术+系统性盆腔淋巴结清扫术±腹主动脉旁淋巴结清扫术;②术后病理确诊的原发性宫颈癌(基于2018年FIGO标准)[19];③具备完整的术前基线资料;④术前1周完成标准血液检测(血常规、肝肾功能及凝血功能)。排除标准包括:①非标准术式(未行根治性子宫切除或淋巴结清扫不充分);②合并活动性感染(C反应蛋白>10 mg/L)、慢性炎症性疾病(如炎症性肠病、类风湿关节炎等)、免疫系统疾病(含自身免疫性疾病及人类免疫缺陷病毒感染)、血液系统疾病(血红蛋白<90 g/L或血小板<100×10^9/L)或严重肝肾功能不全(Child-Pugh C级或肾小球滤过率估计值<30 mL/min/1.73 m^2);③合并其他恶性肿瘤或接受新辅助治疗/姑息性手术;④失访或关键节点数据缺失。本研究的流程图如图1所示。研究获得了重庆医科大学附属第一医院伦理委员会(2021-174)及重庆医科大学妇女儿童医院伦理委员会批准[(2023)伦审(科)002号]。

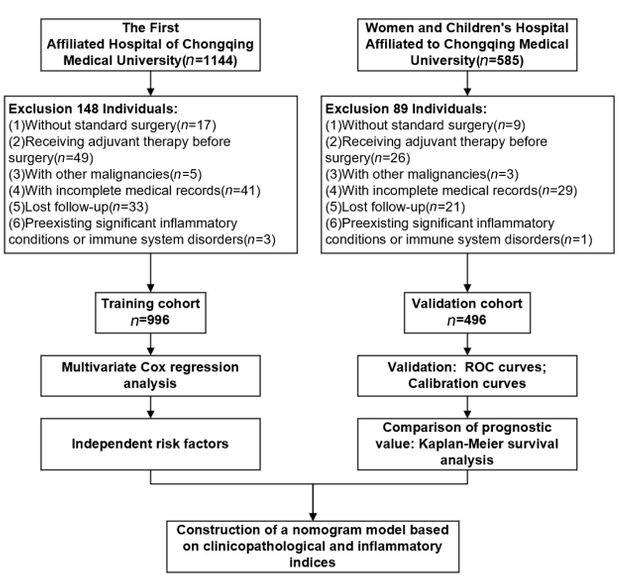


图1 宫颈癌患者筛选流程图

Figure 1 Flow chart of eligible cervical cancer patients

随访:所有患者在接受根治性子宫切除术伴盆腔淋巴结清扫术后,根据多学科讨论和国际指南判定是否接受辅助治疗(化疗和/或放疗)。对于具有以下病理风险因素的患者:切缘受累、淋巴结转移、宫旁浸润、淋巴脉管间隙浸润(lymphovascular space invasion,LVSI)、深部宫颈间质浸润、非鳞状组织学类型及肿瘤较大者,于术后4~6周内给予外照射放疗。原则上,在放疗期间同期给予含铂方案化疗,除非患者拒绝或无法耐受化疗[20]。所有患者自手术日起每3~6个月随访1次,持续2年;第3至5年每6~12个月随访1次;此后每年随访1次[21]。随访计划至少包括盆腔-直肠检查及病史采集。必要时,还会增加血清肿瘤标志物检测、阴道残端细胞学检查及影像学检查。随访截止日期为2025年1月31日。

复发:需经>2名妇科肿瘤医生通过体格检查、生化指标、影像学检查和病理活检确诊[22]。复发类型包括:局部复发(阴道残端复发和中央盆腔复发)及远处转移(腹主动脉旁淋巴结转移、腹膜转移及其他器官转移)[20]。无复发生存期(recurrence-free survival,RFS)定义为从诊断日期到复发或最后1次随访的持续时间;总生存期(overall survival,OS)则定义为从诊断到死亡或最后1次随访的持续时间[23]。

1.2 数据收集

回顾性收集患者的临床病理资料,包括年龄、体质指数(body mass index,BMI)、FIGO分期、肿瘤直径、病理类型、分级、宫旁浸润、肌层浸润、LVSI、阴道切缘阳性、辅助治疗和SIRI。此外,在手术前1周收集血常规检查结果,包括白细胞计数、中性粒细胞计数、单核细胞计数、淋巴细胞计数和血小板计数。SIRI的计算公式为:SIRI=中性粒细胞计数×单核细胞计数/淋巴细胞计数。通过约登指数[24]确定SIRI的最佳截断值。

1.3 统计学分析

对年龄、BMI、FIGO分期、肿瘤直径、病理类型、分级、宫旁浸润、肌层浸润、LVSI、阴道切缘阳性、辅助治疗和SIRI进行了单因素Cox回归分析,并进一步将其中具有统计学意义的变量纳入多因素Cox回归分析,其中P<0.05的变量被认定为独立影响因素。进一步将筛选出的变量纳入列线图模型,用以预测患者1、3和5年的RFS。通过受试者工作特征(receiver operating characteristic,ROC)曲线及其曲线下面积(area under the curve,AUC)量化模型对宫颈癌复发与非复发患者的区分能力,并利用校准曲线评估模型预测的1、3及5年RFS与实际观察结果的一致性。此外,采用DeLong检验对模型间AUC差异进行统计学比较。鉴于数据存在样本不平衡特性,进一步计算精确率-召回率曲线下面积(area under the precision-recall curve ,AUPRC),以客观评估模型对复发事件的识别精度。同时,运用Kaplan-Meier法进行风险分层,并通过Log-rank检验(双侧α=0.05)验证风险分组在RFS和OS中的临床效用。统计分析使用SPSS 26.0和R 4.3.0软件进行,双尾P<0.05被认为具有统计学意义。

2 结果

2.1 患者临床特征

本研究共纳入1 492例宫颈癌患者。训练队列996例(患者来自重庆医科大学附属第一医院),其中复发96例(9.64%),死亡64例(6.43%);验证队列496例(患者来自重庆医科大学附属妇女儿童医院),其中复发57例(11.49%),死亡35例(7.06%)。训练队列及验证队列中复发患者与未复发患者的临床特征见表1。在训练队列中,复发与未复发患者的年龄及BMI分布无显著差异;但复发组显著存在以下高风险特征:更高的FIGO分期比例,更大的肿瘤直径,更差的病理类型,更高的低分化比例,更高的比例合并宫旁浸润、肌层浸润、LVSI、阴道切缘阳性,更高的辅助治疗比例和更高

表1 训练队列及验证队列宫颈癌患者临床资料特征[例(%),$\bar{x}\pm s$]

Table 1 Clinical characteristics of cervical cancer patients in the training cohort and validation cohort

Variables	Training cohort				Validation cohort			
	None-recurrence n=900	Recurrence n=96	t/χ^2	P	None-recurrence n=439	Recurrence n=57	t/χ^2	P
Age (years)	48.12±9.12	48.72±10.26	−0.608	0.543	47.91±9.30	47.53±8.61	0.296	0.767
BMI (kg/m^2)	23.39±3.21	23.05±3.37	0.969	0.333	23.41±3.30	22.69±3.72	1.531	0.126
FIGO stage			134.6	<0.001			48.996	<0.001
Ⅰ	503(55.90)	22(22.90)			233(53.10)	18(31.60)		
Ⅱ	321(35.70)	27(28.10)			166(37.80)	15(26.30)		
Ⅲ	76(8.40)	47(49.00)			40(9.10)	24(42.10)		
Tumor size			35.068	<0.001			24.253	<0.001
<4 cm	626(69.60)	38(39.60)			306(69.70)	21(36.80)		
≥4 cm	274(30.40)	58(60.40)			133(30.30)	36(63.20)		
Histology			10.986	0.001			3.567	0.059
Squamous cell carcinoma	758(84.20)	68(70.80)			380(86.60)	44(77.20)		
None-squamous cell carcinoma	142(15.80)	28(29.20)			59(13.40)	13(22.80)		
Grade			16.140	<0.001			4.669	0.097
1	313(34.80)	19(19.80)			138(31.40)	11(19.30)		
2	500(55.60)	57(59.40)			259(59.00)	37(64.90)		
3	87(9.70)	20(20.80)			42(9.60)	9(15.80)		
Parametrial invasion			37.143	<0.001			21.209	<0.001
No	875(97.20)	81(84.40)			427(97.30)	48(84.20)		
Yes	25(2.80)	15(15.60)			12(2.70)	9(15.80)		
Depth of invasion			38.117	<0.001			22.819	<0.001
<1/2	581(64.60)	31(32.30)			296(67.40)	20(35.10)		
≥1/2	319(35.40)	65(67.70)			143(32.60)	37(64.90)		
LVSI			79.599	<0.001			26.486	<0.001
Negative	795(88.30)	52(54.20)			393(89.50)	37(64.90)		
Positive	105(11.70)	44(45.80)			46(10.50)	20(35.10)		
Resection margin involvement			27.806	<0.001			18.174	<0.001
No	891(99.00)	88(91.70)			437(99.50)	53(93.00)		
Yes	9(1.00)	8(8.30)			2(0.50)	4(7.00)		
Adjuvant therapy			9.24	0.002			5.565	0.018
No	317(35.2)	19(19.80)			162(36.90)	12(21.10)		
Yes	583(64.8)	77(80.20)			277(63.10)	45(78.90)		
SIRI	0.85±0.78	1.22±0.78	−4.491	<0.001	0.85±0.93	1.16±0.90	−2.360	0.019

的SIRI水平(P<0.05)。

2.2 SIRI最佳风险阈值的确定及预后分析

由于训练队列中复发患者相较于未复发患者具有更高的SIRI,且单因素Cox回归分析表明,SIRI是宫颈癌复发的危险因素(P<0.001),进一步通过ROC曲线和最大约登指数(约登指数=敏感性+特异性-1)评估,SIRI预测宫颈癌复发的最佳截断值为0.995(AUC=0.709;敏感度,69.8%;特异度,70.7%)(图2)。

基于SIRI的最佳截断值,将训练队列和验证队列宫颈癌患者分为两组:SIRI≥0.995的患者为高SIRI组,SIRI<0.995的患者为低SIRI组。Kaplan-Meier生存分析结果显示,高SIRI组患者的RFS、OS均较低SIRI组更差(图3,表2、3)。

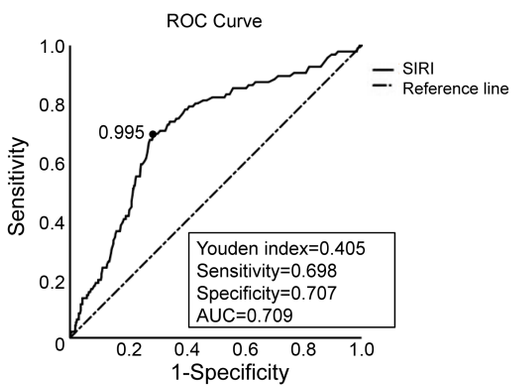


图2 SIRI预测宫颈癌患者复发的ROC曲线

Figure 2 ROC curve of SIRI in predicting recurrence for cervical cancer patients

2.3 宫颈癌患者复发的独立危险因素

进一步通过单因素和多因素Cox回归分析表明,FIGO分期(P<0.001)、肿瘤直径(P<0.001)、病理类型(P<0.001)、分级(P=0.007)、宫旁浸润(P<0.001)、肌层浸润(P=0.019)、LVSI(P=0.019)、阴道切缘阳性(P=0.010)、辅助治疗(P=0.012)和SIRI(P<0.001)是宫颈癌患者复发的独立影响因素(表4)。

2.4 宫颈癌复发的列线图预测模型的建立与验证

基于多因素Cox回归分析,我们构建了一个整合临床病理参数(FIGO分期、肿瘤直径、病理类型、分级、宫旁浸润、肌层浸润、LVSI、阴道切缘阳性、辅助治疗)及SIRI的预测宫颈癌患者RFS的列线图模型(图4)。基于该模型中预测因子的评分,可以计算出宫颈癌患者复发的风险概率。

如表5、图5所示,训练队列中,列线图模型展现出最优的预测效能,AUC=0.886(95%*CI*:0.853~0.919),显著高于临床病理参数(AUC=0.837,95%*CI*:0.795~0.880)和SIRI(AUC=0.702,95%*CI*:0.647~0.758);列线图模型较SIRI的AUC提升0.184(95%*CI*:0.125~0.243,P<0.001),较临床病理参数提升0.049(95%*CI*:0.017~0.081,P=0.003)。验证队列中,列线图模型仍保持良好预测性能(AUC=0.838,95%*CI*:0.780~0.896),其效能同样优于临床病理参数(AUC=0.790,95%*CI*:0.717~0.863)和SIRI(AUC=0.682,95%*CI*:0.606~0.758);列线图模型较SIRI的AUC提升0.156(95%*CI*:0.073~0.239,P<0.001),较临床病理参数提升0.048(95%*CI*:-0.019~0.115,P=0.159),

表2 训练队列中宫颈癌患者低SIRI组与高SIRI组的RFS及OS比较

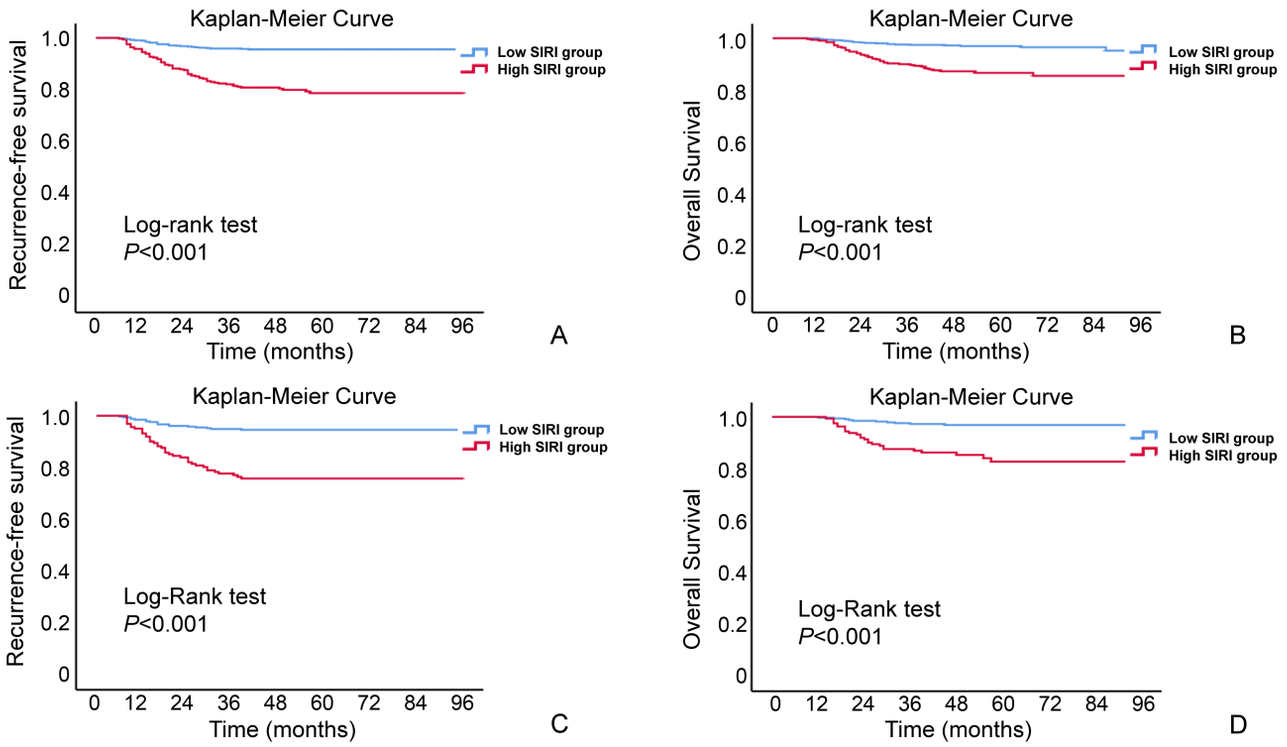
Table 2 Comparisons of RFS and OS between low- and high-SIRI groups in cervical cancer patients of the training cohort

Groups	All patients (n=996)	Recurrence (n=96)	3-year RFS (95%*CI*)	5-year RFS (95%*CI*)	P	Death (n=64)	3-year OS(95%*CI*)	5-year OS(95%*CI*)	P
Low-SIRI group	665	29	95.90% (94.33%~97.47%)	95.60% (94.03%~97.17%)	<0.001	21	97.40% (96.22%~98.57%)	97.40% (96.22%~98.57%)	<0.001
High-SIRI group	331	67	81.60% (77.48%~85.72%)	78.80% (74.10%~83.50%)		43	89.70% (85.67%~92.32%)	86.70% (82.97%~90.42%)	

表3 验证队列中宫颈癌患者低SIRI组与高SIRI组的RFS及OS比较

Table 3 Comparisons of RFS and OS between low- and high-SIRI groups in cervical cancer patients of the validation cohort

Groups	All patients (n=496)	Recurrence (n=57)	3-yearRFS (95%*CI*)	5-year RFS (95%*CI*)	P	Death (n=35)	3-year OS (95%*CI*)	5-year OS (95%*CI*)	P
Low-SIRI group	334	20	94.90% (92.54%~97.25%)	94.60% (92.25%~96.95%)	<0.001	10	97.10% (95.14%~99.06%)	96.10% (93.36%~98.84%)	<0.001
High-SIRI group	162	37	78.10% (71.63%~84.57%)	76.80% (70.33%~83.27%)		25	86.40% (80.91%~91.89%)	80.90% (73.65%~88.15%)	



A and B: Kaplan-Meier curves of RFS (A) and OS (B) for high- and low-SIRI groups in the training cohort; C and D: Kaplan-Meier curves of RFS (C) and OS (D) for high- and low-SIRI groups in the validation cohort

图3 高、低SIRI组患者的Kaplan-Meier生存曲线

Figure 3 Kaplan-Meier survival curves for patients in the high- and low-SIRI groups

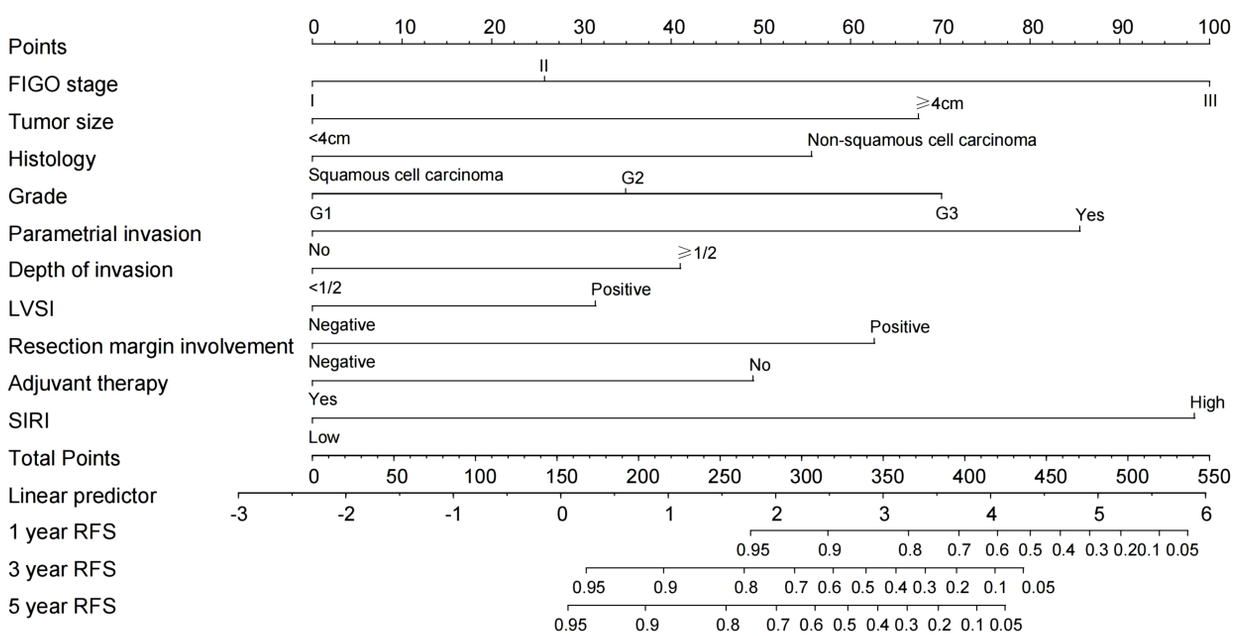


图4 宫颈癌患者1、3、5年无复发生存率的列线图预测模型

Figure 4 The nomogram prediction model for 1-, 3-, and 5-year RFS in patients with cervical cancer

表4 训练队列宫颈癌患者RFS的单因素与多因素Cox回归分析

Table 4 Univariate and multivariate Cox regression analyses of RFS in cervical cancer patients of the training cohort

Variables	Univariate analysis					Multivariate analysis				
	B	*SE*	*HR*	95% *CI*	*P*	*B*	*SE*	*HR*	95% *CI*	*P*
Age (years) (≥50 *vs* <50)	0.263	0.206	1.301	0.869~1.947	0.201	–	–	–	–	–
BMI(kg/m^2)	−0.031	0.033	0.969	0.909~1.033	0.337	–	–	–	–	–
FIGO stage										
Ⅰ	–	–	1	–	<0.001	–	–	1	–	<0.001
Ⅱ	0.634	0.287	1.885	1.073~3.309	0.027	0.272	0.31	1.312	0.715~2.410	0.381
Ⅲ	2.422	0.259	11.263	6.784~18.699	0	1.428	0.313	4.172	2.260~7.702	<0.001
Tumor size (cm) (≥4 *vs* <4)	1.186	0.209	3.273	2.174~4.928	<0.001	0.998	0.23	2.712	1.728~4.255	<0.001
Histology (No Squamous cell carcinoma *vs* Squamous cell carcinoma)	0.758	0.225	2.133	1.374~3.313	0.001	0.827	0.249	2.288	1.405~3.724	<0.001
Grade										
1	–	–	1	–	<0.001	–	–	1	–	0.007
2	0.618	0.265	1.856	1.104~3.119	0.02	0.527	0.281	1.693	0.976~2.939	0.061
3	1.251	0.32	3.495	1.865~6.549	<0.001	1.077	0.342	2.937	1.501~5.747	0.002
Parametrial invasion (Yes vs No)	1.690	0.281	5.419	3.122~9.407	<0.001	1.332	0.295	3.789	2.125~6.753	<0.001
Depth of invasion (≥1/2 vs <1/2)	1.280	0.218	3.597	2.344~5.517	<0.001	0.593	0.253	1.809	1.102~2.971	0.019
LVSI (positive vs negative)	1.716	0.205	5.562	3.721~8.314	<0.001	0.581	0.247	1.788	1.102~2.901	0.019
Resection margin involvement(Yes vs No)	1.834	0.37	6.26	3.034~12.915	<0.001	1.050	0.409	2.858	1.281~6.377	0.01
Adjuvant therapy (Yes vs No)	0.759	0.256	2.137	1.293~3.530	0.003	−0.754	0.301	0.47	0.261~0.849	0.012
SIRI (High vs Low)	1.610	0.222	5.003	3.235~7.735	<0.001	1.437	0.232	4.21	2.672~6.634	<0.001

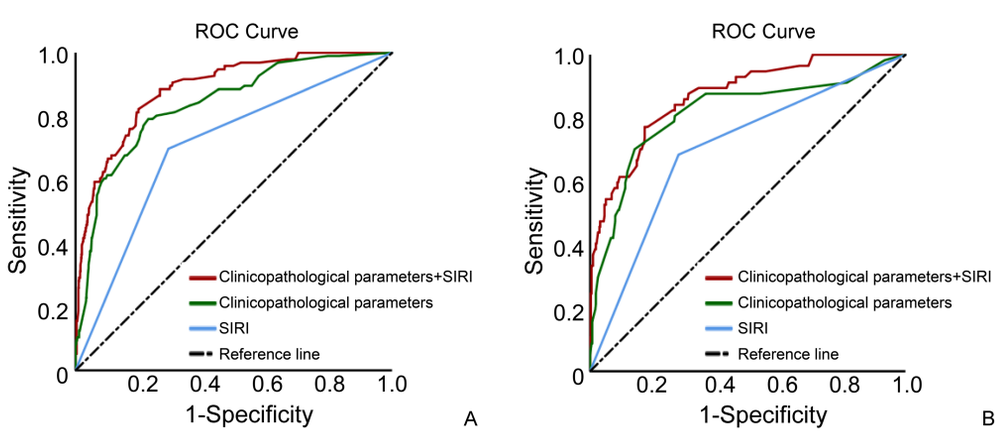


图5 训练队列(A)及验证队列(B)各预测指标的ROC曲线

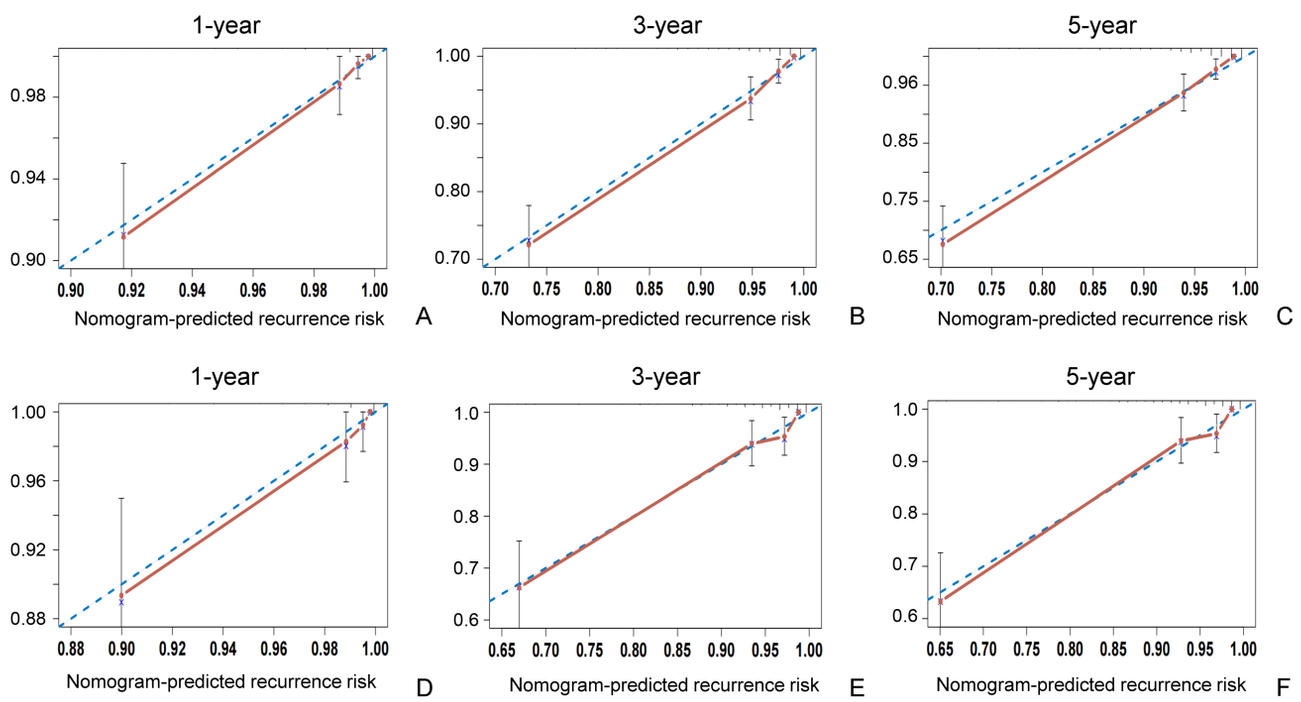
Figure 5 ROC curves of predictive variables in the training cohort (A) and validation cohort (B)

表5 各预测模型预测宫颈癌复发风险的效能比较

Table 5 Performance comparison of predictive models for risk of cervical cancer recurrence

Cohort	Model	AUC(95%*CI*)	ΔAUC(95%*CI*)	AUPRC(95%*CI*)	*P*
Training cohort	SIRI+Clinicopathological Parameters	0.886(0.853~0.919)	-	0.533(0.424~0.636)	-
	Clinicopathological Parameters	0.837(0.795~0.880)	0.049(0.017~0.081)	0.417(0.317~0.510)	0.003[b]
	SIRI	0.702(0.647~0.758)	0.184(0.125~0.243)	0.180(0.136~0.240)	<0.001[a]
Validation cohort	SIRI+Clinicopathological Parameters	0.838(0.780~0.896)	-	0.504(0.369~0.642)	-
	Clinicopathological Parameters	0.790(0.717~0.863)	0.048(-0.019~0.115)	0.421(0.302~0.555)	0.159[b]
	SIRI	0.682(0.606~0.758)	0.156(0.073~0.239)	0.191(0.132~0.281)	<0.001[a]

ΔAUC: the difference in AUC value between each single-parameter model and the SIRI+clinicopathological parameters model. a: the difference in AUC value between the SIRI+clinicopathological parameters model and the SIRI model by DeLong's test. b: the difference in AUC value between the SIRI+clinicopathological parameters model and the clinicopathological parameter model by DeLong's test.



Calibration curves of 1-, 3-, 5-year RFS in the training cohort (A-C); and the validation cohort (D-F)

图6 宫颈癌患者RFS校准曲线

Figure 6 The calibration curves of the nomogram model for RFS

但由于验证队列样本量受限,未显示出明显的统计学差异。针对样本不平衡性,表5结果显示训练队列中列线图模型AUPRC为0.533(95%*CI*:0.424~0.636),优于临床病理参数(AUPRC=0.417,95%*CI*:0.317~0.510)和SIRI(AUPRC=0.180,95%*CI*:0.136~0.240)。在验证队列中,列线图模型AUPRC为0.504(95%*CI*:0.369~0.642),同样显著优于临床病理参数(AUPRC=0.421,95%*CI*:0.302~0.555)和SIRI(AUPRC=0.191,95%*CI*:0.132~0.281)。校准曲线表明两队列的列线图模型预测值与实际值高度一致(图6)。

2.5 模型最佳风险阈值的确定及其预后分析

进一步在训练队列中利用ROC曲线和最大约登指数确定了模型预测宫颈癌复发的最佳风险阈值为0.927(图7)。根据此最佳风险阈值,将3年RFS≥0.927的患者定义为低风险组,3年RFS<0.927的患者定义为高风险组。Kaplan-Meier生存分析显示,在训练队列中,高风险组患者的3年和5年RFS分别为87.20%(95%*CI*,83.08~91.32%)和77.40%(95%*CI*,72.30~82.50%),3年和5年OS分别为86.80%(95%*CI*,

82.68~90.92%)和83.70%(95%*CI*, 79.19~88.21%),低风险组患者的3年和5年RFS均为97.80%(95%*CI*, 96.82~98.78%),3年和5年OS均为98.60%(95%*CI*, 97.82~99.38%),组间比较均有统计学意义(*P*<0.001),以上生存差异在验证队列中得到了验证(图8)。

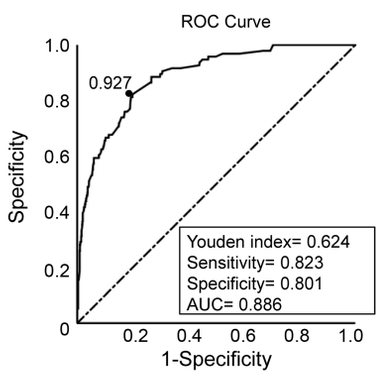
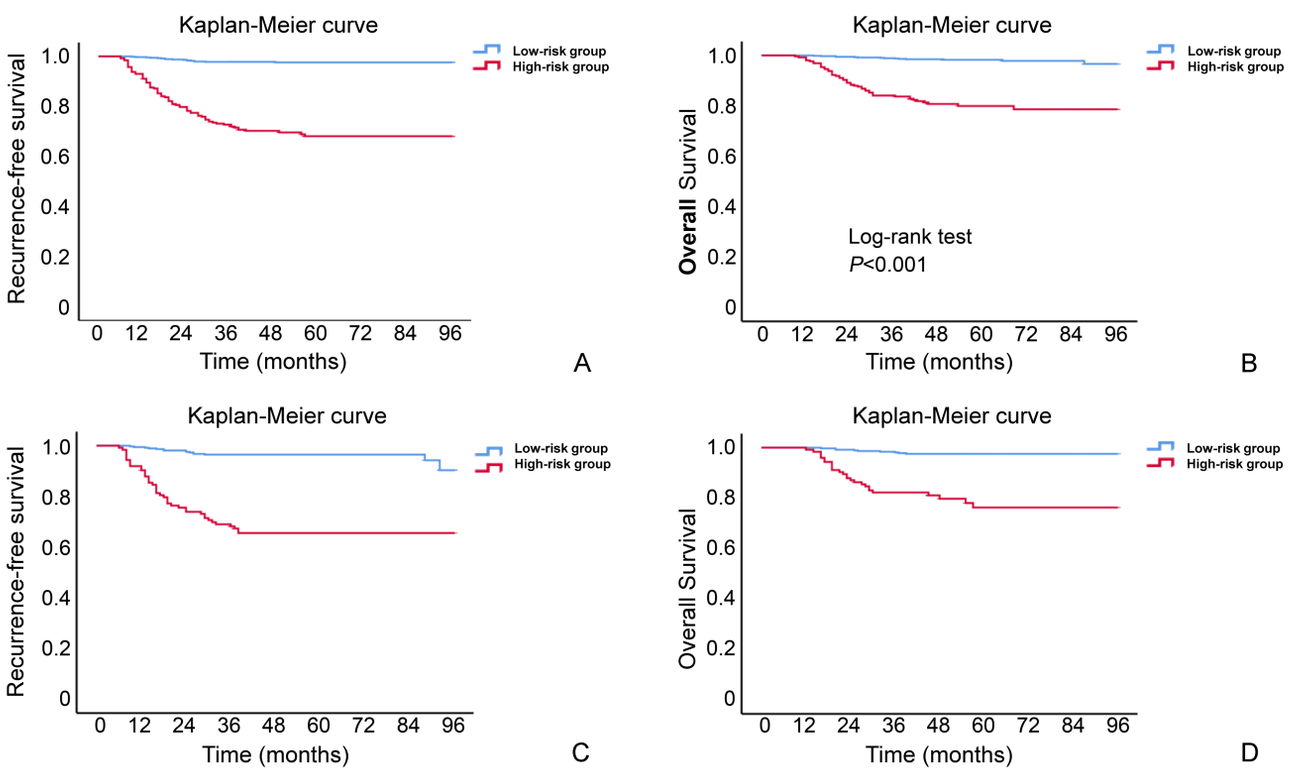


图7 模型预测宫颈癌复发的ROC曲线

Figure 7 ROC curve of the nomogram model for cervical cancer recurrence

3 讨论

宫颈癌是妇科最常见的恶性肿瘤之一[1]。复发性宫颈癌患者可选用的治疗方式有限,其预后情况通常不佳,死亡率随之显著升高[25]。因此准确预测患者复发概率并进行个体化预后管理显得尤为重要。本研究结果表明,SIRI可作为宫颈癌复发的独立危险因素。生存分析显示,高SIRI组患者的OS、RFS显著劣于低SIRI组,这一结果与近期多项研究结论相互印证[26-29]。基于此,本研究构建了一个整合SIRI与临床病理特征的宫颈癌复发预测模型。该模型采用列线图形式直观呈现各预测因子的相对权重,以量化的形式评估个体患者的复发风险。例如,对于具有以下特征的患者:FIGO Ⅱ期(31.6分)、肿瘤直径≥4 cm(67.5分)、鳞状细胞癌(0分)、中分化(G2,40.3分),同时合并宫旁浸润(85分)和肌层浸润(41分),但无淋巴血管间隙浸润(LVSI阴性,0分)且手术切缘阴性(0分),在接受辅助治疗(0分)且SIRI高表达(97.5分)的情况下,其总评分达362.9分,对应1年RFS约为81%。在



A and B: Kaplan-Meier survival curves of RFS (A) and OS (B) for high- and low-risk groups in the training cohort; C and D: Kaplan-Meier survival curves of RFS (C) and OS (D) for high- and low-risk groups in the validation cohort

图8 高、低危组患者的Kaplan-Meier生存曲线

Figure 8 Kaplan-Meier survival curves for high- and low-risk groups

训练队列中,整合临床病理参数与SIRI的联合预测模型,其AUC显著高于单一SIRI指标或单纯临床病理参数($P<0.05$)。验证队列中该模型仍表现出优于SIRI单指标的预测效能,尽管相较于临床病理参数差异未达统计学显著性,但AUC提升0.048,说明该模型具有潜在增量预测价值,需通过扩大样本量进一步验证。依据该模型所确定的最佳风险阈值,患者被划分为高风险组和低风险组。该模型的综合风险分层能力在训练队列和验证队列均得到了充分评估,结果一致显示高风险组患者的预后显著劣于低风险组。此外,校准曲线的内部和外部验证进一步证实了该模型具有较高的预测精度和良好的一致性。

然而,SIRI在预测宫颈癌预后方面的具体机制在很大程度上仍不明确。基于现有证据,我们推测其潜在的机制可能是:SIRI整合中性粒细胞、单核细胞及淋巴细胞三系参数,能更精准捕捉肿瘤微环境的系统炎症特征。具体而言,中性粒细胞通过促进肿瘤转移、血管生成和免疫抑制,充当癌症发展的调节剂[30]。中性粒细胞可因多种趋化因子和细胞因子的释放而加速血管生成,增强肿瘤细胞的黏附能力,进而促进肿瘤的远处转移[31]。其次,单核细胞可能通过分化为肿瘤相关巨噬细胞(tumor-associated macrophages,TAMs),影响肿瘤的发生。TAMs通过产生促炎细胞因子和刺激肿瘤血管生成,而加速肿瘤生长[32]。此外,淋巴细胞,尤其是肿瘤浸润淋巴细胞,在细胞介导的肿瘤免疫中发挥重要作用。较低的淋巴细胞计数会削弱全身免疫系统,使肿瘤细胞能够逃避免疫监视[33]。

值得一提的是,目前临床针对宫颈癌术后辅助治疗的适应证判定,主要取决于患者是否合并中高危临床病理因素[34]。根据美国国家综合癌症网络(national comprehensive cancer network,NCCN)及欧洲肿瘤内科学会(european society for medical oncology,EMSO)指南的推荐,对于具有以下高危因素的患者,在完成子宫切除术后,应考虑接受辅助放疗或联合化疗:肿瘤直径≥4 cm、宫颈深部间质浸润、分化不良、LVSI阳性、切缘阳性、淋巴结转移[21,35]。然而,仍有一些潜在的高危患者未能及时接受辅助治疗。这类患者的术后病理评估结果虽然处于指南所界定的中低危范畴,但可能由于处于促炎微环境的激活状态,存在隐匿性的高危特征,从而导致预后不良[28]。本研究基于经典临床病理参数和SIRI构建的列线图模型可以在一定程度上对宫颈癌患者进行更精细的风险分层和更具针对性的预后管理。具体来说,本研究发现根据列线图风险阈值划分的高危组患者,其RFS和OS远低于非高危组患者。对于按照指南接受相应辅助治疗的高危人群中的大多数患者,现有的辅助治疗方案可能无法有效控制这些患者的复发,因此可能需要推荐这些患者接受同步放化疗(如果原来的辅助治疗方案仅包括放疗)或适当增加辅助治疗的周期。同时,在医生的指导下,患者可考虑包括靶向药物治疗、免疫治疗等多种辅助治疗方案,以期进一步改善预后。

本研究尚存在一定局限性。首先,模型基于回顾性数据建立,存在患者选择偏倚、缺乏随机分配及数据收集不完整等问题,未来前瞻性研究可更精准地识别预后影响因素。此外,作为一项多中心研究,不同医疗机构的外科医师及病理科医生在治疗管理标准上可能存在差异,这对结果可能产生混杂影响,但同时这一特点也使研究结论更具普适性。

综上所述,本研究揭示了SIRI与宫颈癌术后复发的关联,为优化临床管理提供了新思路。通过将SIRI与传统临床病理预后因素整合,构建了兼具较高预测效能与临床实用性的列线图风险分层模型。该模型通过量化宫颈癌个体复发风险,为指导临床治疗决策提供参考。

利益冲突 本文所有作者声明不存在利益冲突

参考文献:

[1] SUNG H, FERLAY J, SIEGEL R L, *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. DOI: 10.3322/caac.21660.

[2] ARBYN M, WEIDERPASS E, BRUNI L, *et al*. Estimates of incidence and mortality of cervical cancer in 2018: a worldwide analysis [J]. Lancet Glob Health, 2020, 8(2): e191-e203. DOI: 10.1016/S2214-109X(21)00554-4.

[3] FALCARO M, CASTAñON A, NDLELA B, *et al*. The effects of the national HPV vaccination programme in England, UK, on cervical cancer and grade 3 cervical intraepithelial neoplasia incidence: a register-based observational study [J]. Lancet, 2021, 398(10316): 2084-2092. DOI: 10.1016/S0140-6736(21)02178-4.

[4] DE JUAN A, REDONDO A, RUBIO M J, *et al*. SEOM clinical guidelines for cervical cancer (2019) [J]. Clin Transl Oncol, 2020, 22(2): 270-278. DOI: 10.1007/s12094-019-02271-z.

[5] WENDEL NAUMANN R, LEATH C A, 3RD. Advances in immunotherapy for cervical cancer [J]. Curr Opin Oncol,

2020, 32(5): 481-487. DOI: 10.1097/CCO.0000000000000663.

[6] WRIGHT J D, MATSUO K, HUANG Y, *et al*. Prognostic Performance of the 2018 International Federation of Gynecology and Obstetrics Cervical Cancer Staging Guidelines [J]. Obstet Gynecol, 2019, 134(1): 49-57. DOI: 10.1097/AOG.0000000000003311.

[7] JIANG K, AI Y, LI Y, *et al*. Nomogram models for the prognosis of cervical cancer: A SEER-based study [J]. Front Oncol, 2022, 12: 961678. DOI: 10.3389/fonc.2022.961678.

[8] QUERLEU D, CIBULA D, ABU-RUSTUM N R. 2017 Update on the Querleu-Morrow Classification of Radical Hysterectomy [J]. Ann Surg Oncol, 2017, 24(11): 3406-3412. DOI: 10.1245/s10434-017-6031-z.

[9] YANG F, ZHENG Y, LUO Q, *et al*. Knockdown of NCAPD3 inhibits the tumorigenesis of non-small cell lung cancer by regulation of the PI3K/Akt pathway. BMC Cancer. 2024; 24(1):408. DOI: 10.1186/s12885-024-12131-x.

[10] SUN W, ZHANG L, LUO M, *et al*. Pretreatment hematologic markers as prognostic factors in patients with nasopharyngeal carcinoma: Neutrophil-lymphocyte ratio and platelet-lymphocyte ratio [J]. Head Neck, 2016, 38 Suppl 1: E1332-1340. DOI: 10.1002/hed.24224.

[11] CHEN T, TANG M, ZHOU Y, *et al*. Pretreatment lymphocyte-to-monocyte ratio as a prognostic factor and influence on dose-effect in fractionated stereotactic radiotherapy for oligometastatic brain metastases in non-small cell lung cancer patients [J]. Front Oncol, 2023, 13: 1216852. DOI: 10.3389/fonc.2023.1216852.

[12] VAN WIJK L, DE KLEIN G W, KANTERS M A, *et al*. The ultimate preoperative C-reactive protein-to-albumin ratio is a prognostic factor for survival after pancreatic cancer resection [J]. Eur J Med Res, 2020, 25(1): 46. DOI: 10.1186/s40001-020-00444-z.

[13] XU S, CAO S, GENG J, *et al*. High prognostic nutritional index (PNI) as a positive prognostic indicator for non-small cell lung cancer patients with bone metastasis [J]. Clin Respir J, 2021, 15(2): 225-231. DOI: 10.1111/crj.13288.

[14] KIM J S, CHOI M, KIM S H, *et al*. Systemic inflammation response index correlates with survival and predicts oncological outcome of resected pancreatic cancer following neoadjuvant chemotherapy [J]. Pancreatology, 2022, 22(7): 987-993. DOI: 10.1016/j.pan.2022.08.009.

[15] QI Q, ZHUANG L, SHEN Y, *et al*. A novel systemic inflammation response index (SIRI) for predicting the survival of patients with pancreatic cancer after chemotherapy [J]. Cancer, 2016, 122(14): 2158-2167. DOI: 10.1002/cncr.30057.

[16] JIN Y N, LIU B Q, PENG K W, *et al*. The prognostic value of adding systemic inflammation response index to Epstein-Barr virus DNA in childhood nasopharyngeal carcinoma: A real-world study [J]. Head Neck, 2022, 44(6): 1404-1413. DOI: 10.1002/hed.27033.

[17] CAI H, CHEN Y, ZHANG Q, *et al*. High preoperative CEA and systemic inflammation response index (C-SIRI) predict unfavorable survival of resectable colorectal cancer [J]. World J Surg Oncol, 2023, 21(1): 178. DOI: 10.1186/s12957-023-03056-z.

[18] KöSE O, KöSE E, GöK K, *et al*. The Role of the Systemic Immune-Inflammation Index in Predicting Postoperative Complications in Ovarian Cancer Patients: A Retrospective Cohort Study. Cancers (Basel). 2025; 17(7): 1124. DOI: 10.3390/cancers17071124.

[19] MATSUO K, MACHIDA H, MANDELBAUM R S, *et al*. Validation of the 2018 FIGO cervical cancer staging system [J]. Gynecol Oncol, 2019, 152(1): 87-93. DOI: 10.1016/j.ygyno.2018.10.026zz.

[20] TU Y, JIANG P, ZHANG J, *et al*. The positive threshold of the immunohistochemical parameter Ki67 for predicting the recurrence of cervical cancer [J]. Int J Gynaecol Obstet, 2022, 158(2): 330-337. DOI: 10.1002/ijgo.14005.

[21] MARTH C, LANDONI F, MAHNER S, *et al*. Cervical cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up [J]. Ann Oncol, 2017, 28(suppl_4): iv72-iv83. DOI: 10.1093/annonc/mdx220.

[22] MICCò M, LUPINELLI M, MANGIALARDI M, *et al*. Patterns of Recurrent Disease in Cervical Cancer [J]. J Pers Med, 2022, 12(5). DOI: 10.1093/annonc/mdx220.

[23] ZHENG Y, SHEN Q, YANG F, *et al*. A nomogram model to predict recurrence of early-onset endometrial cancer after resection based on clinical parameters and immunohistochemical markers: a multi-institutional study [J]. Front Oncol, 2024, 14: 1442489. DOI: 10.3389/fonc.2024.1442489.

[24] VAN DER SCHOUW Y T, VERBEEK A L, RUIJS J H. ROC curves for the initial assessment of new diagnostic tests [J]. Fam Pract, 1992, 9(4): 506-511. DOI: 10.1093/fampra/9.4.506.

[25] ADIGA D, ESWARAN S, PANDEY D, *et al*. Molecular landscape of recurrent cervical cancer [J]. Crit Rev Oncol Hematol, 2021, 157: 103178. DOI: 10.1016/j.critrevonc.2020.103178.

[26] GUO J, LV W, WANG Z, *et al*. Prognostic Value of Inflammatory and Nutritional Markers for Patients With Early-Stage Poorly-to Moderately-Differentiated Cervical Squamous Cell Carcinoma [J]. Cancer Control, 2023, 30:

10732748221148913. DOI: 10.1177/10732748221148913.

[27] CHAO B, JU X, ZHANG L, *et al*. A Novel Prognostic Marker Systemic Inflammation Response Index (SIRI) for Operable Cervical Cancer Patients [J]. Front Oncol, 2020, 10: 766. DOI: 10.3389/fonc.2020.00766.

[28] HUANG H, LIU Q, ZHU L, *et al*. Prognostic Value of Preoperative Systemic Immune-Inflammation Index in Patients with Cervical Cancer [J]. Sci Rep, 2019, 9(1): 3284. DOI: 10.1038/s41598-019-39150-0.

[29] BRUNO M, BIZZARRI N, TEODORICO E, *et al*. The potential role of systemic inflammatory markers in predicting recurrence in early-stage cervical cancer [J]. Eur J Surg Oncol, 2024, 50(1): 107311. DOI: 10.1016/j.ejso. 2023. 107311.

[30] MAHMUD Z, RAHMAN A, MISHU I D, *et al*. Mechanistic insights into the interplays between neutrophils and other immune cells in cancer development and progression [J]. Cancer Metastasis Rev, 2022, 41(2): 405-432. DOI: 10.1007/s10555-022-10024-8.

[31] XIONG S, DONG L, CHENG L. Neutrophils in cancer carcinogenesis and metastasis [J]. J Hematol Oncol, 2021, 14(1): 173. DOI: 10.1186/s13045-021-01187-y.

[32] CHANMEE T, ONTONG P, KONNO K, *et al*. Tumor-associated macrophages as major players in the tumor microenvironment [J]. Cancers (Basel), 2014, 6(3): 1670-1690. DOI: 10.3390/cancers6031670.

[33] MAN Y G, STOJADINOVIC A, MASON J, *et al*. Tumor-infiltrating immune cells promoting tumor invasion and metastasis: existing theories [J]. J Cancer, 2013, 4(1): 84-95. DOI: 10.7150/jca.5482.

[34] JIANG P, HUANG Y, TU Y, *et al*. Combining Clinicopathological Parameters and Molecular Indicators to Predict Lymph Node Metastasis in Endometrioid Type Endometrial Adenocarcinoma [J]. Front Oncol, 2021, 11: 682925. DOI: 10.3389/fonc.2021.682925.

[35] KOH W J, ABU-RUSTUM N R, BEAN S, *et al*. Cervical Cancer, Version 3.2019, NCCN Clinical Practice Guidelines in Oncology [J]. J Natl Compr Canc Netw, 2019, 17(1): 64-84. DOI: 10.6004/jnccn.2019.0001.

(**收稿**:2025-04-18;**修回**:2025-07-18)

(编辑 张艺霖)