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Diffusion-Weighted Magnetic Resonance Imaging for Assessing Response to Neoadjuvant Chemoradiotherapy in Locally Advanced Rectal Carcinoma

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Abstract

Introduction: Locally advanced rectal carcinoma is commonly treated with neoadjuvant chemoradiotherapy (NCRT); however, accurate assessment of treatment response remains challenging because fibrosis, oedema, necrosis, and residual tumour may have overlapping imaging appearances. This study evaluated the role of diffusion-weighted imaging (DWI) and apparent diffusion coefficient (ADC) measurements as quantitative imaging parameters for assessing response to NCRT.

Materials and methods: This prospective observational study was conducted at Vydehi Institute of Medical Sciences and Research Centre, Bengaluru, from June 2024 to December 2025. A total of 24 patients with biopsy-proven rectal adenocarcinoma underwent MRI before NCRT and repeat MRI six to eight weeks after completion of treatment, before surgery. Tumour volume, ADC, mesorectal fascia (MRF) involvement, extramural vascular invasion (EMVI), lymph-node involvement, and histopathological tumour regression grade were assessed. Histopathological tumour regression was graded using the Dworak tumour regression grading system.

Results: Mean tumour volume decreased significantly from 41.24 ± 18.26 cm^3 before NCRT to 2.17 ± 0.73 cm^3 after treatment ($p < 0.001$). MRF involvement decreased from 14 (58.3%) to five (20.8%), EMVI from 11 (45.8%) to two (8.3%), and lymph-node involvement from 20 (83.3%) to six (25.0%). Post-treatment ADC was significantly higher in good responders than in poor responders (1.63 ± 0.10 vs. 0.94 ± 0.15 × 10^{-3} mm^2/s; $p < 0.001$). The percentage change in ADC was also significantly greater in good responders (91.70 ± 20.27% vs. 10.87 ± 18.76%; $p < 0.001$). A post-NCRT ADC cutoff of >1.20 × 10^{-3} mm^2/s demonstrated 94.7% sensitivity, 100.0% specificity, and an area under the curve (AUC) of 0.989. TRG1 was the most frequent histopathological regression grade, observed in 12 (50.0%) patients, followed by TRG2 in 10 (41.7%).

Conclusion: DWI and ADC measurements provide useful quantitative information for assessing treatment response in locally advanced rectal carcinoma following NCRT. Post-treatment ADC and percentage change in ADC demonstrated high discriminatory performance within the study cohort, suggesting their potential role in non-invasive response assessment and preoperative planning. The observed reductions in tumour volume, MRF involvement, EMVI, and lymph-node involvement further support the value of integrating morphological and diffusion-based MRI parameters. However, the small sample size and limited distribution across some tumour regression categories warrant cautious interpretation. The identified ADC cutoff should be considered exploratory rather than an established clinical threshold. Larger multicentre studies with standardized imaging protocols, formal assessment of interobserver agreement, and longer follow-up are warranted to validate these findings and determine their clinical utility.

Categories: Radiology
Keywords: apparent diffusion coefficient, diffusion-weighted imaging, dynamic contrast-enhanced mri, neoadjuvant chemoradiotherapy, rectal carcinoma

Introduction

Rectal cancer is a major global health concern and remains one of the leading malignancies of the gastrointestinal tract, contributing substantially to cancer-related morbidity and mortality worldwide [1]. The burden of rectal cancer is also increasing in developing countries, including India, where changing lifestyles and delayed diagnosis contribute to presentation at advanced stages [2,3]. Locally advanced rectal cancer (LARC), particularly tumours involving the T3-T4 stages and/or regional lymph nodes, is generally managed with neoadjuvant chemoradiotherapy (NCRT) followed by total mesorectal excision [4]. Neoadjuvant treatment aims to achieve tumour downstaging, improve local control, reduce the risk of recurrence, increase the possibility of sphincter-preserving surgery, and potentially reduce metastatic disease [5]. However, treatment response is heterogeneous, with only a proportion of patients achieving pathological complete response, while others demonstrate partial or minimal tumour regression [6]. Therefore, reliable non-invasive methods for assessing treatment response are important to guide

preoperative decision-making and support individualized treatment strategies [7].

Magnetic resonance imaging (MRI) is the preferred imaging modality for local staging, restaging, and post-treatment assessment of rectal cancer because of its excellent soft-tissue contrast and ability to evaluate tumour extent, mesorectal fascia (MRF), circumferential resection margin, extramural vascular invasion (EMVI), and regional lymph nodes [8]. Conventional T1- and T2-weighted sequences provide important morphological information; however, assessment after NCRT can be challenging because treatment-related fibrosis, oedema, necrosis, and residual viable tumour may have overlapping imaging appearances [9]. Diffusion-weighted imaging (DWI) provides additional functional information regarding tumour microstructure and cellularity. DWI assesses the movement of water molecules within tissues, with restricted diffusion and lower apparent diffusion coefficient (ADC) values generally reflecting increased cellularity. Following effective treatment, tumour cell death and structural changes may result in increased ADC values [10]. Thus, combining DWI with conventional morphological sequences may provide a more comprehensive assessment of post-treatment tumour changes.

Quantitative assessment of ADC before and after NCRT may therefore provide useful information regarding treatment response. Changes in ADC, including the percentage change in ADC (ΔADC), have been investigated as potential imaging biomarkers for differentiating responders from non-responders [11]. An increase in ADC following treatment may reflect reduced tumour cellularity and treatment-related tissue changes, while the magnitude of this increase may vary according to the degree of tumour regression. In addition to diffusion parameters, morphological MRI assessment, including tumour volume, MRF involvement, EMVI, and lymph-node status, may provide complementary information regarding treatment-related changes. Evaluating these quantitative and morphological parameters together may offer a more comprehensive characterization of treatment response and residual disease, potentially contributing to preoperative treatment planning [12-16].

Despite increasing evidence supporting the role of DWI and quantitative ADC assessment in rectal cancer response evaluation, region-specific data from India remain limited. Differences in patient characteristics, disease presentation, treatment practices, and available imaging resources highlight the need for studies evaluating these techniques in the Indian population. Furthermore, the combined assessment of quantitative diffusion parameters and morphological tumour characteristics warrants further evaluation in this setting. Evaluation of quantitative MRI biomarkers such as ADC, together with morphological tumour assessment, may improve non-invasive assessment of response to NCRT and assist in treatment planning for patients with LARC. Therefore, the present study aimed to evaluate the role of DWI and ADC measurements in assessing response to NCRT in patients with LARC.

Materials And Methods

Study design and setting

A prospective observational study was conducted in the Department of Radiodiagnosis, Vydehi Institute of Medical Sciences and Research Centre (VIMS & RC), Bengaluru, Karnataka, India, from June 2024 to December 2025. The study included patients with biopsy-proven locally advanced rectal adenocarcinoma who were planned for NCRT. The study was approved by the Institutional Ethics Committee (IEC), VIMS & RC, Bengaluru, Karnataka, India (IEC No. VIEC/2023/APP/PG/114; dated 19/02/2024), and written informed consent was obtained from all participants before enrolment. The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [17].

Study population

Patients with biopsy-proven rectal adenocarcinoma fulfilling the criteria for locally advanced disease were included. Locally advanced rectal carcinoma was defined as a tumour staged clinically as T3 or T4 and/or associated with regional lymph-node involvement on pretreatment imaging. Patients with recurrent rectal carcinoma, previous pelvic radiotherapy, treatment with targeted therapy or immunotherapy, incomplete NCRT or poor treatment compliance, contraindications to MRI, known gadolinium contrast allergy, or impaired renal function were excluded. Patients in whom the interval between post-NCRT MRI and surgery exceeded three months were also excluded. A total of 24 patients were included using purposive sampling. Patients with distant metastases were not excluded because the study primarily evaluated local tumour response to NCRT using MRI and pathological tumour regression. The presence of distant metastatic disease was therefore recorded as a baseline clinical characteristic while local tumour response remained the primary imaging assessment.

Sample size

The sample size was calculated based on an anticipated sensitivity of 75%, as reported by Iafrate et al. [18]. The sample size was calculated using the formula:

$$n = \frac{Z^2_{\alpha/2} P(1-P)}{d^2}$$

Where Zα/2 = 1.96 at a 95% confidence level, P = 0.75, and d = 0.18. Thus, the calculated minimum sample size was approximately 23 participants and was rounded to 24 participants for the present study.

Participant flow

During the study period, 30 patients were screened for eligibility. Six patients were excluded according to the predefined exclusion criteria, and 24 patients were subsequently enrolled and included in the final analysis. The participant flow is presented in Figure *1*.

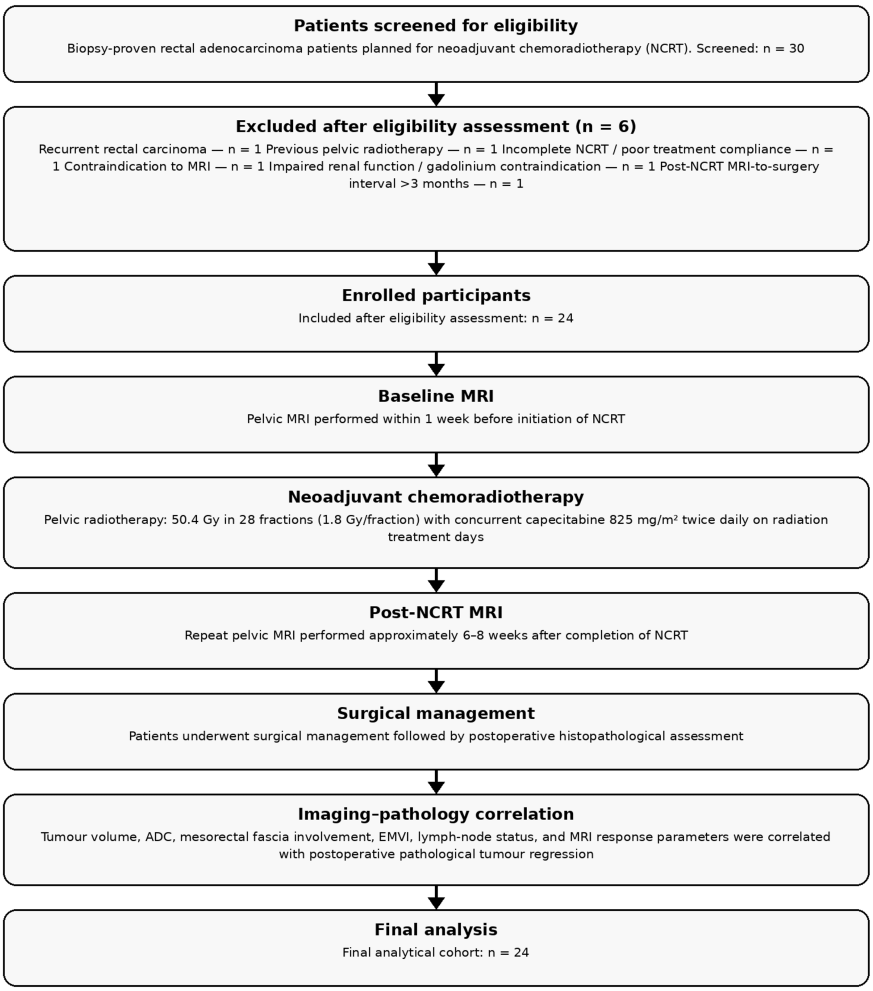


FIGURE 1: Participant flow chart

ADC: apparent diffusion coefficient, EMVI: extramural vascular invasion

Neoadjuvant chemoradiotherapy

All eligible patients underwent standard NCRT before surgical management. Radiotherapy was delivered to the pelvis to a total dose of 50.4 Gy in 28 fractions, at 1.8 Gy per fraction, with concurrent chemotherapy. Concurrent chemotherapy consisted of capecitabine at a dose of 825 mg/m² twice daily on radiation treatment days. The NCRT regimen was completed before the post-treatment MRI assessment.

MRI protocol

Baseline MRI of the pelvis was performed within one week before initiation of NCRT. Follow-up MRI was performed approximately six to eight weeks after completion of NCRT and before surgery. MRI examinations were performed on a Siemens 1.5-Tesla Magnetom Aera MRI system (Siemens Healthineers, Erlangen, Germany) using a pelvic phased-array coil. Patients were instructed to fast for approximately three hours before the examination. The imaging protocol included axial, sagittal, and coronal T2-weighted sequences, T1-weighted sequences, fat-suppressed T2-weighted sequences, DWI, and ADC mapping. DWI was acquired using b-values of 0, 500, and 1000 s/mm² [16]. ADC maps were automatically generated from the diffusion-weighted images. Contrast-enhanced imaging was performed following intravenous administration of

Resoimage (Gadoterate Meglumine Injection USP; Arco Lifesciences/Trident Medlife Private Limited, Nagpur, India) at a dose of 0.2 mL/kg.

Assessment of tumour volume and ADC

Tumour volume was assessed by manual delineation of the tumour on consecutive axial T2-weighted images. The tumour area was outlined on each relevant slice, and the total tumour volume was calculated by summing the tumour areas across the slices using syngo.via imaging software (version VB60; Siemens Healthineers). ADC measurements were obtained from the ADC maps using manually placed regions of interest (ROIs) within the solid component of the tumour. Areas of necrosis, cystic degeneration, haemorrhage, the rectal lumen, and adjacent normal tissue were avoided while placing the ROI. The mean ADC value was recorded for each examination [16,19]. ADC measurements were obtained before NCRT and after completion of NCRT.

Representative pre- and post-NCRT MRI images demonstrating tumour morphology, diffusion characteristics, and ADC measurements are presented in Figure *2*. The figure illustrates the identification of the tumour on T2-weighted images, corresponding diffusion characteristics on DWI, and ADC assessment using an ROI.

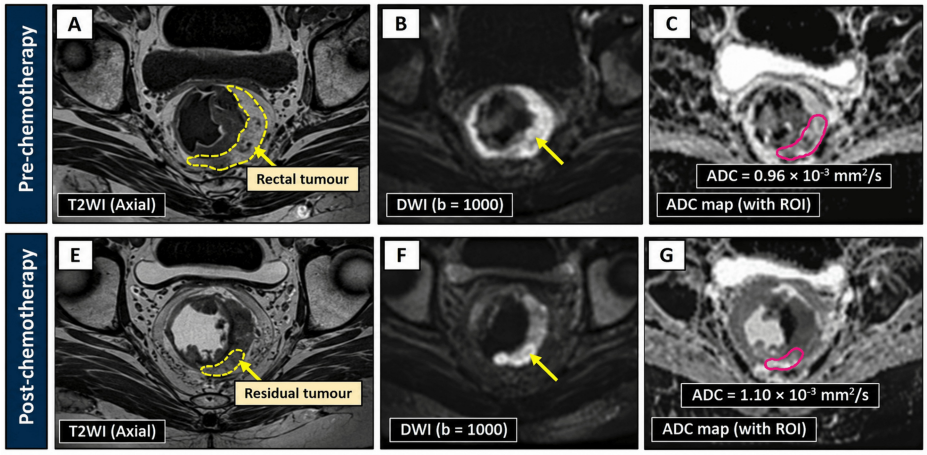


FIGURE 2: Representative pre- and post-neoadjuvant chemoradiotherapy MRI findings with diffusion-weighted imaging and apparent diffusion coefficient assessment in a patient with mid-rectal adenocarcinoma.

(A) Pretreatment axial T2-weighted image demonstrating an endoluminal, semicircumferential rectal tumour with heterogeneous signal intensity. (B) Corresponding pretreatment DWI (b = 1000 s/mm²) demonstrating restricted diffusion within the tumour. (C) Pretreatment ADC map showing a mean ADC value of 0.96 × 10^{-3} mm²/s, with the ROI indicated. (E) Post-treatment axial T2-weighted image demonstrating a reduction in tumour extent, with residual semicircumferential wall involvement. (F) Corresponding post-treatment DWI demonstrating persistent restricted diffusion within the residual tumour. (G) Post-treatment ADC map showing an increased mean ADC value of 1.10 × 10^{-3} mm²/s. The ADC value increased by 14.6% following NCRT, suggesting a treatment-related reduction in tumour cellularity. Overall, the imaging findings demonstrate partial morphological regression with persistent residual tumour.

Abbreviations: ADC, apparent diffusion coefficient; DWI, diffusion-weighted imaging; NCRT, neoadjuvant chemoradiotherapy; ROI, region of interest; T2WI, T2-weighted imaging.

The percentage change in ADC following NCRT was calculated as:

Percentage change in ADC = [(Post-treatment ADC − Pre-treatment ADC) / Pre-treatment ADC] × 100

Assessment of MRI response

The pre- and post-NCRT MRI examinations were assessed for tumour characteristics and treatment response. The parameters evaluated included tumour volume, ADC values, MRF involvement, EMVI, and regional lymph-node status. The imaging findings were compared between the pre-NCRT and post-NCRT examinations to assess treatment-related changes in local tumour extent. Radiological treatment response was assessed based on changes in tumour morphology, tumour volume, diffusion characteristics, and contrast enhancement, in accordance with previously described MRI-based response assessment approaches in LARC [19,20].

ADC measurements were considered complementary quantitative parameters in the overall assessment of treatment response and were interpreted alongside conventional morphological MRI findings. The study was not designed to differentiate individual post-treatment tissue changes, such as fibrosis, oedema, necrosis, or haemorrhage, using ADC maps alone.

Tumour regression was subsequently compared with postoperative histopathological findings. Histopathological tumour regression was graded using the Dworak tumour regression grading system, which categorizes tumour regression from TRG 0 to TRG 4, with higher grades indicating greater tumour regression [21]. TRG 0 indicates no tumour regression, whereas TRG 4 indicates complete regression with no residual tumour cells.

Definition of good and poor responders

Based on the overall post-NCRT MRI assessment, patients were stratified into two groups according to their radiological response to treatment. Group A (Good Responders) comprised patients demonstrating marked tumour regression with substantial reduction in tumour volume and reduction or resolution of imaging features suggestive of viable residual tumour. Group B (Poor Responders) comprised patients demonstrating minimal or no tumour regression, limited reduction in tumour volume, and persistent imaging features suggestive of viable residual tumour [19,20]. These response categories represented the overall radiological assessment and were not intended to establish ADC as an independent or sole determinant of treatment response.

MRI image interpretation

The MRI examinations were reviewed independently by two radiologists. The readers had 10 years of experience in abdominal and pelvic MRI interpretation. The readers were blinded to the postoperative histopathological findings at the time of MRI assessment. In cases of disagreement, the final imaging assessment was established by consensus between the readers. Formal interobserver agreement was not calculated.

Data collection and statistical analysis

Data were entered into Microsoft Excel (Microsoft 365, Microsoft Corporation, Redmond, WA, USA) and analysed using IBM SPSS Statistics version 26.0 (IBM Corporation, Armonk, NY, USA). Continuous variables were expressed as mean ± standard deviation, while categorical variables were expressed as frequencies and percentages. McNemar's test was used to compare paired categorical variables before and after NCRT. A paired-samples t-test was used for within-patient continuous variables, and an independent-samples t-test was used for comparisons between good and poor responders. Effect sizes were reported using Cohen's dz for paired comparisons and Cohen's d for independent-group comparisons. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the ability of post-NCRT ADC and percentage change in ADC (ΔADC) to discriminate between good and poor responders, with sensitivity, specificity, area under the curve (AUC), and 95% confidence intervals reported. A two-sided $p < 0.05$ was considered statistically significant.

Results

The study included 24 participants. The largest proportion belonged to the 40-49-year age group (nine, 37.5%), followed by 50-59 years (eight, 33.3%) and <40 years (seven, 29.2%). Males constituted 15 (62.5%) participants and females nine (37.5%). Mid-rectal tumours were most common (12, 50.0%), followed by lower (eight, 33.3%) and upper rectal tumours (four, 16.7%). Distant metastasis was present in three (12.5%) participants (Table *1*).

Variable	Category	n (%)
Age group (years)	<40	7 (29.2%)
	40–49	9 (37.5%)
	50–59	8 (33.3%)
Sex	Male	15 (62.5%)
	Female	9 (37.5%)
Diabetes mellitus	Present	1 (4.2%)
Hypertension	Present	1 (4.2%)
Tumour location	Lower rectum	8 (33.3%)
	Mid rectum	12 (50.0%)
	Upper rectum	4 (16.7%)
Distant metastasis	Present	3 (12.5%)

TABLE 1: Baseline demographic and clinical characteristics of study participants (n = 24)

Data are presented as n (%). Abbreviations: NCRT, neoadjuvant chemoradiotherapy.

Following NCRT, MRF involvement decreased from 14 (58.3%) to five (20.8%), EMVI from 11 (45.8%) to two (8.3%), and lymph-node involvement from 20 (83.3%) to six (25.0%). Mean tumour volume also decreased from 41.24 ± 18.26 cm^3 to 2.17 ± 0.73 cm^3 ($t = 9.953$, $df = 23$, $p < 0.001$) (Table *2*).

Parameter	Pre-NCRT	Post-NCRT	Statistical value	df	Effect size	p-value
Mesorectal Fascia involvement	14 (58.3%)	5 (20.8%)	McNemar's $\chi^2 = 9.00$	1	-	0.004
Extramural Vascular Invasion present	11 (45.8%)	2 (8.3%)	McNemar's $\chi^2 = 9.00$	1	-	0.004
Lymph node involvement	20 (83.3%)	6 (25.0%)	McNemar's $\chi^2 = 14.00$	1	-	< 0.001
Tumour volume, mean ± SD (cm^3)	41.24 ± 18.26	2.17 ± 0.73	t = 9.953	23	Cohen's dz = 2.03	p < 0.001

TABLE 2: Pre- and post-NCRT tumour characteristics and changes in local disease status (n = 24)

Categorical data are presented as n (%) and continuous data as mean ± standard deviation (SD). McNemar's test was used to compare paired categorical variables, and the paired t-test was used to compare pre- and post-NCRT tumour volume. Cohen's dz was used as the effect size for the paired continuous comparison. Abbreviations: NCRT, neoadjuvant chemoradiotherapy; MRF, mesorectal fascia; EMVI, extramural vascular invasion; SD, standard deviation. P < 0.05 was considered statistically significant.

Pre-treatment ADC values were comparable between good and poor responders (0.859 ± 0.0839 vs. 0.852 ± 0.0409 × 10^{-3} mm^2/s; $p = 0.861$). Post-treatment ADC was significantly higher among good responders (1.63 ± 0.10 vs. 0.94 ± 0.15 × 10^{-3} mm^2/s; $p < 0.001$). The percentage change in ADC was also significantly greater among good responders (91.70 ± 20.27% vs. 10.87 ± 18.76%; $p < 0.001$). These findings indicate that post-treatment ADC values and their percentage changes differed significantly between the two radiological response groups, whereas pretreatment ADC values were comparable (Table *3*).

ADC parameter	Good responders (n = 19)	Poor responders (n = 5)	Statistical value	df	Effect size	p-value
Pre-treatment ADC (×10^{-3} mm^2/s)	0.859 ± 0.0839	0.852 ± 0.0409	t = 0.178	22	Cohen's d = 0.09	0.861
Post-treatment ADC (×10^{-3} mm^2/s)	1.63 ± 0.10	0.94 ± 0.15	t = 12.877	22	Cohen's d = 6.47	<0.001
Percentage change in ADC (%)	91.70 ± 20.27	10.87 ± 18.76	t = 8.039	22	Cohen's d = 4.04	<0.001

TABLE 3: Comparison of ADC parameters between good and poor responders (n = 24)

Data are presented as mean ± SD. An independent-samples t-test was used to compare ADC parameters between good and poor responders. Cohen's d was reported as the effect size. Abbreviations: ADC, apparent diffusion coefficient; SD, standard deviation; NCRT, neoadjuvant chemoradiotherapy. P < 0.05 was considered statistically significant.

TRG1 was the most frequent regression grade, observed in 12 (50.0%) participants, followed by TRG2 in 10 (41.7%). TRG0 and TRG4 were each observed in one (4.2%) participant, while TRG3 was not observed. Thus, TRG1 and TRG2 together accounted for 22 (91.7%) participants (Table *4*).

Tumour regression grade	N (%)
TRG 0	1 (4.2%)
TRG 1	12 (50.0%)
TRG 2	10 (41.7%)
TRG 3	0 (0.0%)
TRG 4	1 (4.2%)
Total	24 (100.0%)

TABLE 4: Tumour regression grade distribution following NCRT (n = 24)

Data are presented as n (%). Abbreviations: TRG, tumour regression grade; NCRT, neoadjuvant chemoradiotherapy.

Good responders had significantly lower pre-treatment tumour volume than poor responders (37.05 ± 15.59 vs. 57.18 ± 20.57 cm^3; p = 0.025). Post-treatment tumour volume was also significantly lower among good responders (1.31 ± 0.44 vs. 2.87 ± 0.93 cm^3; p < 0.001). The differences in tumour volume between the two response groups were observed at both pre-treatment and post-treatment assessments (Table *5*).

Tumour volume parameter	Good responders (n = 19)	Poor responders (n = 5)	Statistical value	df	Effect size	p-value
Pre-treatment tumour volume (cm^3)	37.05 ± 15.59	57.18 ± 20.57	t = −2.413	22	Cohen's d = 1.21	0.025
Post-treatment tumour volume (cm^3)	1.31 ± 0.44	2.87 ± 0.93	t = −5.489	22	Cohen's d = 2.76	<0.001

TABLE 5: Comparison of tumour volume between good and poor responders (n = 24)

Data are presented as mean ± SD. An independent-samples t-test was used to compare tumour volume between good and poor responders. Cohen's d was reported as the effect size. Abbreviations: NCRT, neoadjuvant chemoradiotherapy; SD, standard deviation. P < 0.05 was considered statistically significant.

A post-NCRT ADC cut-off of >1.20 × 10^{-3} mm^2/s showed 94.7% sensitivity and 100.0% specificity, with an AUC of 0.989 (95% CI: 0.958-1.000; p < 0.001). A ΔADC cut-off of >45% demonstrated 94.7% sensitivity and 100.0% specificity, with an AUC of 0.979 (Table 6).

ADC parameter	Cut-off	Sensitivity	Specificity	AUC	95% CI	p-value
Post-NCRT ADC (×10^{-3} mm^2/s)	>1.20	94.7%	100.0%	0.989	0.958-1.000	<0.001
ΔADC (%)	>45.0%	94.7%	100.0%	0.979	0.931-1.000	<0.001

TABLE 6: Diagnostic performance of post-NCRT ADC parameters for treatment response (n = 24)

Data are presented as sensitivity, specificity, area under the receiver operating characteristic curve (AUC), 95% confidence interval (CI), and p-value. ROC curve analysis was used to evaluate the ability of post-NCRT ADC and percentage change in ADC (ΔADC) to discriminate between good and poor treatment responders. Abbreviations: ADC, apparent diffusion coefficient; ΔADC, percentage change in ADC; AUC, area under the curve; CI, confidence interval; NCRT, neoadjuvant chemoradiotherapy; ROC, receiver operating characteristic.

Discussion

The present study demonstrated a substantial reduction in tumour burden following NCRT, with mean tumour volume decreasing from 41.24 ± 18.26 cm^3 before treatment to 2.17 ± 0.73 cm^3 after treatment (p < 0.001). This reduction was accompanied by significant decreases in MRF involvement from 14 (58.3%) to five (20.8%), EMVI from 11 (45.8%) to two (8.3%), and lymph-node involvement from 20 (83.3%) to six (25.0%). These findings demonstrate that conventional morphological MRI parameters can provide useful information regarding changes in local tumour extent following NCRT. Similar findings have been reported, with post-treatment tumour volume and volumetric changes showing associations with pathological treatment response [22].

DWI provided important functional information regarding treatment response. Post-treatment ADC values were significantly higher in good responders than in poor responders (1.63 ± 0.10 vs. 0.94 ± 0.15 × 10^{-3} mm^2/s; p < 0.001), while the percentage increase in ADC was also significantly greater among good responders (91.70 ± 20.27% vs. 10.87 ± 18.76%; p < 0.001). In contrast, pretreatment ADC values did not differ significantly between the two groups (p = 0.861). The increase in ADC following NCRT may reflect treatment-induced reduction in tumour cellularity and increased extracellular water content. Similar findings have been reported, demonstrating the potential value of ADC changes for assessing response to NCRT [23,24]. However, the diagnostic performance of ADC has varied across studies, supporting the need for standardized acquisition, measurement, and response criteria [19,20]. Therefore, ADC measurements should be interpreted alongside morphological findings, as post-treatment fibrosis, oedema, necrosis, and mucinous changes may influence diffusion characteristics. Importantly, ADC measurements should be considered complementary quantitative imaging parameters rather than independent indicators capable of differentiating individual post-treatment tissue components such as fibrosis, oedema, necrosis, or haemorrhage. Their interpretation should therefore be integrated with conventional morphological MRI findings and other established imaging parameters.

Tumour volume was also significantly lower among good responders. Good responders had a lower pretreatment tumour volume than poor responders (37.05 ± 15.59 vs. 57.18 ± 20.57 cm^3; p = 0.025), and post-treatment tumour volume was also significantly lower (1.31 ± 0.44 vs. 2.87 ± 0.93 cm^3; p < 0.001). These findings suggest that tumour burden, both before and after NCRT, may provide useful information regarding treatment response. Previous studies have similarly demonstrated the potential value of tumour volume and volumetric changes in response assessment [22,23,25]. Nevertheless, residual tumour volume should be interpreted cautiously because fibrosis, oedema, necrosis, and viable residual tumour may coexist after treatment and may not always be reliably distinguished on conventional morphological imaging.

Histopathological assessment showed that TRG1 was the most frequent regression grade, observed in 12 (50.0%) participants, followed by TRG2 in 10 (41.7%). According to the Dworak tumour regression grading system, higher TRG indicates greater tumour regression [21]. In the present study, post-treatment ADC and ΔADC demonstrated high apparent discriminatory performance within the study cohort, with AUCs of 0.989 and 0.979, respectively. These findings suggest a potential complementary role for diffusion-based quantitative parameters in treatment response assessment. However, the observed diagnostic performance should be interpreted cautiously because of the small sample size, limited representation of some tumour regression categories, and the exploratory nature of the derived ADC thresholds. The findings should not be interpreted as establishing ADC-based thresholds for routine clinical decision-making or as suggesting that ADC measurements can replace conventional morphological MRI assessment.

Strengths and limitations

The strengths of the present study include its prospective design, standardized pre- and post-NCRT MRI assessment, and incorporation of both quantitative tumour volume and ADC measurements for evaluating treatment response. The study also assessed clinically relevant MRI features, including MRF involvement, EMVI, lymph node status, and histopathological tumour regression grade, providing a comprehensive assessment of treatment response. However, the study has certain limitations. The small sample size of 24 participants, single-centre design, purposive sampling, and relatively short study period may limit the generalizability of the findings. Interobserver agreement between the radiologists was not formally assessed, which may have introduced variability in image interpretation and quantitative measurements. In addition, post-treatment MRI findings may be influenced by fibrosis, oedema, necrosis, and other treatment-related changes. The limited distribution of patients across some TRG categories also restricts the strength of histopathological response comparisons. Longer-term clinical and oncological outcomes were not evaluated. Furthermore, the study was not designed to differentiate individual post-treatment tissue components using ADC measurements alone, and ADC should be interpreted as a complementary rather than a standalone imaging biomarker. A separate parameter-wise correlation between post-treatment MRI findings and surgical histopathological findings for MRF involvement and EMVI was not performed, limiting the assessment of their individual pathological accuracy. The ADC cutoffs derived from ROC curve analysis should be considered exploratory thresholds within the present study cohort and were not intended to establish universally applicable clinical decision limits. Their diagnostic performance requires validation in larger, independent patient populations. Larger multicentre studies with standardized imaging protocols, formal assessment of interobserver agreement, independent histopathological validation of imaging biomarkers, and longer follow-up are warranted to validate these findings and establish the clinical utility of diffusion-weighted MRI and ADC measurements.

Conclusions

Diffusion-weighted MRI and ADC measurements provide useful quantitative information for assessing treatment response following NCRT in patients with locally advanced rectal carcinoma. Significant reductions in tumour volume, MRF involvement, EMVI, and lymph-node involvement were observed following treatment. Good responders demonstrated significantly higher post-treatment ADC values and greater percentage increases in ADC than poor responders. Post-NCRT ADC and ΔADC showed high discriminatory performance between good and poor responders, suggesting their potential role as non-invasive imaging biomarkers of treatment response. Histopathological assessment revealed that Dworak TRG1 was the most frequent regression grade, followed by TRG2. However, the small sample size and limited representation of certain TRG categories warrant cautious interpretation of these findings. Larger multicentre studies incorporating standardized imaging protocols, formal assessment of interobserver agreement, and longer follow-up are needed to validate these results and establish the clinical utility of diffusion-weighted MRI and ADC measurements in routine practice.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Mounika Malreddygari, Doddamani Diwakar, Suresh A, Swara B. S

Acquisition, analysis, or interpretation of data: Mounika Malreddygari, Doddamani Diwakar, Suresh A, Swara B. S

Drafting of the manuscript: Mounika Malreddygari, Doddamani Diwakar, Suresh A, Swara B. S

Critical review of the manuscript for important intellectual content: Mounika Malreddygari, Doddamani Diwakar, Suresh A, Swara B. S

Disclosures

Human subjects: Informed consent for treatment and open access publication was obtained or waived by all participants in this study. Institutional Ethics Committee, Vydehi Institute of Medical Sciences and Research Centre, Bengaluru issued approval VIEC/2023/APP/PG/114. **Animal subjects:** All authors have confirmed that this study did not involve animal subjects or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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