Volume 24, No 4 | International Journal of Radiation Research, October 2026

Impact of anemia on tumor regression in locally advanced rectal cancer: A comparison between MRI-guided short-course radiotherapy and long-course chemoradiotherapy

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► ***Original article***

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Received: September 2025
Final revised: February 2026
Accepted: April 2026

Int. J. Radiat. Res., October 2026; 24(4): 1215-1221

DOI: 10.61186/ijrr.24.4.36

Keywords: *Rectal neoplasms, neoadjuvant therapy, chemoradiotherapy, radiotherapy, image-guided, anemia, treatment outcome.*

ABSTRACT

Background: To evaluate the impact of anemia on tumor regression in locally advanced rectal cancer (LARC) patients who are undergoing MRI-guided short-course radiotherapy (MRI-guided SCRT) or long-course chemoradiotherapy (LCCRT). ***Materials and Methods:*** This retrospective study analysed 189 patients with LARC who received neoadjuvant treatment followed by curative resection at a single institution. Patients were classified as anemic or nonanemic according to baseline hemoglobin levels. Tumor regression grade (TRG), tumor downstaging, and pathological complete response (pCR) were compared across the two radiotherapy approaches. Potential predictors of tumor regression were evaluated using univariable analysis and subsequently examined with multivariable logistic regression models. ***Results:*** 157 patients underwent LCCRT and 32 patients underwent MRI-guided SCRT. The baseline characteristics of the two groups were comparable (P>0.05). An overall efficacy analysis revealed no significant differences between MRI-guided SCRT and LCCRT in terms of TRG, pCR, or tumor downstaging (P>0.05). Subgroup analysis revealed that in the LCCRT cohort, anemia was associated with worse TRG and lower pCR rates (P<0.05), whereas the MRI-guided SCRT cohort showed no statistically significant association (P>0.05). Multivariate logistic regression demonstrated that anemia was an independent adverse determinant of both TRG and pCR (P<0.05), whereas the radiotherapy modality itself was not independently related to treatment outcome (P>0.05). ***Conclusions:*** MRI-guided SCRT demonstrated a comparable overall efficacy to LCCRT in patients with LARC. The efficacy of MRI-guided SCRT was unaffected by anemia, whereas anemia significantly impaired tumor regression outcomes in LCCRT patients.

INTRODUCTION

For patients with locally advanced rectal cancer (LARC), the established standard of care consists of neoadjuvant chemoradiotherapy (nCRT) followed by total mesorectal excision (TME) [1,2], resulting in significant improvements in survival outcomes, lower local recurrence rates, and higher rates of sphincter-preserving surgeries [3]. However, substantial variability in tumor response to nCRT is observed among patients, and the factors driving this variability remain unclear.

Anemia is commonly observed in LARC patients who are receiving nCRT, with a reported prevalence that ranges from 30% to 67% [4]. Anemia has strongly been associated with poorer outcomes[5], largely due to anemia-induced hypoxia, which disrupts oxygen delivery within the tumor microenvironment [6–8]. Hypoxia is known to promote more aggressive tumor behaviour, upregulate the expression of angiogenic factors, and reduce the sensitivity of tumors to radiotherapy [9]. Consequently, anemia is recognized as a key barrier to achieving optimal tumor regression in rectal cancer patients.

Advances in MRI-guided radiotherapy (MRI-guided RT) have enabled these challenges to be addressed. MRI-guided linear accelerators (MR-Linac) integrate high-resolution imaging with accurate radiation delivery, enabling superior soft-tissue visualization, real-time target monitoring, and

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[DOI: 10.61186/ijrr.24.4.36]

adaptive treatment workflows [10–12]. These capabilities improve target conformity while limiting unnecessary irradiation of adjacent normal tissue [10,13], potentially mitigating the impact of hypoxia and improving the efficacy of radiotherapy in anemic patients [14]. Moreover, MRI-guided short-course radiotherapy (SCRT), with its shorter treatment duration, may reduce the impact of prolonged hypoxia compared with conventional long-course chemoradiotherapy (LCCRT) [15].

Despite the theoretical advantages of MRI-guided SCRT, its performance in the setting of anemia has not been well characterized, and whether it differs from LCCRT in its sensitivity to anemia-related hypoxia remains uncertain. Comparative evidence on pathological response between these modalities in anemic and nonanemic patients is limited. This study addresses this gap by evaluating tumor regression grade (TRG), pathological complete response (pCR), and tumor downstaging across anemia subgroups, with the aim of determining whether MRI-guided SCRT provides more stable treatment outcomes among patients with anemia.

MATERIALS AND METHODS

Study population

Approval for the study protocol was obtained from the Institutional Ethics Committee (Approval No. SCCHCEC-02-2024-044; March 7, 2024). Due to the retrospective nature of the study, the need for written informed consent was waived. Between 2018 and 2023, 288 patients with LARC treated at Sichuan Cancer Hospital were retrospectively reviewed. All patients had undergone nCRT followed by curative surgical resection. Detailed clinical information was extracted from surgical and diagnostic records; the inclusion and exclusion process are illustrated in figure 1.

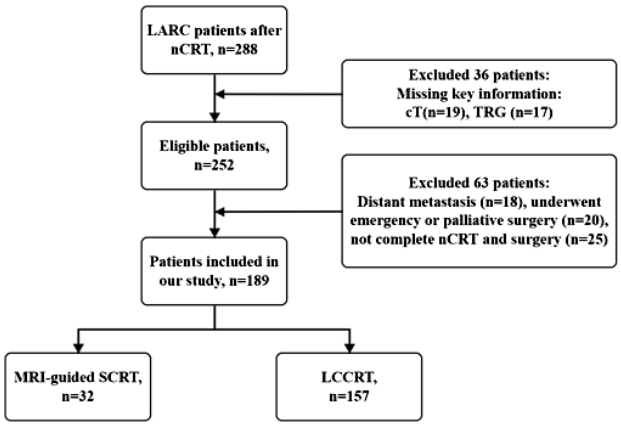


Figure 1. Consort diagram. LARC=Locally advanced rectal cancer; nCRT=Neoadjuvant chemoradiotherapy; TRG=Tumor regression grading; MRI-guided SCRT =MRI-guided neoadjuvant short-course radiotherapy; LCCRT=Long-course concurrent chemoradiotherapy.

Eligibility requirements were defined as an age of at least 18 years, having a histopathologically confirmed rectal adenocarcinoma, and a clinical diagnosis of LARC (cT3-4 or cN+ without distant metastases). Only patients who completed nCRT followed by curative surgery and had complete postoperative pathological data were included in the analysis. Patients were excluded if distant metastases (M1) were present at diagnosis; if key clinical information such as sex, age, tumor markers, or pathological reports was missing; or if they underwent emergency or palliative surgery. Additional exclusion criteria included concurrent malignancies or severe systemic diseases, as well as contraindications to chemoradiotherapy or incomplete nCRT and surgery.

After applying these criteria, 189 patients remained for the final analysis, with 157 receiving LCCRT and 32 undergoing MRI-guided SCRT. Baseline variables included demographic variables (age and sex), tumor-node-metastasis stage (TNM), carcinoembryonic antigen (CEA) level, body mass index (BMI), histological differentiation, distance of the tumor from the anal verge, and TRG.

Hemoglobin assessment

Hemoglobin (Hb) levels were assessed within two weeks before radiotherapy. Anemia was diagnosed the World Health Organization (WHO) criteria: hemoglobin concentration <12 g/dL in women and <13 g/dL in men [16].

Treatments

Patients treated with LCCRT received external beam radiotherapy using a linear accelerator (Synergy®, Elekta, Sweden) using daily fractions of 1.8-2.0 Gy administered five times per week, to a cumulative dose of 50-50.4 Gy over 5-6 weeks, with concurrent capecitabine (Xeloda®, Switzerland) administered at 825 mg/m^2 twice daily. Systemic chemotherapy regimens included CapeOX, composed of capecitabine (Xeloda®, Switzerland) and oxaliplatin (Eloxatin®, France), or modified FOLFOX6 (mFOLFOX6), consisting of 5-fluorouracil (Efudex®, Switzerland), leucovorin (Calcium Folinate Injection®, China), and oxaliplatin (Eloxatin®, France). After 4-6 cycles of chemotherapy, the preoperative treatment response was assessed 7–12 weeks post-nCRT, followed by surgery. Adjuvant chemotherapy with CapeOX or mFOLFOX6 was initiated 3-4 weeks postoperatively.

Patients who underwent MRI-guided SCRT (Unity®, Elekta, Sweden) received radiotherapy delivered via MR-Linac to deliver 25 Gy in five daily fractions of 5 Gy each (figure 2). Chemotherapy consisted of mFOLFOX6, followed by preoperative assessment after 6 cycles. Surgery was subsequently performed, and adjuvant chemotherapy with mFOLFOX6 commenced 3-4 weeks post-operatively.

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Surgical procedures were either low anterior resection or abdominoperineal resection, following total mesorectal excision principles.

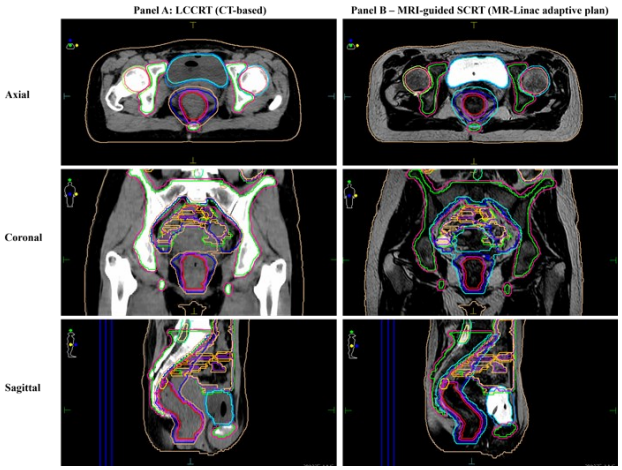


Figure 2. Representative planning images of LCCRT and MRI-guided SCRT. Panel **A:** CT-based plan for long-course chemoradiotherapy (LCCRT), showing axial, coronal, and sagittal views with target volumes and organs at risk. Panel **B:** MRI-guided plan for short-course radiotherapy (SCRT) on a 1.5 -T MR-Linac, demonstrating soft-tissue visualization and adaptive dose distribution across the same three planes.

Efficacy assessment

Tumor regression was evaluated by TRG, pCR, and tumor downstaging. Assessment of TRG followed the American Joint Committee on Cancer (AJCC) grading system [17]. TRG 0 is defined by the complete absence of tumor cells, TRG 1 shows scattered single cells or small clusters, TRG 2 is characterized by residual tumor cells with associated stromal changes, and TRG 3 indicates minimal treatment response. TRGs 0–1 was classified as good responses whereas TRGs 2–3 were considered poor responses. The term tumor downstaging refers to a decrease in T stage when comparing pretreatment clinical staging (cT) with postoperative pathological findings (ypT) [18]; pCR was defined as the absence of any remaining tumor cells in either the primary tumor or the regional lymph nodes [19].

Statistical analysis

All the statistical computations were completed in SPSS 25.0 (IBM Corp., USA). Continuous measures were expressed as the mean ± standard deviation; between-group differences were assessed with the independent-samples t test or, when appropriate, the Mann–Whitney U test. Categorical data were compared with either the chi-square test or Fisher's exact test. Variables identified as significant in univariable analyses, along with treatment modality, were included in multivariable logistic regression analyses, and adjusted odds ratios with 95% confidence intervals were used to report the effect estimates. Statistical significance was determined by a two-sided P value <0.05.

RESULTS

Patient characteristics

In total, 189 patients with LARC were analyzed, of whom 157 received LCCRT and 32 were treated with MRI-guided SCRT. Table 1 summarizes the baseline demographic and clinical features. Sex distribution was comparable between groups (male: 64.3% vs. 59.4%; female: 35.7% vs. 40.6%, P>0.05), mean age (56.38 ± 11.24 vs. 51.91 ± 10.52 years, P>0.05), and tumor distance from the anal verge (5.54 ± 2.56 vs. 4.62 ± 1.74 cm, P>0.05). Other baseline characteristics, including body mass index, clinical stage, and carcinoembryonic antigen levels, with comparable results between the two groups (all P>0.05).

Table 1. Patient characteristics.

Patient characteristics	Category	MRI-guided SCRT (n=32) n (%)	LCCRT (n=157) n (%)	*P*
Gender	Male	19(59)	101(64)	0.688
	Female	13(41)	56(36)	
Age	Mean ± SD (year)	51.91±10.52	56.38±11.24	0.052
BMI	Mean ± SD (kg/m²)	23.59±3.18	23.45±3.49	0.923
Clinical T stage	2	2(6)	2(1)	0.153
	3	21(66)	97(62)	
	4	9(28)	58(37)	
Clinical N stage	cN0	1(3)	14(9)	0.474
	cN+	31(97)	143(91)	
Distance from the anal verge	Mean ± SD (cm)	4.62±1.74	5.54±2.56	0.072
Preoperative CEA	Mean ± SD (ng/mL)	12.85±20.11	13.04±24.68	0.822
Anemia	No	22(69)	88(56)	0.239
	Yes	10(31)	69(44)	
ypT	0	9(28)	33(21)	0.224
	1	2(6)	5(3)	
	2	10(31)	34(22)	
	3	11(34)	76(48)	
	4	0(0)	9(6)	
ypN	0	21(66)	114(73)	0.053
	1	11(34)	30(19)	
	2	0(0)	13(8)	
Tumor differentiation	Low	3(9)	14(9)	0.141
	Medium-low	0(0)	22(14)	
	Medium	10(31)	54(34)	
	High-medium	9(28)	27(17)	
	High	4(13)	13(8)	
	Unknown	6(19)	27(17)	
Vascular tumor thrombus	No	28(88)	137(87)	1.000
	Yes	4(13)	20(13)	
Perineural invasion	No	27(84)	124(79)	0.631
	Yes	5(16)	33(21)	
CRM	No	31(97)	156(99)	0.311
	Yes	1(3)	1(1)	

Abbreviations: MRI-guided SCRT =MRI-guided neoadjuvant short-course radiotherapy; LCCRT=Long-course concurrent chemoradiotherapy; BMI=Body mass index; CEA=Carcinoembryonic antigen; CRM=Closest resection margin.

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[DOI: 10.61186/ijrr.24.4.36]

Comparison of efficacy between MRI-guided SCRT and LCCRT

The rates of TRG, pCR, and tumor downstaging were similar in the MRI-guided SCRT and LCCRT groups, and the results were comparable across the two groups (all P>0.05; table 2).

Table 2. Comparison of Tumor Regression of MRI-guided SCRT and LCCRT.

Outcomes	Category	MRI-guided SCRT (n=32) n (%)	LCCRT (n=157) n (%)	*P*
TRG	Good	15(47)	55(35)	0.211
	Poor	17(53)	102(65)	
pCR	Yes	7(22)	30(19)	0.722
	No	25(78)	127(81)	
Downstaging	Yes	22(69)	101(64)	0.680
	No	10(31)	55(36)	

Abbreviations: TRG=Tumor regression grading; pCR=Pathological complete remission; MRI-guided SCRT =MRI-guided neoadjuvant short-course radiotherapy; LCCRT=Long-course concurrent chemoradiotherapy.

Comparison of tumor regression between anemic and non-anemic patients with MRI-guided SCRT and LCCRT

Among patients treated with MRI-guided SCRT, no significant differences in TRG, pCR, or tumor downstaging were observed between anemic and non-anemic individuals (P>0.05). Conversely, in the LCCRT group, anemia was associated with poorer tumor regression outcomes. Anemic patients had a lower proportion of good TRG values (TRG 0–1) than nonanemic patients did (17.2% vs. 43.2%, P=0.015), and the pCR rate was likewise reduced (11.6% vs. 25.0%, P=0.03).

Univariate analysis of tumor regression

Factors potentially associated with tumor regression outcomes were evaluated using univariable analysis, focusing on tumor downstaging, TRG, and pCR. Significant associations were observed between tumor downstaging and pretreatment tumor and nodal stages (clinical T stage and clinical N stage), postoperative pathological stages (ypT and ypN), vascular invasion, and perineural invasion (P<0.05). In contrast, anemia, postoperative pathological stage (ypT and ypN), vascular invasion, and perineural invasion were significantly related to TRG (P<0.05). Similar associations were observed for pCR, which was significantly related to anemia, postoperative pathological stage (ypT and ypN), and vascular and perineural invasion (P<0.05). Radiotherapy treatments were not significantly associated with tumor regression outcomes according to any of the aforementioned metrics (as shown in table 3, P>0.05).

Multivariate analysis of tumor regression

Multivariate logistic regression demonstrated that anemia independently predicted poorer TRG and pCR outcomes. Anemic patients were less likely to achieve good TRG responses (OR = 0.42; P=0.011) or pCRs (OR = 0.37; P=0.019). Radiotherapy treatments (MRI-guided SCRT vs. LCCRT) were not independently associated with tumor regression outcomes (as shown in table 4; P>0.05).

Table 3. Comparison of Tumor Regression Between Anemic and Non-Anemic Patients in MRI-Guided SCRT and LCCRT.

Outcomes	Category	MRI-Guided SCRT			LCCRT		
		Anemia (n=10) n (%)	Non-anemia (n=22) n (%)	*P*	Anemia (n=69) n (%)	Non-anemia (n=88) n (%)	*P*
TRG	Good	4(40)	11(50)	0.712	17(25)	38(43)	**0.015**
	Poor	6(60)	11(50)		52(75)	50(57)	
pCR	Yes	1(10)	6(27)	0.387	8(12)	22(25)	**0.030**
	No	9(90)	16(73)		61(88)	66(75)	
Downstaging	Yes	8(80)	14(64)	0.440	44(64)	58(66)	0.780
	No	2(20)	8(36)		25(36)	30(34)	

Abbreviations: TRG=Tumor regression grading; pCR=Pathological complete remission; MRI-guided SCRT =MRI-guided neoadjuvant short-course radiotherapy; LCCRT=Long-course concurrent chemoradiotherapy.

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Table 4. Univariate Analysis. Determination of characteristics correlated with downstaging, TRG, and pCR in nCRT.

Patient characteristics	Category	Downstaging			TRG			pCR		
		Yes (n=124) n (%)	No (n=65) n (%)	*P*	Good (n=70) n (%)	Poor (n=119) n (%)	*P*	Yes (n=37) n (%)	No (n=152) n (%)	*P*
Gender	Male	79(64)	41(63)	1	44(63)	76(64)	1	21(57)	99(65)	0.448
	Female	45(36)	24(37)		26(37)	43(36)		16(43)	53(35)	
Age	Mean ± SD (year)	55.15±11.50	56.52±10.71	0.565	53.86±11.86	56.66±10.75	0.104	55.43±12.22	55.66±11.01	0.776
BMI	Mean ± SD (kg/m²)	23.59±3.46	23.25±3.40	0.559	23.57±3.71	23.41±3.27	0.821	23.59±3.65	23.44±3.39	0.837
Clinical T stage	2	2(2)	2(3)	**0.000**	3(4)	1(1)	0.585	2(5)	2(1)	0.482
	3	61(49)	57(88)		43(61)	75(63)		23(62)	95(63)	
	4	61(49)	6(9)		24(34)	43(36)		12(32)	55(36)	
Clinical N stage	cN0	15(12)	0(0)	**0.008**	7(10)	8(7)	0.599	4(11)	11(7)	0.702
	cN+	109(88)	65(100)		63(90)	111(93)		33(89)	141(93)	
Distance from the anal verge	Mean ± SD (cm)	5.27±2.35	5.62±2.67	0.547	5.27±2.29	5.46±2.56	0.708	5.27±2.23	5.42±2.52	0.900
Preoperative CEA	Mean ± SD (ng/mL)	11.78±19.70	15.35±30.44	0.102	12.60±25.84	13.25±22.83	0.120	10.02±20.65	13.74±24.66	0.096
Anemia	No	72(58)	38(58)	1	49(70)	61(51)	**0.018**	28(76)	82(54)	**0.027**
	Yes	52(42)	27(42)		21(30)	58(49)		9(24)	70(46)	
ypT	0	42(34)	0(0)	**0.000**	42(60)	0(0)	**0.000**	36(97)	6(4)	**0.000**
	1	7(6)	0(0)		4(6)	3(3)		0(0)	7(5)	
	2	42(34)	2(3)		12(17)	32(27)		0(0)	44(29)	
	3	33(27)	54(83)		12(17)	75(63)		1(3)	86(57)	
	4	0(0)	9(14)		0(0)	9(8)		0(0)	9(6)	
ypN	0	106(85)	29(45)	**0.000**	59(84)	76(64)	**0.002**	34(92)	101(66)	**0.002**
	1	14(11)	27(42)		10(14)	31(26)		3(8)	38(25)	
	2	4(3)	9(14)		1(2)	12(10)		0(0)	13(9)	
Tumor differentiation	Low	12(10)	5(8)	0.358	11(16)	6(5)	0.250	8(22)	9(6)	0.501
	Medium-low	11(9)	11(17)		2(3)	20(17)		1(3)	21(14)	
	Medium	39(31)	25(38)		14(20)	50(42)		1(3)	63(41)	
	High-medium	19(15)	17(26)		7(10)	29(24)		0(0)	36(24)	
	High	14(11)	3(5)		7(10)	10(8)		2(5)	15(10)	
	Unknown	29(23)	4(6)		29(41)	4(3)		25(68)	8(5)	
Radiotherapy treatments	MRI-guided SCRT	22(18)	10(15)	0.837	15(21)	17(14)	0.287	7(19)	25(16)	0.908
	LCCRT	102(82)	55(85)		55(79)	102(86)		30(81)	127(84)	
Vascular tumor thrombus	No	116(94)	49(75)	**0.001**	70(100)	95(80)	**0.000**	37(100)	128(84)	**0.021**
	Yes	8(6)	16(25)		0(0)	24(20)		0(0)	24(16)	
Perineural invasion	No	114(92)	37(57)	**0.000**	68(97)	83(70)	**0.000**	36(97)	115(76)	**0.007**
	Yes	10(8)	28(43)		2(3)	36(30)		1(3)	37(24)	
CRM	No	123(99)	64(98)	1	70(100)	117(98)	0.723	37(100)	150(99)	1
	Yes	1(1)	1(2)		0(0)	2(2)		0(0)	2(1)	

Abbreviations: nCRT=Neoadjuvant chemoradiotherapy; BMI=Body mass index; CEA=Carcinoembryonic antigen; TRG=Tumor regression grading; CRM=Closest resection margin; pCR=Pathological complete remission; MRI-guided SCRT =MRI-guided neoadjuvant short-course radiotherapy; LCCRT=Long-course concurrent chemoradiotherapy.

Table 5. Multifactorial analysis. Determining predictors of downstaging, TRG, and pCR in nCRT.

Patient characteristics	Downstaging			TRG			pCR		
	Odds ratio	95%CI	*p*	Odds ratio	95%CI	*p*	Odds ratio	95%CI	*p*
Anemia	1.143	0.555~2.351	0.717	0.420	0.215~0.818	**0.011**	0.365	0.157~0.848	**0.019**
Radiotherapy treatments	1.151	0.454~2.919	0.767	1.485	0.642~3.433	0.356	1.100	0.410~2.952	0.849
ypN	2.836	1.530~5.255	**0.001**	1.656	0.810~3.386	0.167	3.580	1.046~12.254	**0.042**
Vascular tumor thrombus	1.729	0.566~5.279	0.336	0.696	0.2~2.424	0.570			/
Perineural invasion	4.706	1.922~11.525	**0.001**	11.973	2.625~54.617	**0.001**	6.619	0.827~52.962	0.075

Abbreviations: nCRT=Neoadjuvant chemoradiotherapy;TRG=Tumor regression grading; pCR=Pathological complete remission; CI=confidence interval.

DISCUSSION

This study compared MRI-guided SCRT and LCCRT in LARC, focusing on differences between anemic and non-anemic patients. Pathological response was comparable between SCRT and LCCRT in the overall cohort. Baseline anemia was an independent adverse factor for TRG and pCR. The negative association with anemia was evident in patients treated with LCCRT, whereas it was not observed in the MRI-guided SCRT cohort.

The similar pathological outcomes observed with short-course and long-course regimens align with current standards in neoadjuvant treatment for rectal cancer. Short-course radiotherapy combined with subsequent systemic therapy and delayed

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[DOI: 10.61186/ijrr.24.4.36]

surgical intervention is supported by randomized evidence within total neoadjuvant therapy programs, including the RAPIDO trial [20]. Trials evaluating the interval between SCRT and surgery, including the Stockholm III trial, also reported greater tumor regression with delayed resection after SCRT [21]. These data provide a clinical context in which SCRT-based approaches represent an established option rather than a compromise in efficacy. Relevant radiotherapy strategies for digestive tract tumors have been previously reported [22].

The adverse association between anemia and response during LCCRT aligns with that in prior rectal cancer cohorts, showing that reduced regression and lower complete response rates were observed in patients with low pretreatment hemoglobin levels. A recent study evaluating anemia in patients receiving preoperative chemoradiotherapy similarly reported impaired tumor response in anemic patients [23]. The radiobiological basis is well described: oxygen enhances the effectiveness of photon radiation through oxygen-dependent fixation of DNA damage, whereas hypoxia reduces radiosensitivity and contributes to resistance [9]. The interaction between tumor hypoxia and the response to radiotherapy has also been discussed in the hypofractionated radiotherapy era [24].

One major finding of this study is the identification of a pattern linked to the treatment modality among patients with anemia. In this cohort, anemia was not associated with inferior TRG or pCR after MRI-guided SCRT. Research on the clinical application of online adaptive radiotherapy with 1.5 T MR-Linac systems has confirmed its feasibility in rectal cancer, enabling daily visualization of targets and organs at risk and plan adjustments for pelvic anatomic changes [25]. In anemic patients, where conventional chemoradiotherapy may be more vulnerable to hypoxia-associated impairment, the observed stability of the response with MRI-guided SCRT supports further evaluation of MRI-guided SCRT as a practical neoadjuvant option.

Certain limitations should be acknowledged. The analysis was retrospective in design and performed at a single center, with potential selection bias and residual confounding. The MRI-guided SCRT cohort was small, limiting the precision of the subgroup analyses. Systemic therapy regimens and sequencing were not fully uniform and may have influenced the pathological response. Hemoglobin concentration was assessed only before radiotherapy and without longitudinal monitoring or standardized anemia correction, and no direct hypoxia biomarkers were available. An evaluation of long-term efficacy, treatment-related toxicity, and quality-of-life outcomes was not performed in this analysis. Future prospective multicentre investigations with standardized systemic therapy, longitudinal hemoglobin monitoring, and confirmation of these findings will require future studies with longer follow-up periods and improved strategies for patient selection.

CONCLUSION

MRI-guided SCRT and LCCRT exhibited comparable overall efficacy in patients with LARC. Among the anemic patients, the efficacy of MRI-guided SCRT remained consistent, whereas anemia significantly reduced treatment effectiveness in the LCCRT group. MRI-guided SCRT may serve as a viable alternative for LARC patients, particularly those with anemia, offering a potential option with comparable efficacy and distinct advantages in terms of treatment duration and precision.

Acknowledgments: The authors would like to sincerely thank all the researchers and organizations that contributed to this study.

Conflict of interest: None declared.

Funding: The study was supported by the Central guidance local science and technology development program (Grant No. 24ZYQA029), the National Key Research and Development Program of China (No.2022YFC2401500), Science and Technology Project of Lanzhou City (Grant No. 2023-1-9), Gansu Province Project of Science and Technologies (Grant No. 20JR10RA680, 22CX8JA149) and the Lanzhou heavy Ion Accelerator High-end user Project (HIR20GY007).

Ethical consideration: This study was approved by the ethical review committee of the Sichuan Cancer Hospital (Application No. SCCHCEC-02-2024-044; approval date: March 7, 2024) with a waiver for informed consent.

Author contributions: J.T., Conceptualization; writing-review and editing; methodology; project administration; supervision. Qian Peng, Writing-review and editing; resources; supervision. L.H., Conceptualization; writing-original draft; data curation. G.L., Resources; data curation. Q.Z., Writing-review and editing; resources; supervision. H.L., Data curation; project administration. SL. and H.G., Data curation; supervision.

Data availability statement: The datasets generated during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Possible AI usage: No artificial intelligence (AI) tools were used in the preparation of this manuscript.

REFERENCES

1. Siegel RL, Miller KD, Wagle NS, Jemal A (2023) Cancer statistics, 2023. *CA Cancer J Clin*, ***73***: *17-48*.
2. Wo JY, Anker CJ, Ashman JB, Bhadkamkar NA, *et al.* (2021) Radiation therapy for rectal cancer: executive summary of an

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[DOI: 10.61186/ijrr.24.4.36]

ASTRO clinical practice guideline. *Pract Radiat Oncol,* ***11****: 13-25*.
3. Vuijk FA, van de Water C, Lent-van Vliet S, van der Valk MJM, *et al.* (2021) Intra-tumoral genomic heterogeneity in rectal cancer: mutational status is dependent on preoperative biopsy depth and location. *Cancers,* ***13****: 2271*.
4. van Halteren HK, Houterman S, Verheij CDGW, Lemmens VEPP, Coebergh JWW (2004) Anaemia prior to operation is related with poorer long-term survival in patients with operable rectal cancer. *Eur J Surg Oncol,* ***30****: 628-632*.
5. Bruns ERJ, Borstlap WA, van Duijvendijk P, van der Zaag-Loonen HJ, *et al.* (2019) Association of preoperative anemia with postoperative course and oncological outcome in patients undergoing rectal cancer surgery: a multicenter snapshot study. *Dis Colon Rectum,* ***62****: 823-831*.
6. Vaupel P, Mayer A, Höckel M (2006) Impact of hemoglobin levels on tumor oxygenation: the higher, the better? *Strahlenther Onkol,* ***182****: 63-71*.
7. Becker A, Stadler P, Lavey RS, Hänsgen G, *et al.* (2000) Severe anemia is associated with poor tumor oxygenation in head and neck squamous cell carcinomas. *Int J Radiat Oncol Biol Phys,* ***46****: 459-466*.
8. Hoff CM (2012) Importance of hemoglobin concentration and its modification for the outcome of head and neck cancer patients treated with radiotherapy. *Acta Oncol,* ***51****: 419–432*.
9. Vaupel P, Thews O, Höckel M (2001) Treatment resistance of solid tumors: role of hypoxia and anemia. *Med Oncol,* ***18****: 243-259*.
10. Boldrini L, Intven M, Bassetti M, Valentini V, Gani C (2021) MR-guided radiotherapy for rectal cancer: current perspective on organ preservation. *Front Oncol,* ***11****: 619852*.
11. Gani C, Boldrini L, Valentini V (2019) Online MR-guided radiotherapy for rectal cancer: new opportunities. *Clin Transl Radiat Oncol,* ***18****: 66-67*.
12. Tchelebi LT, Romesser PB, Feuerlein S, Hoffe S, Latifi K, Felder S, Chuong MD (2020) Magnetic resonance-guided radiotherapy for rectal cancer: expanding opportunities for non-operative management. *Cancer Control,* ***27****: 1073274820969449*.
13. Lee SL, Bassetti M, Meijer GJ, Mook S (2021) Review of MR-guided radiotherapy for esophageal cancer. *Front Oncol*, ***11****: 628009*.
14. Bonomo P, Lo Russo M, Nachbar M, Boeke S, Gatidis S, Zips D, Thorwarth D, Gani C (2021) 1.5-T MR-linac planning study comparing two strategies of rectal boost irradiation. *Clin Transl Radiat Oncol*, ***26****: 86-91*.
15. Klüter S, Katayama S, Spindeldreier CK, Koerber SA, *et al.* (2020) Prospective clinical evaluation of feasibility and patient acceptance of magnetic resonance-guided radiotherapy in Germany. *Strahlenther Onkol,* ***196****: 691-698*.
16. World Health Organization (2011) Haemoglobin concentrations for the diagnosis of anaemia and assessment of severity. Geneva: World Health Organization (WHO/NMH/NHD/MNM/11.1).
17. Chen HY, Feng LL, Li M, Ju HQ, *et al.* (2021) College of American Pathologists tumor regression grading system for long-term outcome in patients with locally advanced rectal cancer. *Oncologist,* ***26****: e780–e793*.
18. Edge SB and Compton CC (2010) The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. *Ann Surg Oncol,* ***17****: 1471-1474*.
19. Boldrini L, Lenkowicz J, Orlandini LC, Dinapoli N, *et al.* (2020) Radiomics-based prediction of pathological complete response in rectal cancer: intercontinental validation. *Radiother Oncol,* ***152****: S405*.
20. Bahadoer RR, Dijkstra EA, van Etten B, Marijnen CAM, *et al.* (2021) Short-course radiotherapy followed by chemotherapy versus preoperative chemoradiotherapy for locally advanced rectal cancer (RAPIDO): a randomised phase 3 trial. *Lancet Oncol,* ***22****: 29-42*.
21. Pettersson D, Lörinc E, Holm T, Iversen H, Cedermark B, Glimelius B, Martling A (2015) Tumour regression in the randomized Stockholm III trial of radiotherapy regimens for rectal cancer. *Br J Surg*, ***102****: 972-978*.
22. Chen G, Jiang S, Kong L, Yang T, Sun X, Xu T, Fan L, Xie Q, Zhao H (2025) Radiotherapy for digestive tract tumors: an overview of different approaches, side effects, and recent advances. *Int J Radiat Res,* ***23****: 757-769*.
23. Yalçın B, Ökten B, Tuncay E, Mermut Ö (2024) Hemoglobin level as a prognostic factor of neoadjuvant chemoradiotherapy in patients with rectal cancer. *Istanb Med J*, ***25****: 293-297*.
24. Gao HQ, Wan YZ, Bu XM, Fan XY, *et al.* (2021) How to deal with the relationship between hypoxia and radiotherapy in the hypofractionated radiotherapy era? *Int J Radiat Res,* ***19****: 759-769*.
25. Intven MPW, de Mol van Otterloo SR, Mook S, Doornaert PAH, *et al.* (2021) Online adaptive MR-guided radiotherapy for rectal cancer: feasibility of the workflow on a 1.5-T MR-linac. *Radiother Oncol,* ***154****: 172-178*.

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