



· 专题论著 ·



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机体组分在直肠癌患者术后长期预后预测中的价值及模型建立

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〔摘要〕背景与目的：既往研究探讨了骨骼肌和脂肪组织的组成和分布对结直肠癌患者预后预测的意义，但多未对直肠癌与结肠癌患者群体加以区分。本研究旨在探究机体组分与直肠癌患者长期预后的关系，并建立术后预测模型。**方法：**回顾性收集2018年1月—2021年12月于青岛大学附属医院接受手术治疗的直肠癌患者的临床资料。纳入标准：① 年龄 ≥ 18 岁；② 术前经肠镜检查 and 活组织病理学检查确诊为直肠癌；③ 行外科手术完整切除者；④ 术前1个月内行腹部计算机断层成像（computed tomography, CT）扫描。排除标准：① 临床资料缺失；② 肿瘤多发转移；③ 肿瘤T分期为0或为原位癌；④ 严重伪影导致CT成像质量差，难以区分脂肪和肌肉；⑤ 无法获得随访结果的患者。本研究已获得青岛大学附属医院医学伦理委员会批准（批件号：QYFYWZLL30313），伦理审批环节已豁免知情同意。通过CT扫描观察到的骨骼肌横截面积及皮下脂肪横截面积除以身高的平方得到骨骼肌指数（skeletal muscle index, SMI）和皮下脂肪指数（subcutaneous adipose tissue index, SATI）。采用单因素和多因素COX回归分析确定影响直肠癌患者无复发生存期（recurrence-free survival, RFS）及总生存期（overall survival, OS）的危险因素。根据多因素分析结果，构建列线图预测模型，并通过受试者工作特征（receiver operating characteristic, ROC）曲线、校准曲线和决策曲线（decision curve analysis, DCA）对列线图的预测能力和准确性进行评估，并进行内部验证。**结果：**共有696例患者被纳入本研究，96例（13.8%）患者出现术后复发，89例（12.8%）患者死亡。多因素COX回归分析显示，SMI、SATI、肿瘤T分期、N分期是影响患者术后RFS和OS的独立因素。基于以上独立预测因素分别构建直肠癌患者的RFS及OS的列线图预测模型，3、4和5年RFS的ROC曲线的曲线下面积（area under curve, AUC）分别为0.862、0.846和0.824；3、4和5年OS的AUC分别为0.886、0.898和0.875，通过校

基金项目：山东省自然科学基金面上项目（ZR2022MH252）。

利益冲突：作者声明无利益冲突。

伦理批件：QYFYWZLL30313。

知情同意：豁免。

引用本文：刘 硕，卢 云，胡继霖，等. 机体组分在直肠癌患者术后长期预后预测中的价值及模型建立 [J]. 中国癌症杂志, 2025, 35(7): 672-684.

Funding: General Program of Shandong Provincial Natural Science Foundation (ZR2022MH252).

Conflicts of interest: authors declare no conflicts of interest.

Ethical approval: QYFYWZLL30313.

Informed consent: exemption.

Cite this article: LIU Shuo, LU Yun, HU Jilin, et al. The predictive value and model establishment of body composition in the long-term prognosis of patients after rectal cancer surgery [J]. China Oncol, 2025, 35(7): 672-684.

准曲线和DCA对模型进行评估, 并进行内部验证, 显示模型的预测准确性较好。**结论:** CT机体组分是直肠癌患者RFS和OS的独立预测因素, 在此基础上开发的列线图模型对直肠癌患者预后较好的预测价值。

[**关键词**] 直肠癌; 计算机体层成像机体组分; 骨骼肌指数; 皮下脂肪指数; 列线图模型

中图分类号: R735.3+7 文献标志码: A

DOI: 10.19401/j.cnki.1007-3639.2025.07.006

The predictive value and model establishment of body composition in the long-term prognosis of patients after rectal cancer surgery LIU Shuo¹, LU Yun¹, HU Jilin¹, YANG Wenchang¹, ZHAO Rizhi², XU Wenda¹, YANG Hanyu¹, LU Zechen¹, MA Zheng¹, DU Zhaolin¹, GAO Yunzhi¹, GAO Yuan¹ (1. Department of Gastrointestinal Surgery, The Affiliated Hospital of Qingdao University, Qingdao 266000, Shandong Province, China; 2. Department of Gastrointestinal Surgery, Rizhao Traditional Chinese Medicine Hospital, Rizhao 276800, Shandong Province, China)

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[**Abstract**] **Background and Purpose:** Previous studies have investigated the prognostic significance of skeletal muscle and adipose tissue composition and distribution in colorectal cancer patients, yet most have not differentiated between rectal and colon cancer patient cohorts. This study aimed to explore the relationship between body composition and long-term prognosis, and to develop a postoperative predictive model. **Methods:** Clinical data of rectal cancer patients who underwent surgical treatment at Qingdao University Affiliated Hospital from January 2018 to December 2021 were retrospectively collected. Inclusion criteria: ① Age > 18 years; ② Preoperative colonoscopy and pathological diagnosis of colorectal cancer; ③ Complete surgical resection; ④ Abdominal computed tomography (CT) scan 1 month before surgery. Exclusion criteria: ① Clinical data is missing; ② Multiple metastases of tumors; ③ Tumor T stage 0 or carcinoma in situ; ④ Severe artifacts lead to poor quality CT imaging, making it difficult to distinguish between fat and muscle; ⑤ Inability to obtain follow-up results. This study has been approved by the Medical Ethics Committee of the Affiliated Hospital of Qingdao University (approval number: QYFYWZLL30313), and informed consent has been waived in the ethical approval process. The skeletal muscle index (SMI) and subcutaneous adipose tissue index (SATI) were calculated by dividing the areas of skeletal muscle and subcutaneous fat observed on CT scans by the square of the patient's height. Univariate and multivariate COX regression analyses were conducted to identify risk factors influencing recurrence-free survival (RFS) and overall survival (OS) in rectal cancer patients. Based on the results of the multivariate analysis, a nomogram prediction model was developed, its predictive power and accuracy were assessed using the receiver operating characteristic (ROC) curve, calibration plots and decision curve analysis (DCA), and internal validation was conducted. **Results:** A total of 696 patients were included in this study, with 96 (13.8%) patients experiencing postoperative recurrence and 89 (12.8%) patients dying. Multivariate COX regression analysis showed that SMI, SATI, tumor T stage and N stage were independent factors affecting the postoperative RFS and OS of patients. Nomogram prediction models for RFS and OS in rectal cancer patients were constructed based on the above independent predictors. The area under ROC curve (AUC) for 3-, 4- and 5-year RFS was 0.862, 0.846 and 0.824, respectively; the AUC for 3-, 4- and 5-year OS was 0.886, 0.898 and 0.875, respectively. The models were evaluated using calibration curves and decision curves, and internal validation was performed, which showed that the prediction accuracy of the models was good. **Conclusion:** CT body composition is an independent predictor of RFS and OS in rectal cancer patients, and the nomogram model developed based on these factors demonstrates good predictive value for patient prognosis.

[**Key words**] Rectal cancer; Computed tomography body composition; Skeletal muscle index; Subcutaneous adipose tissue index; Nomogram model

结直肠癌 (colorectal cancer, CRC) 是中国第二大常见癌症, 并且是癌症相关死亡的第4大原因^[1]。手术是CRC最常用的治疗手段, 近年来, 由于诊疗水平的进步, CRC患者的5年生存率有所提高^[2]。然而, 预计至2035年, 全球CRC死亡人数将大幅增加^[3]。因此, 尽早识别与CRC患者肿瘤学结局相关的因素变得愈发重要。有研究^[4-5]表明, 年龄、性别等社会人口学特征与肿瘤患者预后有关。此外, 机体营养状态也会影响肿瘤患者预后^[6-7]。在此背景下, 准确评估机体营养状态尤为重要。长期以来, 体重指数 (body mass index, BMI) 是评估机体营养状

态的常用指标, 但无法准确区分肌肉和脂肪, 这可能导致对某种机体组分特点及功能的不当理解。与BMI相比, 包括骨骼肌和脂肪在内的机体组分可准确评估机体营养水平^[7-8]。先前的研究^[9]已经报道了基于计算机体层成像 (computed tomography, CT) 的机体组分对CRC患者预后预测的意义。

CRC患者的长期预后一直是临床关注的重点, 关乎患者的生存期和生存质量。但结肠癌和直肠癌在解剖位置、手术方法和复发模式方面有所不同。既往针对CT机体组分与长期预后关联的研究, 大多将CRC患者作为整体进行分析, 未

对直肠癌与结肠癌患者群体加以区分^[10]。相比之下,本研究聚焦于直肠癌患者,以期进行精确的术后预后评估。另外,关于CRC患者长期预后的研究大多专注于术前客观指标,缺乏对患者营养状态的综合评估。因此,如何精准评估CRC患者的营养状态并进行个性化干预成为亟待解决的问题。本研究旨在探究CT机体组分等营养指标与直肠癌患者长期预后的内在联系,并结合肿瘤T、N分期,建立联合预测模型。该模型有助于帮助医疗专业人员精准地判断患者预后不良的风险,制订个性化的治疗干预方案,从而改善患者的预后,为直肠癌患者的围手术期管理和长期预后评估提供新的思路和方法。

1 资料和方法

1.1 患者选择

回顾性分析2018年1月—2021年12月于青岛大学附属医院接受手术治疗的直肠癌患者。纳入标准:① 年龄 ≥ 18 岁;② 术前经肠镜检查 and 活组织病理学检查确诊为直肠癌;③ 行外科手术完整切除者;④ 术前1个月内行腹部CT扫描。排除标准:① 临床资料缺失;② 肿瘤多发转移;③ 肿瘤T分期为0或为原位癌;④ 严重伪影导致CT成像质量差,难以区分脂肪和肌肉;⑤ 无法获得随访结果的患者。纳入患者涵盖不同人口统计学特征,以确保数据具有代表性。样本量大小根据10倍EPV原则确定,即样本数不少于开展回归纳入模型自变量数的10倍。本研究共纳入16项临床指标,纳入样本量满足10倍EPV经验法。本研究已获得青岛大学附属医院医学伦理委员会批准(批件号:QYFYWZLL30313),伦理审批环节已豁免知情同意。

1.2 临床变量

本研究共纳入16项临床指标,主要包括年龄、性别、BMI、骨骼肌指数(skeletal muscle index, SMI)、皮下脂肪指数(subcutaneous adipose tissue index, SATI)、癌胚抗原(carcinoembryonic antigen, CEA)水平、肿瘤大小、肿瘤T分期、肿瘤N分期等。SMI是用于评估人体骨骼肌量相对水平的一个指标,是最常用于定义肌少症的影像学指标。皮下脂肪是指位于皮肤下方的脂肪组织,它是人体脂肪的重要组成部分。SATI就是用于衡量人体皮下脂肪含量或状态的指标,可用于辅助诊断肥胖症及代谢综合征。SMI的计算方法是在第三腰椎(L3)水平的CT扫描中观察到的骨骼肌横截面积除以身高的

平方。SATI则是将L3水平的皮下脂肪横截面积除以身高的平方。所有变量均由专业人员计算或测量得到,评估者对于患者的疾病情况、治疗方式及预测因子均不知情。

1.3 研究终点及随访

研究终点为直肠癌患者长期预后,包括:无复发生存期(recurrence-free survival, RFS),定义为从首次手术切除至肿瘤出现复发、转移的时间;总生存期(overall survival, OS),定义为从手术治疗到患者因任何原因死亡的时间。根据中国临床肿瘤学会CRC诊疗指南^[11]制订随访方案。通过电话或门诊进行随访并确定是否复发或死亡,评估者对患者的预测因子不知情。术后前3年每3个月随访1次,第4~5年每6个月随访1次。在最后1次就诊后的1年内未按预约就诊的患者被视为失访。此外,根据患者的病理学分期,在5年内每6或12个月进行1次胸部和腹盆腔CT扫描,以确定是否发生复发或转移。收集的随访信息包括辅助治疗状态、肿瘤复发情况、复发时间、患者生存时间和死亡时间。随访截至2024年12月31日。

1.4 机体组分分析

选择L3水平的单个CT图像来量化骨骼肌和脂肪组织。使用SliceOonic 5.0版(加拿大TomoVision公司)测量皮下脂肪横截面积和骨骼肌横截面积。基于以前的研究^[12],皮下和肌间脂肪的阈值设置为-190~-30 HU,骨骼肌的阈值设置为-29~150 HU。通过总骨骼肌横截面积除以身高的平方计算得到SMI。用总皮下脂肪横截面积除以身高的平方得到SATI。

1.5 数据准备与预处理

本研究数据来自于青岛大学附属医院的临床电子病历系统。在进行分析之前,我们对原始数据集进行了系统的预处理和质量检查,删除数据缺失的个体,以确保数据质量和分析的稳定性。

1.6 手术方法

所有患者均行术前检查、围手术期前评估和对症治疗。所有患者均接受完整的外科手术切除。根据肿瘤位置及大小决定手术方式,主要包括腹会阴联合切除术(abdominoperineal resection, APR)和低位前切除术(low anterior resection, LAR)。

1.7 统计学处理

连续型变量符合正态分布时,采用 $\bar{x} \pm s$ 进行描述,采用成组 t 检验进行组间比较,不符合正态分布时,采用M(Q1, Q3)进行描述,

组间比较采用非参数秩和检验；分类变量采用 n (%) 进行统计描述，组间比较采用 χ^2 检验或 Fisher 精确概率法。由于连续型变量易掩盖预测因子的实际作用，因此使用通过约登指数获得的截断值将连续型变量转换为分类变量进行分析。使用 SPSS 27.0 对数据进行统计学分析。采用 Kaplan-Meier 法绘制生存曲线，比较患者的生存差异。采用单因素和多因素 COX 回归分析确定影响直肠癌患者 RFS 和 OS 的危险因素。根据多因素分析结果，通过“rms”包构建列线图预测模型，并通过“rms”、“ResourceSelection”和“ggDCA”包绘制受试者工作特征 (receiver operating characteristic, ROC) 曲线、校准曲线和决策曲线 (decision curve analysis, DCA)，进而评估列线图的预测能力和准确性。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 临床资料

本研究共纳入 696 例患者，按照 7:3 比例分为训练组 (487 例) 和验证组 (209 例)，患者纳入和排除流程图见图 1。训练组与验证组的临床特征及机体组分比较详见表 1。组间比较显示，训练组与验证组之间各变量差异无统计学意义 ($P > 0.05$)，具有可比性。

本研究人群包括男性 352 例 (50.6%)，女性 344 例 (49.4%)。男性和女性患者骨骼肌和脂肪组织的分布存在差异。因此，根据性别分界点将患者分为高 CT 机体组和低 CT 机体组。

男性 SMI $< 38.65 \text{ cm}^2/\text{m}^2$ 、女性 SMI $< 36.34 \text{ cm}^2/\text{m}^2$ 的患者分为低 SMI 组，共 399 例 (57.3%)；男性 SMI $\geq 38.65 \text{ cm}^2/\text{m}^2$ 、女性 SMI $\geq 36.34 \text{ cm}^2/\text{m}^2$ 的患者分为高 SMI 组，共 297 例 (42.7%)。男性 SATI $< 62.9 \text{ cm}^2/\text{m}^2$ 、女性 SATI $< 71.7 \text{ cm}^2/\text{m}^2$ 的患者分为低 SATI 组，共 281 例 (40.4%)；男性 SATI $\geq 62.9 \text{ cm}^2/\text{m}^2$ 、女性 SATI $\geq 71.7 \text{ cm}^2/\text{m}^2$ 的患者分为高 SATI 组，共 415 例 (59.6%)。不同分组患者的临床资料详见表 2。

2.2 与直肠癌患者术后 RFS 相关的因素

本研究中共 96 例 (13.8%) 患者术后出现复发 (表 3)，训练组通过多因素 COX 回归分析发现，SATI [风险比 (hazard ratio, HR) = 2.717, 95% CI: 1.505~4.905, $P < 0.001$]、SMI (HR = 0.329, 95% CI: 0.182~0.595, $P < 0.001$) 是术后出现复发的独立预测因素。Kaplan-Meier 曲线显示，高 SMI、低 SATI、肿瘤分期为 T1-2 期和 N0-1 期的直肠癌患者的 RFS 分别高于低 SMI、高 SATI、肿瘤分期为 T3-4 期和 N2 期的患者 (图 2)。

2.3 与直肠癌患者术后 OS 相关的因素

本研究中共 89 例 (12.8%) 患者术后死亡 (表 4)，训练组通过多因素 COX 回归分析发现，SATI (HR = 3.542, 95% CI: 1.739~7.211, $P < 0.001$)、SMI (HR = 0.132, 95% CI: 0.053~0.330, $P < 0.001$) 是术后导致死亡的独立预测因素。Kaplan-Meier 曲线显示，高 SMI、低 SATI、肿瘤分期为 T1-2 期和 N0-1 期的直肠癌患者的 OS 分别高于低 SMI、高 SATI、肿瘤分期为 T3-4 期和 N2 期的患者 (图 3)。

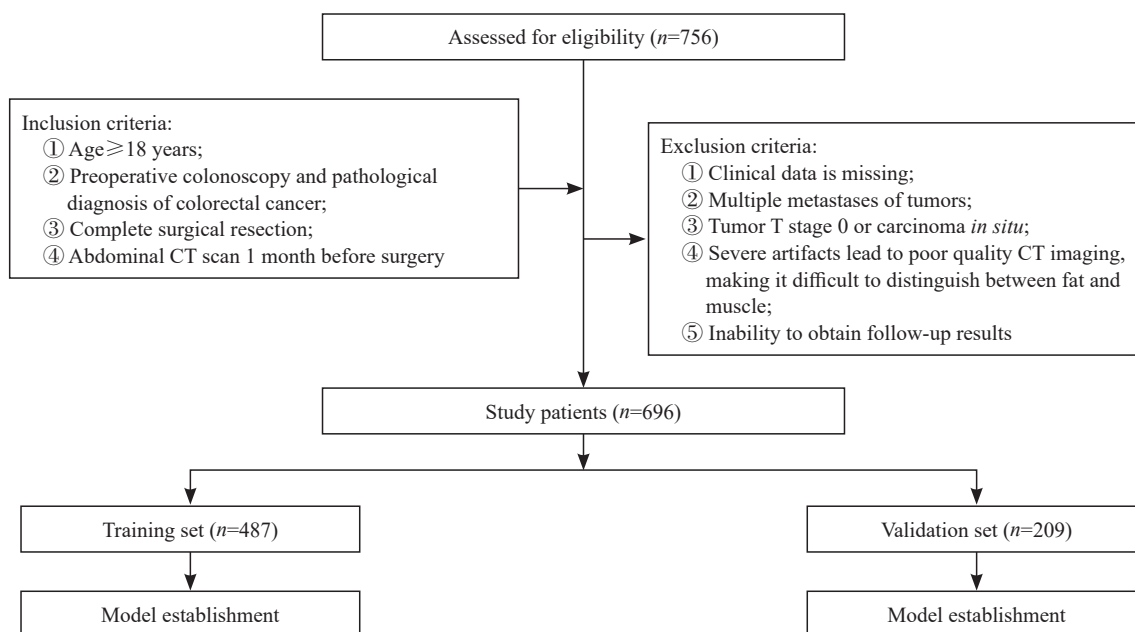


图1 患者纳入和排除流程图

Fig. 1 Patient inclusion and exclusion flow chart

表1 训练组与验证组的临床特征及机体组分比较

Variable	Total (N=696)	Training cohort (N=487)	Validation cohort (N=209)	χ^2/Z value	P value
RFS M(Q1, Q3)	43.0 (38.0, 54.8)	42.0 (38.0, 50.0)	42.0 (38.0, 57.0)	-0.615	0.539
OS M(Q1, Q3)	43.0 (38.0, 58.0)	44.0 (37.0, 57.5)	45.0 (38.0, 58.0)	-0.550	0.582
Gender				0.889	0.346
Male	352 (50.6)	252 (51.7)	100 (47.8)		
Female	344 (49.4)	235 (48.3)	109 (52.2)		
Age/year				0.335	0.563
<65	338 (48.6)	240 (49.3)	98 (46.9)		
≥65	358 (51.4)	247 (50.7)	111 (53.1)		
BMI/(kg·m ⁻²)				0.001	0.976
<22.45	166 (23.9)	116 (23.8)	50 (23.9)		
≥22.45	530 (76.1)	371 (76.2)	159 (76.1)		
CEA/(ng·mL ⁻¹)				0.533	0.465
<4.26	371 (53.3)	264 (54.2)	107 (51.2)		
≥4.26	325 (46.7)	223 (45.8)	102 (48.8)		
Size/cm				0.012	0.914
<5.2	445 (63.9)	312 (64.1)	133 (63.6)		
≥5.2	251 (36.1)	175 (35.9)	76 (36.4)		
T stage				1.435	0.231
T1-T2	131 (18.8)	86 (17.7)	45 (21.5)		
T3-T4	565 (81.2)	401 (82.3)	164 (78.5)		
N stage				0.309	0.578
N0-N1	404 (58.0)	286 (58.7)	118 (56.5)		
N2	292 (42.0)	201 (41.3)	91 (43.5)		
Hypertension				0.094	0.759
Yes	224 (32.2)	155 (31.8)	69 (33.0)		
No	472 (67.8)	332 (68.2)	140 (67.0)		
Diabetes				0.001	0.977
Yes	127 (18.2)	89 (18.3)	38 (18.2)		
No	569 (81.8)	398 (81.7)	171 (81.8)		
Smoke				0.599	0.439
Yes	291 (41.8)	199 (40.9)	92 (44.0)		
No	405 (58.2)	288 (59.1)	117 (56.0)		
Alcohol				0.056	0.813
Yes	295 (42.4)	205 (42.1)	90 (43.1)		
No	401 (57.6)	282 (57.9)	119 (56.9)		
Surgical approach				0.009	0.925
Laparoscopic	672 (96.6)	470 (96.5)	202 (96.7)		
Open	24 (3.4)	17 (3.5)	7 (3.3)		
Surgical procedure				0.288	0.592
LAR	578 (83.0)	402 (82.5)	176 (84.2)		
APR	118 (17.0)	85 (17.5)	33 (15.8)		
Neoadjuvant treatment				0.043	0.836
Yes	86 (12.3)	61 (12.5)	25 (12.0)		
No	610 (87.7)	426 (87.5)	184 (88.0)		
SMI				1.069	0.301
High	297 (42.7)	214 (43.9)	83 (39.7)		
Low	399 (57.3)	273 (56.1)	126 (60.3)		
SATI				0.054	0.816
High	415 (59.6)	289 (59.3)	126 (60.3)		
Low	281 (40.4)	198 (40.7)	83 (39.7)		

表2 低机体组分与高机体组分临床特征比较

Tab. 2 Comparison of clinical characteristics between the low body composition group and the high body composition group

Variable	SMI		χ^2 value	P value	SATI		χ^2 value	P value
	Low (N=399)	High (N=297)			Low (N=281)	High (N=415)		
Gender			12.654	<0.001			12.757	<0.001
Male	225 (56.4)	127 (42.8)			119 (42.3)	233 (56.1)		
Female	174 (43.6)	170 (57.2)			162 (57.7)	182 (43.9)		
Age/year			18.129	<0.001			0.145	0.703
<65	166 (41.6)	172 (57.9)			134 (47.7)	204 (49.2)		
\geq 65	233 (58.4)	125 (42.1)			147 (52.3)	211 (50.8)		
BMI/(kg·m ⁻²)			9.166	0.002			52.526	<0.001
<22.45	112 (28.1)	54 (18.2)			107 (38.1)	59 (14.2)		
\geq 22.45	287 (71.9)	243 (81.8)			174 (61.9)	356 (85.8)		
CEA/(ng·mL ⁻¹)			7.380	0.007			0.015	0.903
<4.26	195 (48.9)	176 (59.3)			149 (53.0)	222 (53.5)		
\geq 4.26	204 (51.1)	121 (40.7)			132 (47.0)	193 (46.5)		
Size/cm			12.208	<0.001			5.565	0.018
<5.2	277 (69.4)	168 (56.6)			165 (58.7)	280 (67.5)		
\geq 5.2	122 (30.6)	129 (43.4)			116 (41.3)	135 (32.5)		
T stage			12.318	<0.001			0.934	0.334
T1-T2	93 (23.3)	38 (12.8)			48 (17.1)	83 (20.0)		
T3-T4	306 (76.7)	259 (87.2)			233 (82.9)	332 (80.0)		
N stage			0.313	0.576			0.586	0.444
N0-N1	228 (57.1)	176 (59.3)			168 (59.8)	236 (56.9)		
N2	171 (42.9)	121 (40.7)			113 (40.2)	179 (43.1)		
Hypertension			0.180	0.671			2.979	0.084
Yes	131 (32.8)	93 (31.3)			80 (28.5)	144 (34.7)		
No	268 (67.2)	204 (68.7)			201 (71.5)	271 (65.3)		
Diabetes			2.038	0.153			0.065	0.799
Yes	80 (20.1)	47 (15.8)			50 (17.8)	77 (18.6)		
No	319 (79.9)	250 (84.2)			231 (82.2)	338 (81.4)		
Smoke			0.001	0.978			0.494	0.482
Yes	167 (41.9)	124 (41.8)			113 (40.2)	178 (42.9)		
No	232 (58.1)	173 (58.2)			168 (59.8)	237 (57.1)		
Alcohol			0.234	0.629			0.001	0.987
Yes	166 (41.6)	129 (43.4)			119 (42.3)	176 (42.4)		
No	233 (58.4)	168 (56.6)			162 (57.7)	239 (57.6)		
Surgical approach			1.342	0.247			0.308	0.579
Laparoscopic	388 (97.2)	284 (95.6)			270 (96.1)	402 (96.9)		
Open	11 (2.8)	13 (4.4)			11 (3.9)	13 (3.1)		
Surgical procedure			3.119	0.077			0.562	0.453
LAR	340 (85.2)	238 (80.1)			237 (84.3)	341 (82.2)		
APR	59 (14.8)	59 (19.9)			44 (15.7)	74 (17.8)		
Neoadjuvant treatment			0.092	0.762			0.763	0.382
Yes	48 (12.0)	38 (12.8)			31 (11.0)	55 (13.3)		
No	351 (88.0)	259 (87.2)			250 (89.0)	360 (86.7)		

[n(%)]

表3 训练组中无进展生存期相关因素的单因素和多因素分析

Tab. 3 Univariate and multivariate analysis of factors associated with RFS in the training cohort

Variable	Univariate			Multivariate		
	HR	95%CI	P value	HR	95% CI	P value
SATI (high vs low)	3.027	1.676-5.467	<0.001	2.717	1.505-4.905	<0.001
SMI (high vs low)	0.296	0.164-0.533	<0.001	0.329	0.182-0.595	<0.001
Sex (female vs male)	1.048	0.649-1.692	0.849			
Age (≥ 65 years vs < 65 years)	1.538	0.941-2.514	0.086			
Hypertension (yes vs no)	0.939	0.560-1.574	0.811			
Diabetes (yes vs no)	1.054	0.575-1.932	0.865			
Smoke (yes vs no)	0.840	0.512-1.379	0.491			
Alcohol (yes vs no)	0.952	0.586-1.548	0.844			
Surgical approach (open vs laparoscopic)	0.328	0.045-2.369	0.269			
Surgical procedure (APR vs LAR)	0.610	0.292-1.277	0.190			
Neoadjuvant treatment (yes vs no)	0.739	0.338-1.619	0.450			
BMI (≥ 21.83 kg/m ² vs < 21.83 kg/m ²)	1.812	0.926-3.549	0.083			
CEA (≥ 4.39 ng/mL vs < 4.39 ng/mL)	1.587	0.979-2.574	0.061			
Size (≥ 5.5 cm vs < 5.5 cm)	0.663	0.390-1.129	0.130			
T stage (T3+T4 vs T1+T2)	7.555	1.850-30.856	0.005	7.205	1.762-29.473	0.006
N stage (N2 vs N0+N1)	6.230	3.456-11.233	<0.001	5.443	3.014-9.829	<0.001

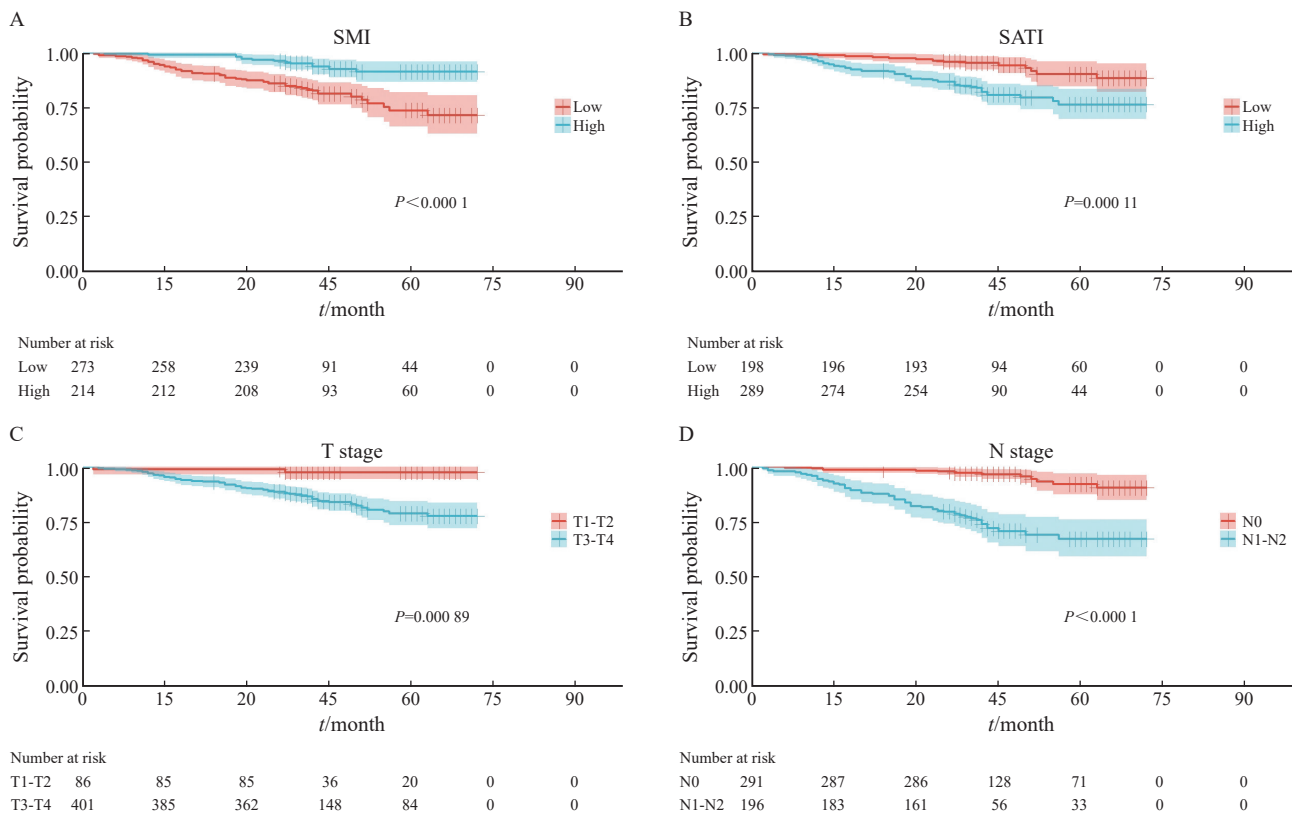


图2 不同分组患者的RFS比较

Fig. 2 Comparison of RFS in different groups of patients

A: Patients with high or low SMI; B: Patients with high or low SATI; C: Patients with T3 and T4 or T1 and T2; D: Patients with N1 and N2 or N0.

表4 训练组中与OS相关因素的单因素及多因素分析

Tab. 4 Univariate and multivariate analysis of factors associated with OS in the training cohort

Variable	Univariate			Multivariate		
	HR	95% CI	P value	HR	95% CI	P value
SATI (high vs low)	4.820	2.367-9.815	<0.001	3.542	1.739-7.211	<0.001
SMI (high vs low)	0.097	0.039-0.243	<0.001	0.132	0.053-0.330	<0.001
Sex (female vs male)	0.793	0.476-1.319	0.371			
Age (≥ 65 years vs < 65 years)	1.744	1.025-2.965	0.040			0.216
Hypertension (yes vs no)	0.906	0.526-1.563	0.723			
Diabetes (yes vs no)	0.675	0.321-1.422	0.301			
Smoke (yes vs no)	0.921	0.549-1.545	0.755			
Alcohol (yes vs no)	0.881	0.525-1.477	0.631			
Surgical approach (open vs laparoscopic)	0.045	0.001-7.094	0.230			
Surgical procedure (APR vs LAR)	1.025	0.533-1.971	0.941			
Neoadjuvant treatment (yes vs no)	0.414	0.150-1.146	0.090			
BMI (≥ 21.83 kg/m ² vs < 21.83 kg/m ²)	1.531	0.776-3.019	0.219			
CEA (≥ 4.39 ng/mL vs < 4.39 ng/mL)	1.457	0.876-2.423	0.147			
Size (≥ 5.5 cm vs < 5.5 cm)	0.573	0.323-1.018	0.057			
T stage (T3+T4 vs T1+T2)	13.201	1.829-95.291	0.011	11.478	1.588-82.952	0.016
N stage (N2 vs N0+N1)	10.374	4.926-21.849	<0.001	7.779	3.683-16.430	<0.001

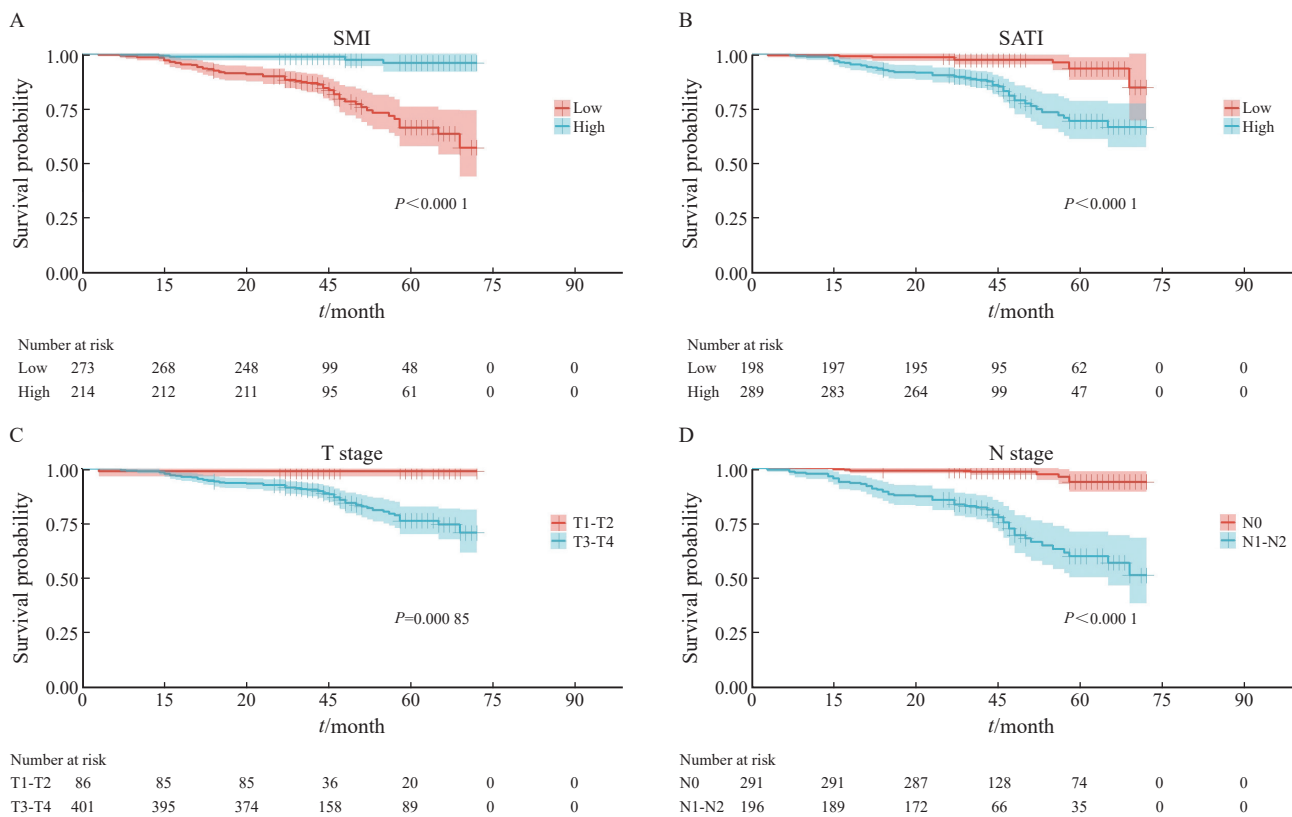


图3 不同分组患者OS比较

Fig. 3 Comparison of OS in different groups of patients

A: Patients with high or low SMI; B: Patients with high or low SATI; C: Patients with T3 and T4 or T1 and T2; D: Patients with N1 and N2 or N0.

2.4 预测模型

根据多因素分析结果, 我们于训练集中分别构建预测术后RFS和OS的预测列线图模型(图4A、4B)。ROC曲线分析证实CT机体组分对术后RFS和OS的预测能力。在训练集中, 模型A预测3、4和5年RFS的ROC曲线的曲线下面积(area under curve, AUC)分别为0.862、0.846和0.824(图5A), 模型B预测3、4和5年OS的AUC分别为0.886、0.898和0.875(图5B)。在验证集中, 预测3、4和5年RFS的AUC分别为0.825、0.866和0.838(图5C), 预测3、4和5年OS的AUC分别为0.876、0.912和0.877(图5D)。上述结果表

明, 本研究所构建的模型A与模型B具有较高的准确率。

此外, 训练集预测模型3、4和5年RFS(图6A1~6A3)及OS(图6B1~6B3)的校准曲线和验证集模型3、4和5年RFS(图6C1~6C3)及OS(图6D1~6D3)的校准曲线表明, 模型具有良好的预测性能; DCA中, Y轴表示净收益, X轴表示相应的风险阈值, 蓝线表示所有患者都不接受治疗, 绿线假设所有患者都接受治疗, 红线代表预测模型。训练集模型RFS(图7A)及OS(图7B)以及验证集模型RFS(图7C)及OS(图7D)的DCA表明, 模型具有较好的临床获益性。

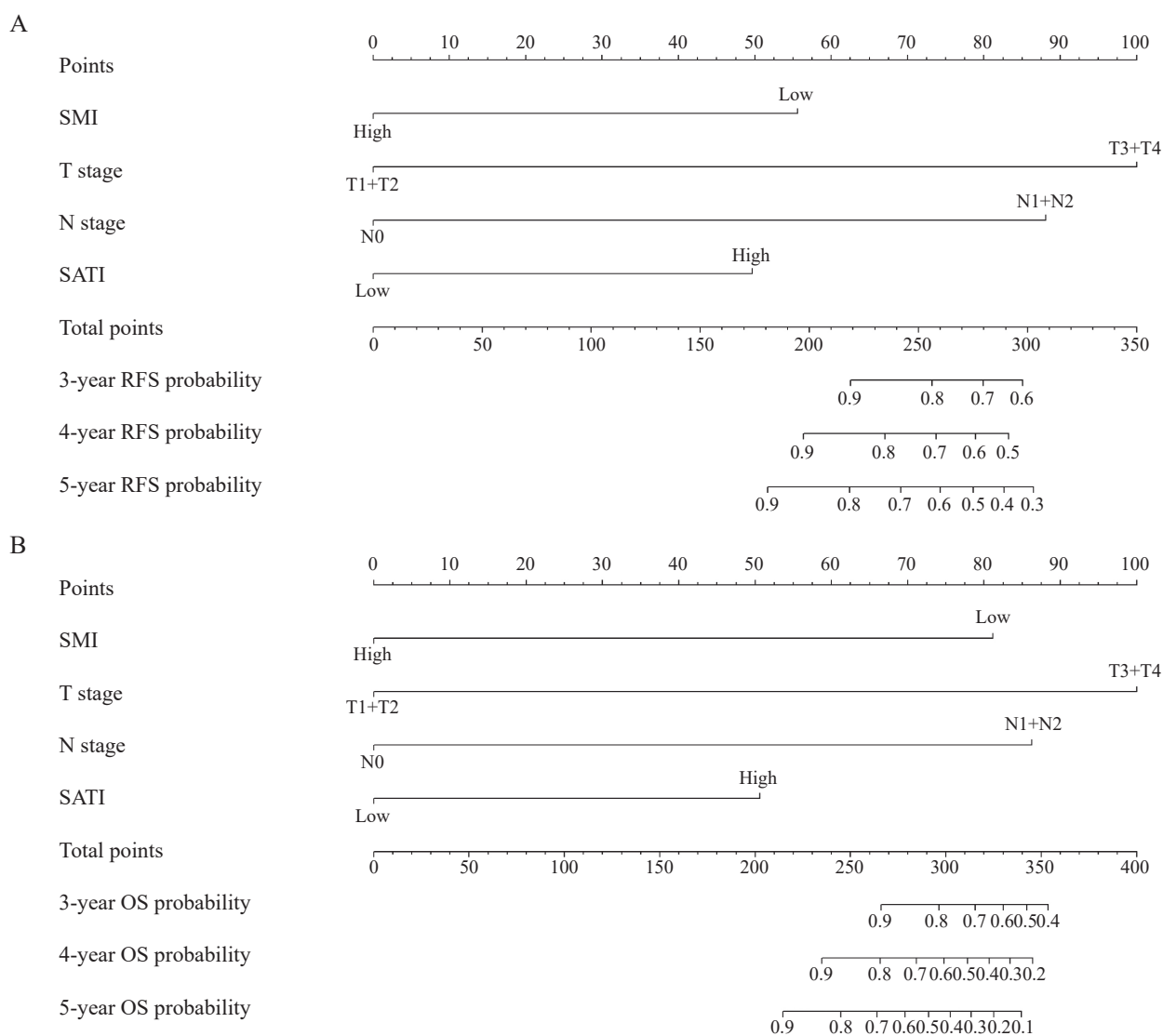


图4 基于独立危险因素构建的列线图模型

Fig. 4 The nomogram models based on independent risk factors

A: Model A (predict the risk of 3-, 4-, and 5-year adverse RFS in patients with rectal cancer); B: Model B (predict the risk of 3-, 4-, and 5-year adverse OS in patients with rectal cancer).

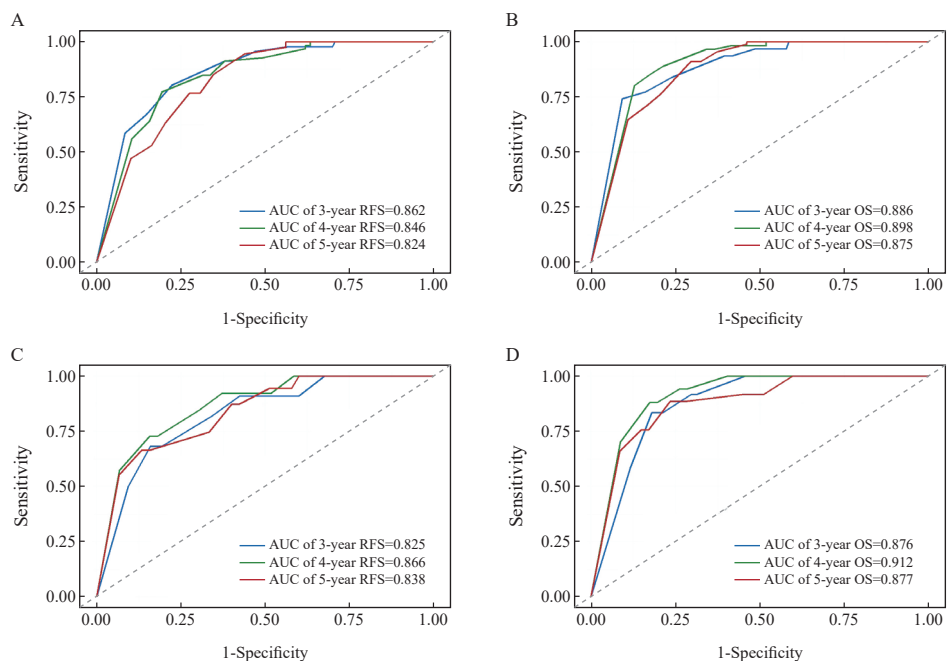


图5 训练集与验证集OS及RFS预测模型的ROC曲线

Fig. 5 ROC curves of OS and RFS prediction models for the training set and validation set

A: ROC curve of model for predicting 3,4,5-year RFS in the training set; B: The ROC curve of model for predicting 3-, 4-, and 5-year OS in the training set; C: The ROC curve of model for predicting 3,4, and 5-year RFS in the validation set; D: The ROC curve of model for predicting 3-, 4-, and 5-year OS in the validation set.

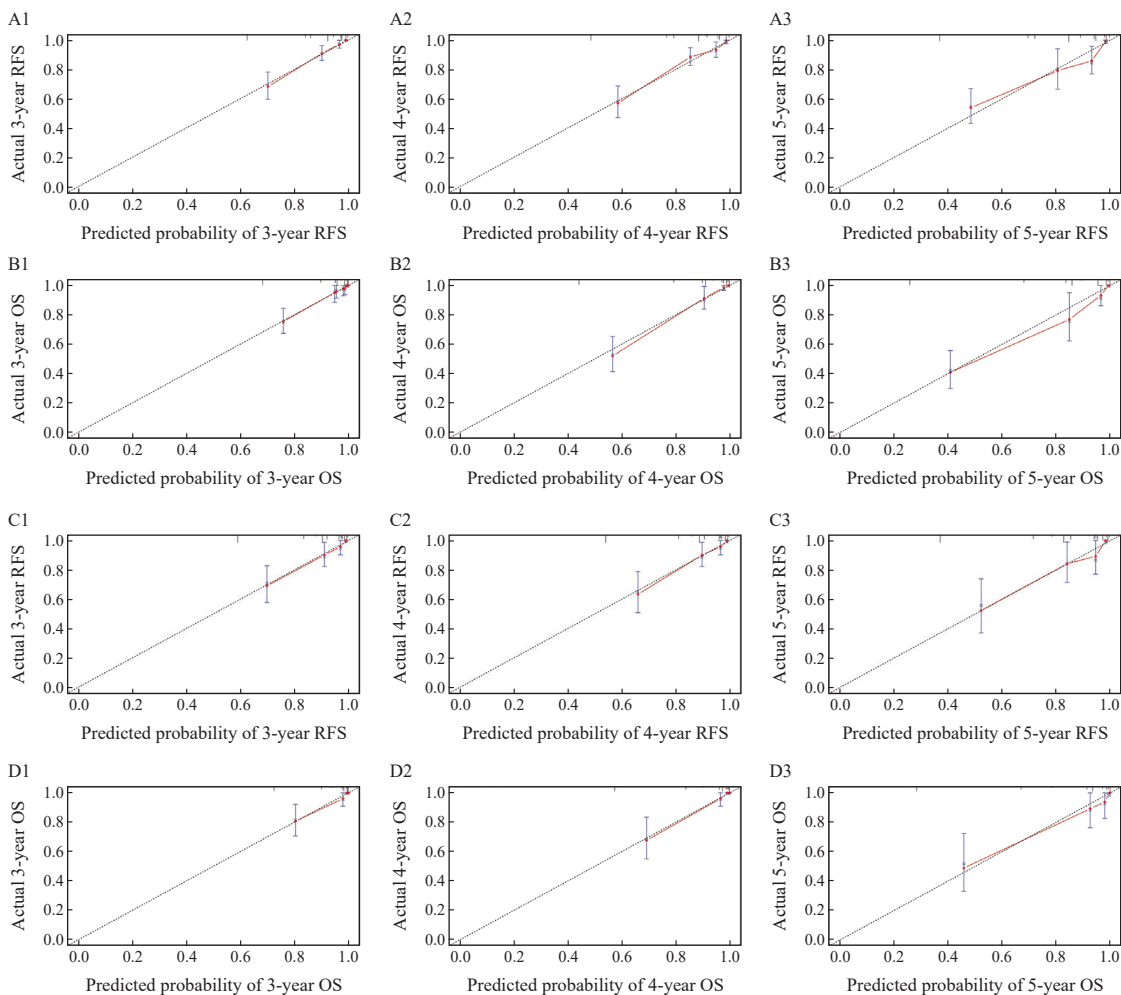


图6 训练集与验证集OS及RFS预测模型的校准曲线

Fig. 6 Calibration diagram of OS and RFS prediction models for the training set and validation set

The calibration plots of the 3-year (A1), 4-year (A2) and 5-year (A3) RFS of the prediction model in the training set. The calibration plots of the 3-year (B1), 4-year (B2) and 5-year (B3) OS of the prediction model in the training set. The calibration plots of 3-year (C1), 4-year (C2) and 5-year (C3) RFS in the validation set. The calibration plots of the 3-year (D1), 4-year (D2) and 5-year (D3) OS in the validation set.

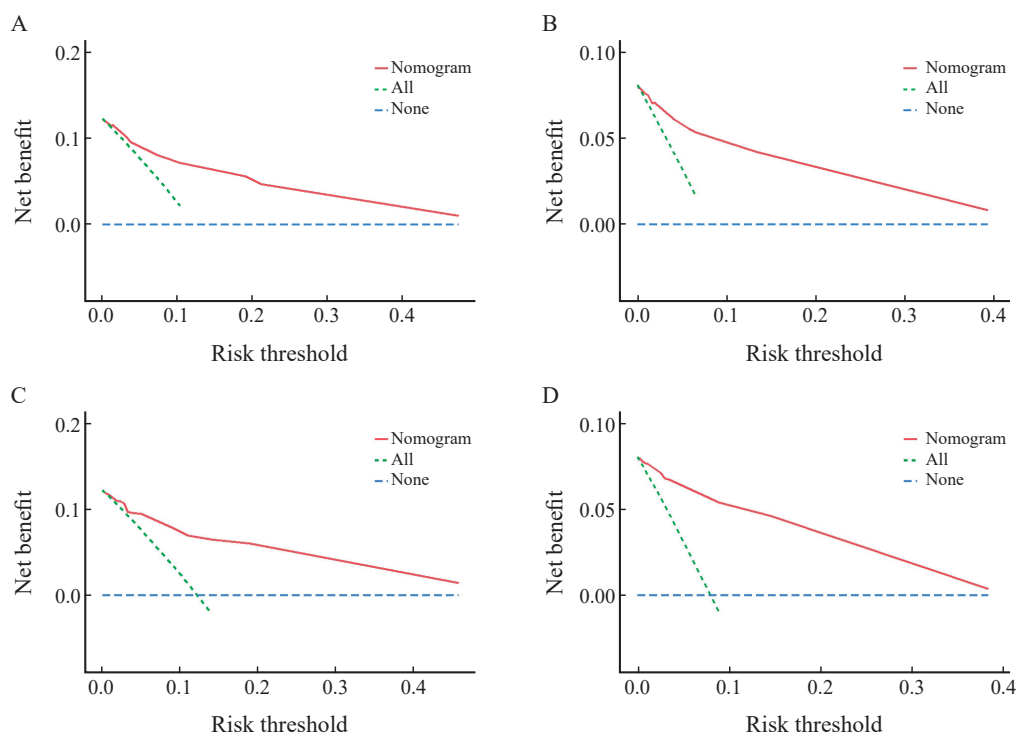


图7 训练集与验证集OS及RFS预测模型的DCA曲线

Fig. 7 DCA curves of OS and RFS prediction models for the training set and validation set

A: Decision curve analysis of the model for predicting RFS in the training set; B: Decision curve analysis of the OS prediction model in the training set; C: Validation of the decision curve analysis of the RFS model; D: Validation of the decision curve analysis of the OS model.

3 讨 论

直肠癌患者的术后长期预后越来越受到关注。本研究分析了直肠癌患者CT测量的机体组分的临床意义,发现低SMI及高SATI是术后预后不良的独立预测因素,并据此构建了一种新的直肠癌患者预后预测模型。为患者预后评估提供了有力且个性化的工具。

肌少症是一种进行性骨骼肌疾病,常见于肿瘤患者,与多种不良反应有关。基于CT测量L3水平的骨骼肌被认为是评估肌少症的主要标准^[13]。然而,目前并没有确定的临界值来定义肌少症。一些研究应用了Prado等^[14]研究中使用的临界值,将肌少症定义为男性SMI $<52.40\text{ cm}^2/\text{m}^2$,女性SMI $<38.50\text{ cm}^2/\text{m}^2$ 。在亚洲患者中,男性的临界值通常较低,定义为男性SMI $<36\text{ cm}^2/\text{m}^2$ ^[15]。本研究中男性和女性SMI的截断值分别为 $38.65\text{ cm}^2/\text{m}^2$ 及 $36.34\text{ cm}^2/\text{m}^2$ 。

肌少症已被证实可影响多种癌症患者的长期预后,如CRC、食管癌、头颈癌、恶性淋巴瘤及胰腺癌等^[12, 16-18]。大量研究表明,肌少症与CRC患者术后并发症增加及OS降低有关。Abe等^[19]的研究证实,肌少症是术后结局恶化的有力预测指标,包括住院时间延长和感染性并发症发生率增加。此外,一项纳入6 600例

CRC患者的meta分析^[20]表明,无论在肿瘤切除之前还是之后观察到的肌少症都与较差的OS和DFS相关。Takiguchi等^[21]研究发现,术前肌少症与CRC患者术后的预后相关,并且在肌少症缓解后预后会显著改善。尽管这些研究表明,肌少症会影响CRC患者的预后,但大都未建立完整的预测模型。相比之下,本研究充分结合术前客观营养指标建立了完整的预测模型,同时模型具有较高的准确率及临床适用性。尽管肌少症影响癌症患者预后的机制尚不清楚,但有研究^[22-23]表明,肌少症可能反映更具侵袭性的肿瘤生物学的代谢活性增加,导致全身炎症和肌肉萎缩,从而提高癌症的患病风险并降低治疗的有效性。此外,肌少症与严重化疗相关不良反应的发生率高度相关,这些变化包括因癌症特异性治疗而继发的骨骼肌量减少^[24]。因癌症治疗而继发不良反应的易感性增加、身体储备功能下降,造成恶性循环,并且在某些情况下,无法再进行针对癌症的进一步治疗^[25]。本研究证实低SMI是直肠癌患者术后RFS和OS较差的独立预测因素,与既往研究结果^[9, 26-27]一致。

腹部肥胖是许多慢性病的重要危险因素,会增加消化系统肿瘤的发病率,特别是CRC,其发病率高,预后差^[28]。CRC患者的肥胖会增

加许多代谢紊乱的风险,包括高血压、心脑血管疾病和糖尿病,同样,肥胖又会加剧与CRC相关的风险因素^[29-30]。消化系统肿瘤在解剖学上生长于脂肪组织附近,当脂肪细胞与癌细胞相互作用时,它们可能会去分化为前脂肪细胞或癌症相关脂肪细胞,这些分化后的脂肪细胞会分泌脂肪因子,从而刺激肿瘤细胞的黏附、迁移和侵袭^[31]。Pacquelet等^[32]研究发现,肌间脂肪面积/皮下脂肪面积比值高与较差的生存结局相关,肌间脂肪面积/皮下脂肪面积比值需分别精确测量肌间脂肪面积与皮下脂肪面积,这种繁琐的测量流程显著增加了临床操作的工作量,严重限制了其在日常临床实践中的广泛应用。因此我们试图探寻一项更加简单易得且准确率高的指标来预测直肠癌患者的长期预后。鉴于上述现状,本研究创新性地引入SATI这一指标,并探索其在直肠癌患者预后预测中的应用价值,为临床提供更为高效、可靠的预后评估工具。结果显示,术前高SATI是RFS及OS更差的独立预测因素。

本研究证实CT机体组分是直肠癌术后RFS及OS的独立预测因子。在此基础上结合肿瘤T、N分期建立了预后预测模型,经过验证,表现出相对较好的性能。同时,一项在研前瞻性研究(注册号为ChiCTR2500104756)试图通过影像学数据及临床数据开发针对CRC患者预后的高性能自动分割预后模型,此研究与本研究类似,有望准确预测直肠癌患者的预后进而指导临床干预。与传统的通过TNM分期预测肿瘤患者预后的方法相比,诺莫图可以综合考虑与研究终点相关的多种因素,综合评估患者出现某一疾病结局的风险,更加准确、直观和全面。而且,它可以根据每个个体的具体特征提供个性化的预测。

本研究具有一定局限性。研究样本来自单中心,且样本量相对有限,这可能限制了研究结果的通用性且不可避免地存在选择偏倚。未来应扩大样本量,包括多中心数据并进行前瞻性研究,以验证模型的可靠性和通用性。另外,预测模型使用时需专业人员掌握一定的影像学技能,如机体组分的测量和计算。当机体组分数据不可获得时,可将患者CT图像与其他便于测量的图像对比,从而获知预后风险。

综上所述,CT机体组分是直肠癌患者RFS和OS的独立预测指标,在此基础上开发的列线图模型对直肠癌患者预后具有较好的预测价值。

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刘硕: 实施研究, 收集及分析数据, 绘制图表, 完成论文的撰写及修改; 卢云, 胡继霖, 杨文昶: 引导研究方向与研究设计, 论文修订及审核; 赵日志, 许文达, 杨涵宇, 路泽琛, 马正, 杜兆麟, 高运治: 收集数据及完善患者随访; 高源: 引导研究方向与研究设计, 论文修订及审核。

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(收稿日期: 2025-05-21 修回日期: 2025-07-16)

(责任编辑: 李广涛)