Journal of Surgical Radiology

Site: https://journalsurgrad.com/

ISSN Print 2156-213X| ISSN Online: 2156-4566 Volume: 05 Issue: 07 Open Access

Research Article

MRI-based Assessment of Tumor Downstaging and Regression after Neoadjuvant Chemo-radiotherapy in Locally Advanced Rectal Cancer: A Prospective Analysis using mr-TRG

Dr. Sairah Elizabeth Benny[1]*, Dr. Natarajan V[2], Dr. S. B. Nishitha[3]

[1] Radiation Oncologist, Department of Radiation Oncology, Apollo Hospitals, Bengaluru, Karnataka, India.

[2] Senior Consultant, Department of Radiation Oncology, Apollo Hospitals, Bannerghatta Road, Bengaluru, Karnataka, India.

[3] Assistant Professor, Department of Pharmacology, Shri Atal Bihari Vajpayee Medical College and Research Institute, Bengaluru, Karnataka, India.

*Corresponding Author

Dr. Sairah Elizabeth Benny
Email:
bethbenny94@gmail.com

Article History
Received: 20-06-2026
Revised: 15-07-2026
Accepted: 20-07-2026
Published: 30-07-2026

Citations:
Benny SE, Natarajan V, Nishitha SB. MRI-based assessment of tumor downstaging and regression after neoadjuvant chemo-radiotherapy in locally advanced rectal cancer: a prospective analysis using mr-TRG. J Surg Radiol, V5 (7) 412-422

Abstract: ***Introduction:*** High-resolution pelvic MRI plays a pivotal role in staging and restaging of locally advanced rectal cancer (LARC). MRI-detected extramural venous invasion (mrEMVI) and tumour deposits (TDs) are established adverse prognostic factors, but their response to neoadjuvant chemo-radiotherapy (NACRT) is less well characterised. This study assessed the radiological response of the primary tumour, mrEMVI and TDs to NACRT using the mrTRG and mr-vTRG scoring systems. **Methods:** Thirty-three consecutive patients with cT3 or cT4 rectal adenocarcinoma underwent baseline pelvic MRI, long-course NACRT (50.4 Gy in 28 fractions with concurrent capecitabine 650 mg/m² BID) and restaging MRI six weeks after treatment completion. Changes in T- and N-stage, cranio-caudal length, circumferential extent, mesorectal nodes, mrEMVI and TDs were analysed using Wilcoxon signed-rank and Stuart-Maxwell tests. **Results:** The mean age was 55.94 years; 54.5% were male. Baseline mrEMVI was present in 42.4% and TDs in 30.3%. After NACRT, mean cranio-caudal length reduced by 55.5% and circumferential extent by 31.1% ($p<0.001$ each). T-stage downstaging occurred in 87.9%, nodal downstaging in 81.8% and prognostic group improvement in 81.8% of patients. Among EMVI-positive patients, 87.6% achieved a favourable mr-vTRG score (1 or 2), and 60% of TD-positive patients achieved complete regression. Overall mrTRG demonstrated good response (score 2) in 24.2% and moderate response (score 3) in 66.7% of patients. **Conclusions:** Long-course NACRT with concurrent capecitabine produces significant downstaging and radiological regression of high-risk MRI features in LARC. Systematic assessment of EMVI and TDs on pre- and post-treatment MRI using the mr-vTRG system helps to identify poor responders who may benefit from treatment intensification.

Keywords: Rectal cancer; MRI; Extramural venous invasion; Tumour deposits; Neoadjuvant chemo-radiotherapy; mr-vTRG; mrTRG.

INTRODUCTION

Colorectal cancer (CRC) is one of the most common malignancies worldwide, and rectal cancer accounts for a substantial proportion of this burden. According to GLOBOCAN 2022, an estimated 729,833 new rectal cancer cases and 343,817 deaths occurred globally, with 70,038 new cases and 40,993 deaths reported from India alone.[1] The incidence exhibits marked geographical variation, with the highest rates in Australia, New Zealand and Europe, and the lowest in Southern Asia and sub-Saharan Africa.[2] Although screening and lifestyle modifications have reduced incidence in some Western populations, the overall burden remains considerable, and approximately 20% of patients present with metastatic disease at diagnosis.[3]

Rectal cancer typically follows an adenoma–carcinoma sequence driven by cumulative genetic and epigenetic alterations.[4] Adenocarcinoma represents nearly 90% of all colorectal malignancies.[5] Modifiable risk factors include obesity, red and processed meat intake, tobacco and alcohol use, whereas physical activity, fiber-rich diet, aspirin and NSAID use appear protective.[6] Inflammatory bowel disease, hereditary syndromes and a personal or family history of adenomatous polyps significantly increase the lifetime risk.[7]

The management of locally advanced rectal cancer (LARC) has evolved substantially since William Ernest Miles' description of abdominoperineal resection in 1908.[8] Total mesorectal excision (TME), introduced by Heald in 1982, remains the surgical cornerstone, and multimodality treatment combining neoadjuvant chemo-radiotherapy (NACRT) with TME has become the standard of care for cT3–T4 disease.[9,10] Preoperative chemo-radiotherapy improves local control, downstages the tumour, facilitates sphincter preservation and reduces local recurrence rates.[11,12]

High-resolution pelvic magnetic resonance imaging (MRI) is the preferred modality for local staging and restaging owing to its superior soft-tissue resolution.[13] Beyond T- and N-classification, MRI identifies several key prognostic descriptors including circumferential resection margin (CRM) involvement, extramural

venous invasion (EMVI) and tumour deposits (TDs).[14] EMVI, first characterised on MRI by Brown et al., is defined as serpiginous extension of intermediate tumour signal within a perirectal vascular structure beyond the muscularis propria.[15] Its reported prevalence ranges from 9% to more than 50%, and MRI-detected EMVI (mrEMVI) is an independent predictor of distant metastasis and reduced disease-free survival.[16,17]

Tumour deposits are discrete foci of tumour within pericolic or perirectal adipose tissue without histological evidence of residual lymph node structure, vascular or neural elements.[18] They frequently coexist with EMVI and adversely influence overall and disease-free survival.[19,20] MRI-based tumour regression grade (mrTRG) evaluates the proportion of residual tumour signal versus fibrosis on post-treatment T2-weighted imaging, while an analogous mr-vTRG score has been proposed to quantify EMVI regression after NACRT.[21,22] Complete or near-complete replacement of intravascular tumour signal by fibrosis (mr-vTRG 1–2) has been associated with significantly improved oncological outcomes.[23]

Despite the growing recognition of mrEMVI and TDs as prognostic biomarkers, systematic evaluation of their response to NACRT in Indian patients with LARC is limited. The present study was undertaken to identify EMVI and TDs in cT3 and cT4 rectal cancer patients on baseline MRI and to quantify their radiological response using the mrTRG and mr-vTRG scoring systems on restaging MRI following long-course NACRT, with the aim of identifying poor responders who may benefit from treatment intensification.

MATERIALS AND METHODS

Study Design and Setting

This prospective analytical study was conducted at the Department of Radiation Oncology, Apollo Hospital, Bengaluru, India, between July 2022 and January 2024. The study protocol was approved by the Institutional Ethics Committee, and written informed consent was obtained from all participants prior to enrolment.

Sample Size

Sample size was estimated using the proportion of good response (defined as reduced distant metastasis after NACRT) of 25% reported by Schaap et al.,[23] with a 95% confidence level and 15% absolute precision, yielding a minimum required sample size of 33 patients.

Patient Selection

Consecutive patients aged 18 years and above with histopathologically proven, non-metastatic, locally advanced (cT3 or cT4) rectal adenocarcinoma planned for long-course NACRT were included. Patients with synchronous distant metastases, those undergoing postoperative adjuvant radiotherapy and those without a pre-treatment MRI were excluded.

MRI Protocol and Interpretation

All patients underwent a baseline high-resolution pelvic MRI performed on a 1.5-T or 3-T system with dedicated pelvic phased-array coils. The standard protocol included high-resolution T2-weighted turbo spin-echo sequences in axial, sagittal and oblique-axial planes perpendicular to the tumour axis, together with diffusion-weighted imaging. Two experienced radiologists interpreted all studies independently, and discrepancies were resolved by consensus.

The following MRI parameters were recorded on both pre- and post-treatment scans: tumour location (upper, mid or lower rectum), cranio-caudal length, circumferential extent expressed as clock-face hours, T-stage, number of mesorectal and extramesorectal nodes, involvement of the mesorectal fascia, presence of EMVI and TDs. EMVI was diagnosed and scored on a 5-point scale (0–4) according to the criteria proposed by Smith et al.,[16] and TDs were defined per the AJCC 8th edition guidelines.[24]

Neoadjuvant Chemo-radiotherapy

All patients received concurrent NACRT consisting of external beam radiotherapy 50.4 Gy delivered in 28 fractions of 1.8 Gy over five and a half weeks using three-dimensional conformal radiotherapy (3DCRT), intensity-modulated radiotherapy (IMRT), image-guided radiotherapy (IGRT) or volumetric modulated arc (RapidArc) techniques. Concurrent oral capecitabine was administered at a dose of 650 mg/m² twice daily, five days per week during radiotherapy.[25,26]

Response Assessment

A restaging MRI of the pelvis using an identical protocol was performed six weeks after completion of NACRT. Response of the primary tumour was assessed using the 5-point mrTRG scale,[21] and EMVI response was graded using the mr-vTRG system,[22] in which score 1 represents complete replacement of intravascular tumour signal by fibrosis, score 2 represents 50–75% fibrosis, score 3 represents 25–49% fibrosis, score 4 represents less than 25% fibrosis, and score 5 represents no discernible regression. TD response was classified as complete or significant regression on the basis of nodule size and signal characteristics.

Statistical Analysis

Statistical analysis was performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarised as mean ± standard deviation (SD) and median with interquartile range (IQR); categorical variables were expressed as frequencies and percentages. Because most continuous variables were not normally distributed, paired comparisons between pre- and post-treatment values were performed with the Wilcoxon signed-rank test. Changes in ordinal

categorical variables (T-stage, N-stage, prognostic group, EMVI status, TD status) were assessed with the Stuart-Maxwell test. A two-sided p-value <0.05 was considered statistically significant.

RESULTS

Patient Characteristics

A total of 33 patients with cT3 or cT4 rectal adenocarcinoma completed NACRT and had paired pre- and post-treatment MRI available for analysis. The demographic and baseline clinical characteristics are summarised in Table 1. The mean age was 55.94 ± 14.03 years, with 54.5% of the cohort in the sixth or seventh decade of life. Three patients were at the extremes of age, including one patient in the 20–29-year group and two patients aged over 80 years, all of whom were female. There was a slight male predominance (18/33, 54.5%).

The tumour was located in the low rectum in 8 patients (24.2%), mid-and-low rectum in 8 (24.2%), mid rectum in 7 (21.2%), upper-and-mid rectum in 5 (15.2%) and upper rectum in 5 (15.2%). The mean pre-treatment cranio-caudal length was 5.51 ± 1.30 cm and the mean circumferential extent was 8.70 ± 2.48 clock-hours. At baseline, 22 patients (66.7%) were staged cT3, 10 (30.3%) cT4a and 1 (3.0%) cT4b. All patients had nodal involvement, with 39.4% harbouring cN2b disease. According to the AJCC 8th edition, 19 patients (57.6%) were classified as stage IIIB and 14 (42.4%) as stage IIIC.

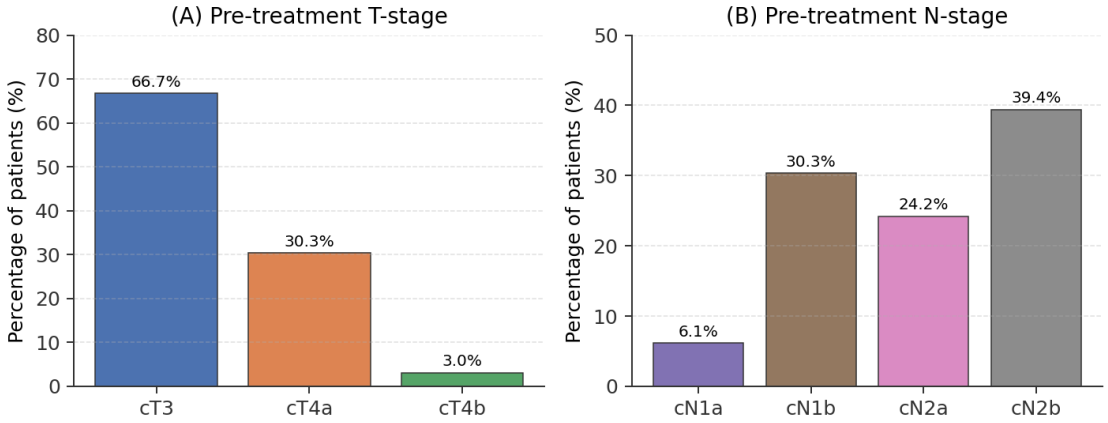

Figure 1. Distribution of pre-treatment (A) T-stage and (B) N-stage across the study cohort (n = 33).

MRI-detected EMVI was present in 14 patients (42.4%), equivocal in 3 (9.1%) and absent in 16 (48.5%). The mean pre-treatment EMVI score was 1.61 ± 1.66. Tumour deposits were identified in 10 patients (30.3%), extramesorectal nodes in 10 (30.3%) and involvement of the mesorectal fascia in 9 (27.3%). Baseline MRI characteristics are summarised in Table 1.

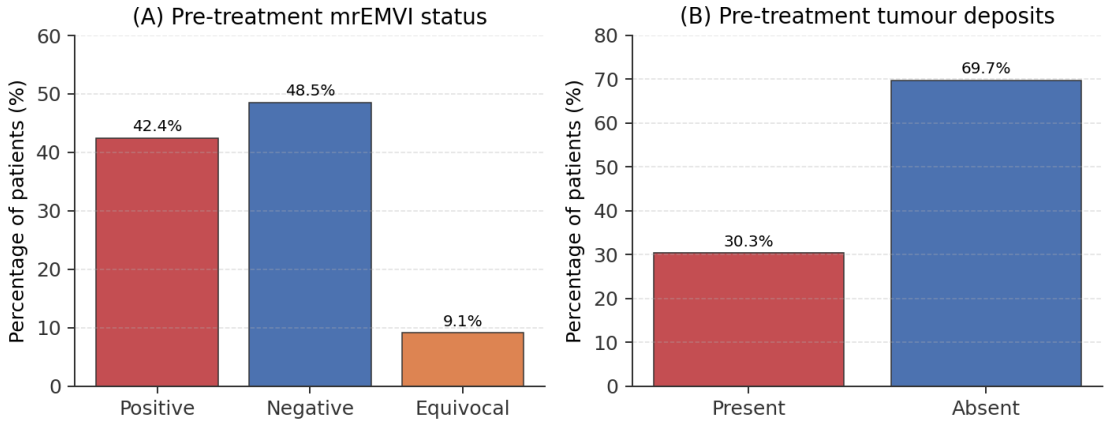

Figure 2. Baseline distribution of (A) MRI-detected extramural venous invasion (mrEMVI) and (B) tumour deposits.

Table 1. Baseline demographic, clinical and MRI characteristics of the study population (n = 33).

Parameter	Value
Age (years), mean ± SD	55.94 ± 14.03
Male, n (%)	18 (54.5)

Female, n (%)	15 (45.5)
Tumour location, n (%)	
Low rectum	8 (24.2)
Mid + low rectum	8 (24.2)
Mid rectum	7 (21.2)
Upper + mid rectum	5 (15.2)
Upper rectum	5 (15.2)
Cranio-caudal length (cm), mean ± SD	5.51 ± 1.30
Circumferential extent (clock-hours), mean ± SD	8.70 ± 2.48
cT3, n (%)	22 (66.7)
cT4a, n (%)	10 (30.3)
cT4b, n (%)	1 (3.0)
cN1a, n (%)	2 (6.1)
cN1b, n (%)	10 (30.3)
cN2a, n (%)	8 (24.2)
cN2b, n (%)	13 (39.4)
Prognostic group IIIB, n (%)	19 (57.6)
Prognostic group IIIC, n (%)	14 (42.4)
MRI-detected EMVI positive, n (%)	14 (42.4)
MRI-detected EMVI equivocal, n (%)	3 (9.1)
Mean EMVI score	1.61 ± 1.66
Tumour deposits, n (%)	10 (30.3)
Mesorectal fascia involvement, n (%)	9 (27.3)
Mesorectal nodes (mean ± SD)	5.73 ± 2.99
Extramesorectal nodes, n (%)	10 (30.3)

Treatment Details

All patients completed the planned 50.4 Gy in 28 fractions with concurrent capecitabine. IMRT and IGRT were each employed in 14 patients (42.4%), RapidArc in 3 (9.1%) and 3DCRT in 2 (6.1%). No patient discontinued treatment because of toxicity.

Change in Quantitative MRI Parameters

Comparison of pre- and post-treatment MRI parameters is presented in Table 2. The mean cranio-caudal length decreased from 5.51 ± 1.30 cm to 2.51 ± 1.17 cm, representing a mean absolute reduction of 3.00 cm (mean percentage reduction 55.5%; Wilcoxon V = 561.0, p<0.001). The mean circumferential extent decreased from 8.70 ± 2.48 to 5.67 ± 2.03 clock-hours (mean reduction 31.1%; Wilcoxon V = 412.0, p<0.001). The mean number of mesorectal nodes fell from 5.73 ± 2.99 to 1.94 ± 2.30, a mean reduction of 72.3% (Wilcoxon V = 496.0, p<0.001).

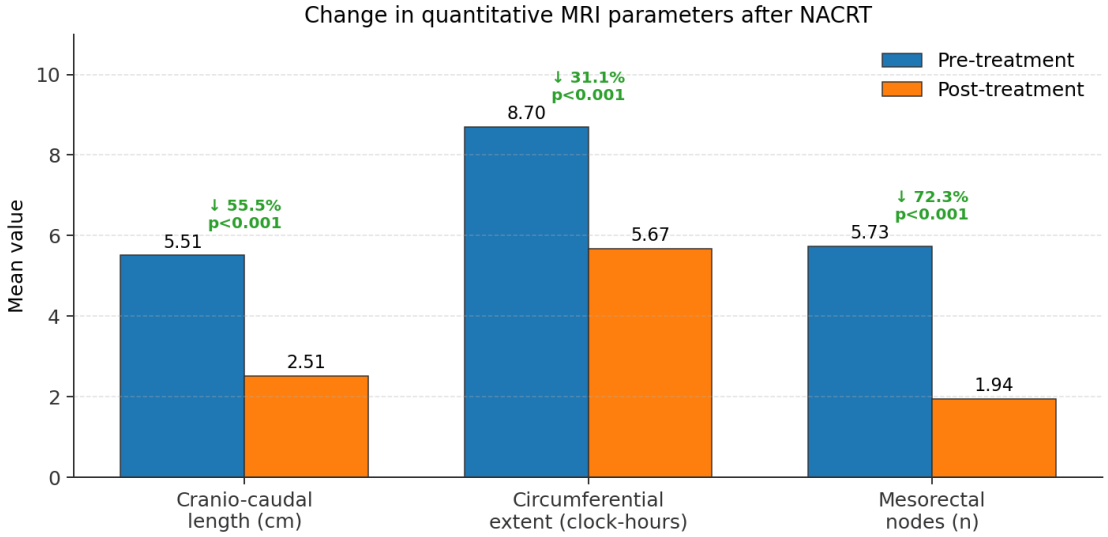

Figure 3. Change in quantitative MRI parameters (cranio-caudal length, circumferential extent and number of mesorectal nodes) between pre- and post-treatment scans. All comparisons were statistically significant (Wilcoxon signed-rank test).

Table 2. Change in quantitative MRI parameters between pre- and post-treatment scans.

Parameter	Pre-treatment mean ± SD	Post-treatment mean ± SD	Mean % change	p-value
Cranio-caudal length (cm)	5.51 ± 1.30	2.51 ± 1.17	-55.5	<0.001
Circumferential extent (clock-hours)	8.70 ± 2.48	5.67 ± 2.03	-31.1	<0.001
Mesorectal nodes (number)	5.73 ± 2.99	1.94 ± 2.30	-72.3	<0.001

T- and N-stage Downstaging

T-stage downstaging was observed in 29 of 33 patients (87.9%). Twenty patients (60.6%) migrated from cT3 to ypT2, 8 patients (24.2%) migrated from cT4a to ypT3, and the single cT4b patient migrated to ypT4a. The overall change in T-stage was highly significant (Stuart-Maxwell $\chi^2 = 29.000$, $p<0.001$). Post-treatment T-stage distribution was ypT2 in 60.6%, ypT3 in 30.3% and ypT4a in 9.1% (Table 3).

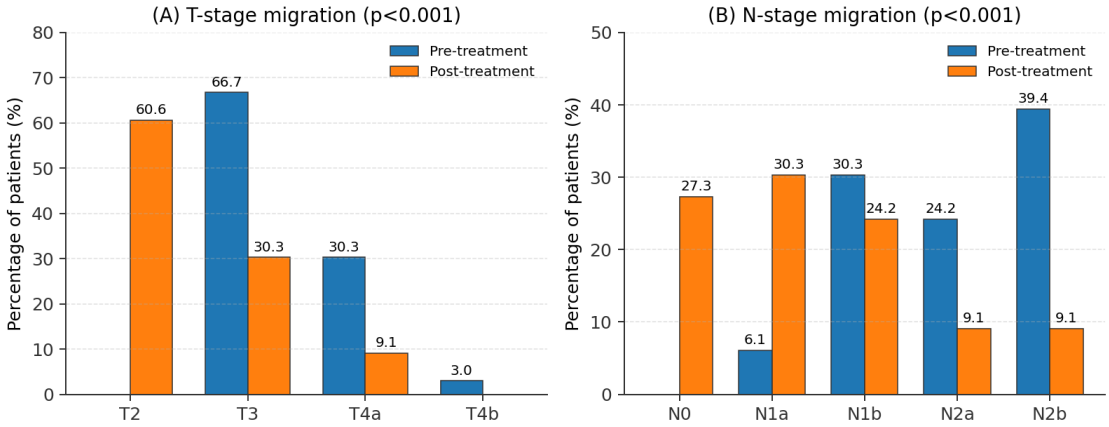

Figure 4. Distribution of (A) T-stage and (B) N-stage before and after neoadjuvant chemo-radiotherapy. Both changes were highly statistically significant on the Stuart-Maxwell test.

Nodal downstaging was equally impressive. Nine patients (27.3%) achieved a complete nodal response (ypN0), while a further 30.3% and 24.2% migrated to ypN1a and ypN1b respectively. Only 6 patients (18.2%) remained ypN2 (Stuart-Maxwell $\chi^2 = 24.827$, $p<0.001$). Consequently, the AJCC prognostic group improved in 27 of 33 patients (81.8%): 7 patients (21.2%) achieved stage I disease, 12 (36.4%) stage IIIA, 10 (30.3%) stage IIIB and only 2 (6.1%) remained stage IIIC (Stuart-Maxwell $\chi^2 = 25.037$, $p<0.001$).

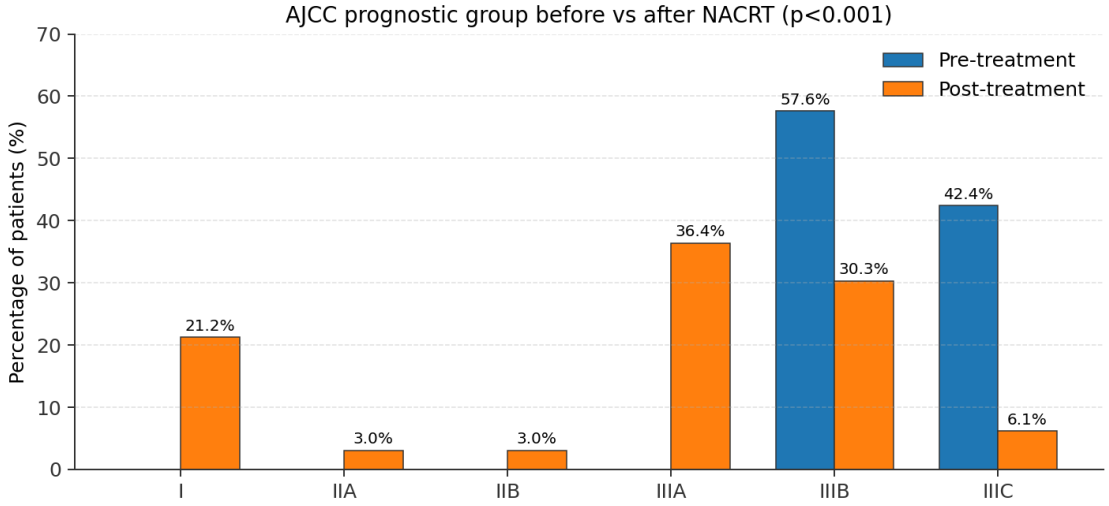

Figure 5. AJCC prognostic group distribution before and after neoadjuvant chemo-radiotherapy (Stuart-Maxwell $\chi^2 = 25.037$, $p<0.001$).

Table 3. Distribution of T-stage, N-stage and AJCC prognostic group before and after neoadjuvant chemo-radiotherapy.

Category	Pre-treatment n (%)	Post-treatment n (%)	p-value
T2	0 (0)	20 (60.6)	<0.001
T3	22 (66.7)	10 (30.3)	
T4a	10 (30.3)	3 (9.1)	
T4b	1 (3.0)	0 (0)	
N0	0 (0)	9 (27.3)	<0.001
N1a	2 (6.1)	10 (30.3)	
N1b	10 (30.3)	8 (24.2)	
N2a	8 (24.2)	3 (9.1)	
N2b	13 (39.4)	3 (9.1)	
Stage I	0 (0)	7 (21.2)	<0.001
Stage IIA	0 (0)	1 (3.0)	
Stage IIB	0 (0)	1 (3.0)	
Stage IIIA	0 (0)	12 (36.4)	
Stage IIIB	19 (57.6)	10 (30.3)	
Stage IIIC	14 (42.4)	2 (6.1)	

Response of Extramural Venous Invasion (mr-vTRG)

Among the 16 patients with baseline mrEMVI (positive or equivocal), 8 (50.0%) demonstrated partial reduction of the venous tumour signal, 7 (43.8%) had complete radiological resolution and only 1 patient (6.2%) had persistent EMVI on restaging (Stuart-Maxwell $\chi^2 = 15.000$, $p = 0.002$). Applying the mr-vTRG scoring system, 7 patients (43.8%) achieved score 1 (complete replacement of intravascular tumour signal by fibrosis) and 7 (43.8%) achieved score 2 (50–75% fibrosis); only 1 patient each (6.2%) scored 3 or 4, and no patient scored 5. Thus 87.6% of EMVI-positive patients were classified as good responders (mr-vTRG 1–2) (Table 4).

Response of Tumour Deposits

Of the 10 patients with tumour deposits at baseline, 6 (60.0%) showed complete regression and 4 (40.0%) showed significant partial regression on the post-treatment MRI (Stuart-Maxwell $\chi^2 = 10.000$, $p = 0.019$). No patient developed new tumour deposits during treatment.

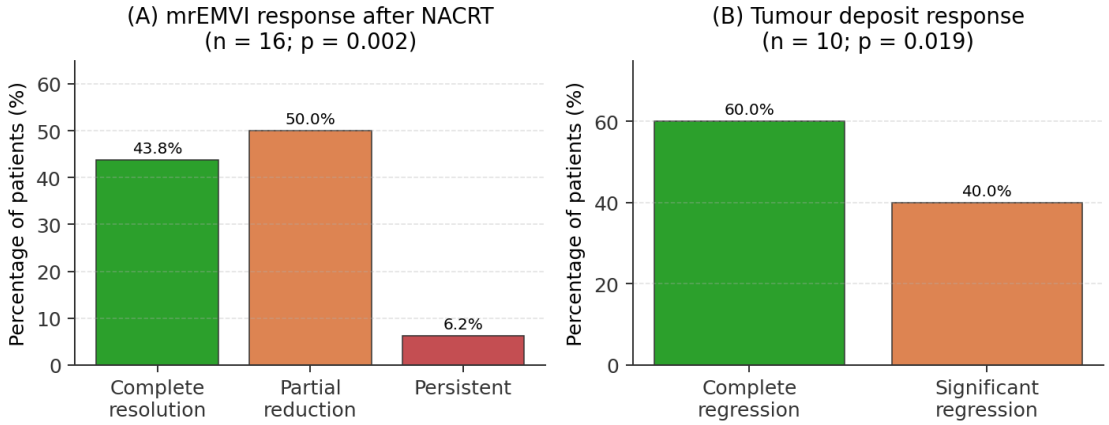

Figure 6. Post-treatment response of (A) MRI-detected extramural venous invasion (mrEMVI) among the 16 baseline EMVI-positive/equivocal patients and (B) tumour deposits among the 10 baseline TD-positive patients.

Overall Tumour Regression (mrTRG)

Overall tumour regression assessed by mrTRG demonstrated that 8 patients (24.2%) achieved a good response (mrTRG score 2), 22 (66.7%) a moderate response (mrTRG score 3) and 3 (9.1%) a slight response (mrTRG score 4). No patient was classified as mrTRG 5 (no response) (Table 4).

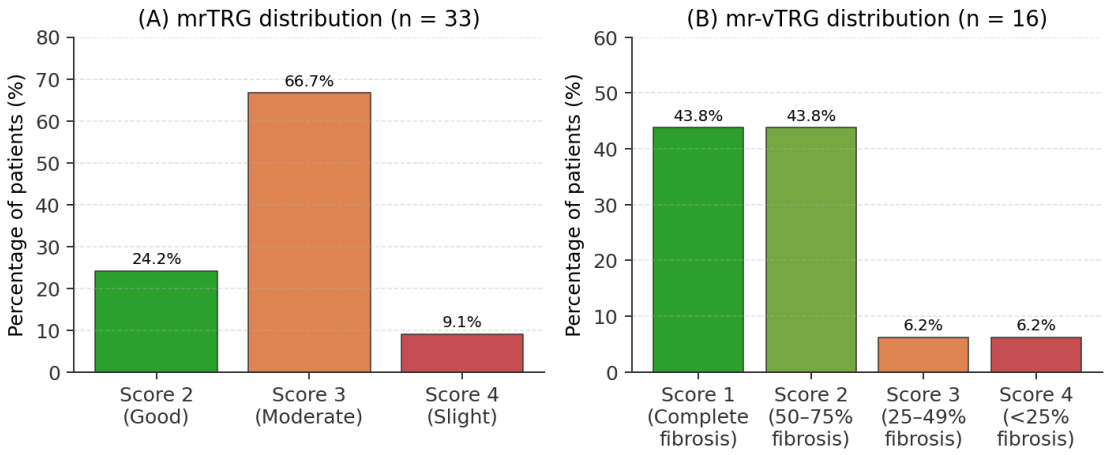

Figure 7. Distribution of (A) mrTRG scores across the whole cohort (n = 33) and (B) mr-vTRG scores among the 16 EMVI-positive patients after neoadjuvant chemo-radiotherapy.

Table 4. Distribution of mrTRG (n = 33) and mr-vTRG (n = 16 EMVI-positive patients) scores after neoadjuvant chemo-radiotherapy.

Score	Interpretation	n (%)	95% CI
mrTRG 2	Good response	8 (24.2)	11.7–42.6
mrTRG 3	Moderate response	22 (66.7)	48.1–81.4
mrTRG 4	Slight response	3 (9.1)	2.4–25.5
mr-vTRG 1	Complete fibrosis	7 (43.8)	20.8–69.4
mr-vTRG 2	50–75% fibrosis	7 (43.8)	20.8–69.4
mr-vTRG 3	25–49% fibrosis	1 (6.2)	0.3–32.3
mr-vTRG 4	<25% fibrosis	1 (6.2)	0.3–32.3

DISCUSSION

The present prospective study demonstrates that long-course NACRT with concurrent capecitabine produces substantial and statistically significant downstaging of locally advanced rectal cancer, with particularly encouraging response of high-risk MRI features such as EMVI and TDs. Approximately 88% of patients with baseline mrEMVI achieved a favourable mr-vTRG score (1 or 2), 60% of patients with baseline TDs achieved complete radiological regression, and 81.8% of patients experienced a reduction in AJCC prognostic group.

Our cohort demographics are consistent with published Indian and international data. Rectal cancer classically affects patients in the sixth and seventh decades, but a rising incidence in patients below 40 years has been reported worldwide over the past two decades.[27,28] In our study, one patient was aged 20–29 years, mirroring the growing burden of early-onset colorectal cancer described in Indian population-based cancer registries.[29] The male preponderance (54.5%) is also in keeping with reported Indian age-adjusted incidence rates of 5.17 per 100,000 in men versus 4.3 per 100,000 in women.[29]

Our baseline stage distribution (66.7% cT3 and 33.3% cT4) is comparable to that reported by Dar et al. (54.4% cT3) in a north Indian series and by Pai et al. (46.3% cT4) in a western Indian cohort.[30,31] A pre-treatment mrEMVI prevalence of 42.4% in our study falls within the previously reported range of 9–58%,[16,17,23] and closely mirrors the 49.5% prevalence reported by Chandramohan et al. in a large Indian cohort of 297 LARC patients.[32] The 30.3% baseline TD prevalence in our study is also consistent with the meta-analytic estimate of 22% (range 5–42%) reported by Nagtegaal et al. across 10,106 patients from 17 studies.[33]

The prognostic weight of mrEMVI has been repeatedly demonstrated. In a large retrospective series of 277 cT3/T4 patients, Schaap et al. reported a 5-year distant metastasis rate of 45.2% in mrEMVI-positive patients with TDs versus 25.7% in mrEMVI-negative patients, and importantly, showed that good post-treatment mr-vTRG responders (score 1–2) had distant metastasis rates identical to baseline mrEMVI-negative patients.[23] Chand et al. independently confirmed the value of mr-vTRG, reporting a 3-year disease-free survival of 87.8% in patients with ≥50% fibrosis of mrEMVI compared with 45.8% in patients with less than 50% fibrosis ($p<0.0001$), together with a hazard ratio of 5.7 for recurrence in poor responders.[21] Our observation that 87.6% of EMVI-positive patients achieved mr-vTRG 1–2 therefore predicts a favourable oncological outcome and is comparable to the response rates observed in these landmark series.

Similarly, Smith et al. reported a 3-year relapse-free survival of 74% in mrEMVI-negative patients versus 34% in EMVI-positive patients,[16] while a meta-analysis of six studies by Siddiqui et al. demonstrated a pooled

relative risk of 3.91 for metastatic disease in mrEMVI-positive rectal cancer.[34] A subsequent systematic review and meta-analysis of 26 studies by Lord et al. confirmed a strong association between TDs and both EMVI and adverse survival.[19]

Beyond static prognostication, dynamic assessment of response on restaging MRI has emerged as an important prognostic biomarker. Chandramohan et al. reported significant reductions in EMVI (49.5% to 31.3%), TDs (47.5% to 31.6%) and mesorectal nodal disease (61.1% to 38.1%) after NACRT, with EMVI, TDs and pelvic side-wall involvement retaining independent adverse prognostic significance on both staging and restaging MRI.[32] Prampolini et al. and Lee et al. have similarly demonstrated that mrEMVI regression after chemo-radiotherapy correlates with improved survival, whereas persistent EMVI predicts early recurrence.[35,36]

Our capecitabine-based radio-sensitisation regimen is supported by robust level 1 evidence. The German AIO/ARO-04 phase III non-inferiority trial by Hofheinz et al. demonstrated that concurrent capecitabine was non-inferior to infusional 5-fluorouracil, with a 5-year overall survival of 76% versus 67% ($p = 0.0004$) and a reduced incidence of distant metastases in the capecitabine arm.[26] The NSABP R-04 trial also confirmed equivalent efficacy of capecitabine and 5-FU.[25] A meta-analysis of 14 randomised trials by Cammà et al. concluded that preoperative radiotherapy significantly reduces overall mortality, cancer-specific mortality and local recurrence in resectable rectal cancer.[37]

From a management perspective, our findings have two clinically important implications. First, the high rate of favourable radiological response confirms that long-course NACRT with capecitabine, delivered predominantly using IMRT/IGRT techniques, is a highly effective downstaging strategy in an Indian tertiary-care setting. Second, and perhaps more importantly, the identification of a small subset of patients (approximately 12%) with poor EMVI regression (mr-vTRG 3–4) and 40% of patients with only partial regression of TDs identifies a clinically actionable 'high-risk' group. These patients may benefit from treatment intensification strategies such as total neoadjuvant therapy (TNT) incorporating consolidation or induction FOLFOX/CAPOX, radiotherapy dose escalation, or closer post-treatment surveillance, as advocated by the RAPIDO and PRODIGE-23 trials.[38,39]

Several limitations of the current study warrant consideration. The sample size, although statistically adequate for the primary end-point, is modest, and the short follow-up period does not permit assessment of long-term outcomes such as overall and disease-free survival. Histopathological correlation of MRI-detected regression, which represents the gold standard, was not performed in this analysis. Additionally, inter-observer variability in reporting mrTRG and mr-vTRG, although minimised by consensus reporting, remains an inherent limitation of any imaging-based grading system.[40] Larger multi-centre studies with prospective histopathological validation and long-term survival follow-up are needed to confirm these observations and to formally integrate mrEMVI and TD response into treatment-decision algorithms.

CONCLUSION

In cT3 and cT4 locally advanced rectal cancer, long-course neoadjuvant chemo-radiotherapy with concurrent capecitabine produces substantial and statistically significant downstaging of the primary tumour, mesorectal nodes, extramural venous invasion and tumour deposits, as assessed on restaging MRI. Nearly 88% of EMVI-positive patients achieved a good radiological response (mr-vTRG 1–2), 60% of patients with tumour deposits demonstrated complete regression, and 81.8% experienced a reduction in AJCC prognostic group. High-resolution pelvic MRI performed before and after NACRT should be considered mandatory in all patients with locally advanced rectal cancer, with detailed assessment of EMVI and TDs using the mr-vTRG scoring system. Poor EMVI/TD responders represent a clinically identifiable high-risk cohort in whom treatment intensification, closer surveillance and consideration of total neoadjuvant therapy strategies may improve oncological outcomes.

REFERENCES

1. Ferlay J, Ervik M, Lam F, Laversanne M, Colombet M, Mery L, et al. Global Cancer Observatory: Cancer Today. Lyon, France: International Agency for Research on Cancer; 2024. Available from: https://gco.iarc.who.int/today.
2. Morgan E, Arnold M, Gini A, Lorenzoni V, Cabasag CJ, Laversanne M, et al. Global burden of colorectal cancer in 2020 and 2040: incidence and mortality estimates from GLOBOCAN. Gut. 2023;72(2):338–44.
3. Ciardiello F, Ciardiello D, Martini G, Napolitano S, Tabernero J, Cervantes A. Clinical management of metastatic colorectal cancer in the era of precision medicine. CA Cancer J Clin. 2022;72(4):372–401.
4. Vogelstein B, Fearon ER, Hamilton SR, Kern SE, Preisinger AC, Leppert M, et al. Genetic alterations during colorectal-tumor development. N Engl J Med. 1988;319(9):525–32.
5. Fleming M, Ravula S, Tatishchev SF, Wang HL. Colorectal carcinoma: pathologic aspects. J Gastrointest Oncol. 2012;3(3):153–73.
6. Dekker E, Tanis PJ, Vleugels JL, Kasi PM, Wallace MB. Colorectal cancer. Lancet. 2019;394(10207):1467–80.
7. Cappell MS. Pathophysiology, clinical presentation, and management of colon cancer. Gastroenterol Clin North Am. 2008;37(1):1–24.

8. Miles WE. A method of performing abdomino-perineal excision for carcinoma of the rectum and of the terminal portion of the pelvic colon. Lancet. 1908;172(4451):1812–3.
9. Heald RJ, Husband EM, Ryall RD. The mesorectum in rectal cancer surgery—the clue to pelvic recurrence? Br J Surg. 1982;69(10):613–6.
10. Heald RJ, Moran BJ, Ryall RD, Sexton R, MacFarlane JK. Rectal cancer: the Basingstoke experience of total mesorectal excision, 1978–1997. Arch Surg. 1998;133(8):894–9.
11. Feeney G, Sehgal R, Sheehan M, Hogan A, Regan M, Joyce M, et al. Neoadjuvant radiotherapy for rectal cancer management. World J Gastroenterol. 2019;25(33):4850–69.
12. Sauer R, Becker H, Hohenberger W, Rödel C, Wittekind C, Fietkau R, et al. Preoperative versus postoperative chemoradiotherapy for rectal cancer. N Engl J Med. 2004;351(17):1731–40.
13. Fernandes MC, Gollub MJ, Brown G. The importance of MRI for rectal cancer evaluation. Surg Oncol. 2022;43:101739.
14. Horvat N, Carlos Tavares Rocha C, Clemente Oliveira B, Petkovska I, Gollub MJ. MRI of rectal cancer: tumor staging, imaging techniques, and management. Radiographics. 2019;39(2):367–87.
15. Brown G, Radcliffe AG, Newcombe RG, Dallimore NS, Bourne MW, Williams GT. Preoperative assessment of prognostic factors in rectal cancer using high-resolution magnetic resonance imaging. Br J Surg. 2003;90(3):355–64.
16. Smith NJ, Barbachano Y, Norman AR, Swift RI, Abulafi AM, Brown G. Prognostic significance of magnetic resonance imaging-detected extramural vascular invasion in rectal cancer. Br J Surg. 2008;95(2):229–36.
17. Sohn B, Lim JS, Kim H, Myoung S, Choi J, Kim NK, et al. MRI-detected extramural vascular invasion is an independent prognostic factor for synchronous metastasis in patients with rectal cancer. Eur Radiol. 2015;25(5):1347–55.
18. Ueno H, Nagtegaal ID, Quirke P, Sugihara K, Ajioka Y. Tumor deposits in colorectal cancer: refining their definition in the TNM system. Ann Gastroenterol Surg. 2023;7(2):225–35.
19. Lord AC, D'Souza N, Pucher PH, Moran BJ, Abulafi AM, Wotherspoon A, et al. Significance of extranodal tumour deposits in colorectal cancer: a systematic review and meta-analysis. Eur J Cancer. 2017;82:92–102.
20. Goldstein NS, Turner JR. Pericolonic tumor deposits in patients with T3N+ M0 colon adenocarcinomas: markers of reduced disease-free survival and intra-abdominal metastases. Cancer. 2000;88(10):2228–38.
21. Chand M, Swift RI, Tekkis PP, Chau I, Brown G. Extramural venous invasion is a potential imaging predictive biomarker of neoadjuvant treatment in rectal cancer. Br J Cancer. 2014;110(1):19–25.
22. Tripathi P, Rao SX, Zeng MS. Clinical value of MRI-detected extramural venous invasion in rectal cancer. J Dig Dis. 2017;18(1):2–12.
23. Schaap DP, Voogt EL, Burger JW, Cnossen JS, Creemers GJ, van Lijnschoten I, et al. Prognostic implications of MRI-detected EMVI and tumor deposits and their response to neoadjuvant therapy in cT3 and cT4 rectal cancer. Int J Radiat Oncol Biol Phys. 2021;111(3):816–25.
24. Amin MB, Edge SB, Greene FL, Byrd DR, Brookland RK, Washington MK, et al., editors. AJCC Cancer Staging Manual. 8th ed. New York: Springer; 2017.
25. Roh MS, Yothers GA, O'Connell MJ, Beart RW, Pitot HC, Shields AF, et al. The impact of capecitabine and oxaliplatin in the preoperative multimodality treatment in patients with carcinoma of the rectum: NSABP R-04. J Clin Oncol. 2011;29(15 Suppl):3503.
26. Hofheinz RD, Wenz F, Post S, Matzdorff A, Laechelt S, Hartmann JT, et al. Chemoradiotherapy with capecitabine versus fluorouracil for locally advanced rectal cancer: a randomised, multicentre, non-inferiority, phase 3 trial. Lancet Oncol. 2012;13(6):579–88.
27. Siegel RL, Torre LA, Soerjomataram I, Hayes RB, Bray F, Weber TK, et al. Global patterns and trends in colorectal cancer incidence in young adults. Gut. 2019;68(12):2179–85.
28. Vuik FE, Nieuwenburg SA, Bardou M, Lansdorp-Vogelaar I, Dinis-Ribeiro M, Bento MJ, et al. Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years. Gut. 2019;68(10):1820–6.
29. Asthana S, Khenchi R, Labani S. Incidence of colorectal cancers in India: a review from population-based cancer registries. Curr Med Res Pract. 2021;11(2):91–6.
30. Dar RA, Chowdri NA, Parray FQ, Shaheen F, Wani SH, Mushtaque M. Pre-operative staging of rectal cancer using multi-detector row computed tomography with multiplanar reformations: single center experience. Indian J Cancer. 2014;51(2):170–5.
31. Pai VD, Jatal S, Ostwal V, Engineer R, Arya S, Patil P, et al. Multivisceral resections for rectal cancers: short-term oncological and clinical outcomes from a tertiary-care center in India. J Gastrointest Oncol. 2016;7(3):345–52.
32. Chandramohan A, Mittal R, Dsouza R, Yezzaji H, Eapen A, Simon B, et al. Prognostic significance of MR identified EMVI, tumour deposits, mesorectal nodes and pelvic side wall disease in locally advanced rectal cancer. Colorectal Dis. 2022;24(4):428–38.
33. Nagtegaal ID, Knijn N, Hugen N, Marshall HC, Sugihara K, Tot T, et al. Tumor deposits in colorectal cancer: improving the value of modern staging—a systematic review and meta-analysis. J Clin Oncol. 2017;35(10):1119–27.

34. Siddiqui MRS, Simillis C, Hunter C, Chand M, Bhoday J, Garant A, et al. A meta-analysis comparing the risk of metastases in patients with rectal cancer and MRI-detected extramural vascular invasion (mrEMVI) vs mrEMVI-negative cases. Br J Cancer. 2017;116(12):1513–9.
35. Prampolini F, Taschini S, Pecchi A, Sani F, Spallanzani A, Gelsomino F, et al. Magnetic resonance imaging performed before and after preoperative chemoradiotherapy in rectal cancer: predictive factors of recurrence and prognostic significance of MR-detected extramural venous invasion. Abdom Radiol. 2020;45(10):2941–9.
36. Lee ES, Kim MJ, Park SC, Hur BY, Hyun JH, Chang HJ, et al. Magnetic resonance imaging-detected extramural venous invasion in rectal cancer before and after preoperative chemoradiotherapy: diagnostic performance and prognostic significance. Eur Radiol. 2018;28(2):496–505.
37. Cammà C, Giunta M, Fiorica F, Pagliaro L, Craxì A, Cottone M. Preoperative radiotherapy for resectable rectal cancer: a meta-analysis. JAMA. 2000;284(8):1008–15.
38. Bahadoer RR, Dijkstra EA, van Etten B, Marijnen CAM, Putter H, Kranenbarg EM, et al. Short-course radiotherapy followed by chemotherapy before total mesorectal excision (TME) versus preoperative chemoradiotherapy, TME, and optional adjuvant chemotherapy in locally advanced rectal cancer (RAPIDO): a randomised, open-label, phase 3 trial. Lancet Oncol. 2021;22(1):29–42.
39. Conroy T, Bosset JF, Etienne PL, Rio E, François É, Mesgouez-Nebout N, et al. Neoadjuvant chemotherapy with FOLFIRINOX and preoperative chemoradiotherapy for patients with locally advanced rectal cancer (UNICANCER-PRODIGE 23): a multicentre, randomised, open-label, phase 3 trial. Lancet Oncol. 2021;22(5):702–15.
40. Shihab OC, Taylor F, Salerno G, Heald RJ, Quirke P, Moran BJ, et al. MRI predictive factors for long-term outcomes of low rectal tumours. Ann Surg Oncol. 2011;18(12):3278–84.
41. 2022;104(3):202-209. doi:10.1308/rcsann.2021.0156. PMID:34519559.