Comparative effectiveness of two abbreviated rectal MRI protocols in assessing tumor response to neoadjuvant chemoradiotherapy in patients with rectal cancer

FILIZ TAŞÇI[1], YAVUZ METIN[2], NURGÜL ORHAN METIN[3], SEMA RAKICI[4],
MELIH GAFFAR GÖZÜKARA[5] and ERENCAN TAŞÇI[6]

[1]Department of Radiology, Faculty of Medicine, Recep Tayyip Erdogan University, 53000 Rize, Turkey;
[2]Faculty of Medicine, Ankara University, 06230 Ankara, Turkey; [3]Radiology Unit, Beytepe Murat Erdi Eker State Hospital,
06800 Ankara, Turkey; [4]Department of Radiation Oncology, Faculty of Medicine, Recep Tayyip Erdogan University,
53000 Rize, Turkey; [5]Health Directorate, Ankara Yıldırım Beyazıt University Faculty of Medicine, 06800 Ankara, Turkey;
[6]Güneysu Physical Therapy Unit, Faculty of Medicine, Recep Tayyip Erdogan University, 53000 Rize, Turkey

Abstract. The present study aimed to compare the effectiveness of two abbreviated magnetic resonance imaging (MRI) protocols in assessing the response to neoadjuvant chemoradiotherapy (CRT) in patients with rectal cancer. Data from the examinations of 62 patients with rectal cancer who underwent neoadjuvant CRT and standard contrast-enhanced rectal MRI were retrospectively evaluated. Standard contrast-enhanced T2-weighted imaging (T2-WI), post-contrast T1-weighted imaging (T1-WI) and diffusion-weighted imaging (DWI) MRI, as well as two abbreviated protocols derived from these images, namely protocol AB1 (T2-WI and DWI) and protocol AB2 (post-contrast fat-suppressed (FS) T1-WI and DWI), were assessed.Measurements of lesion length and width, lymph node short-axis length, tumor staging, circumferential resection margin (CRM), presence of extramural venous invasion (EMVI), luminal mucin accumulation (MAIN), mucinous response, mesorectal fascia (MRF) involvement, and MRI-based tumor regression grade (mrTRG) were obtained. The reliability and compatibility of the AB1 and AB2 protocols in the evaluation of tumor response were analyzed. The imaging performed according to the AB1 and AB2 protocols revealed significant decreases in lesion length, width and lymph node size after CRT. These protocols also showed reductions in lymph node positivity, CRM, MRF, EMVI.Furthermore, both protocols were found to be reliable in determining lesion length and width. Additionally, compliance was observed between the protocols in determining lymph node size and positivity, CRM involvement, and EMVI after CRT. In conclusion, the use of abbreviated MRI protocols, specifically T2-WI with DWI sequences or post-contrast FS T1-WI with DWI sequences, is effective for evaluating tumor response in patients with rectal cancer following neoadjuvant CRT.The AB protocols examined in this study yielded similar results in terms of lesion length and width, lymph node positivity, CRM involvement, EMVI, MAIN, and MRF involvement.

Introduction

Colorectal cancer is the second most common cause of cancer-related deaths in women and the third most common in men worldwide. Rectal cancer has an incidence rate of 40 per 100,000 patients and accounts for more than one-third of colorectal cancer cases. Due to anatomical limitations, rectal cancer is more challenging to resect, has a higher risk of local recurrence, and generally has a worse prognosis (1). Colorectal cancer also has a higher risk of metastasizing to the lungs compared to colon cancer. The 5-year mortality rate for patients diagnosed at Stage IV is approximately 90% (2). The treatment approach for rectal cancer is total mesorectal excision. In individuals with locally advanced rectal cancer (LARC), the use of neoadjuvant chemoradiotherapy (CRT) has resulted in significant improvements in local disease control and fewer side effects compared with adjuvant therapy administered after surgery (3,4).

High-resolution magnetic resonance imaging (MRI) is the preferred method for diagnosing rectal cancer; it plays a crucial role in preoperative diagnosis and staging, in the identification of cases that may benefit from preoperative neoadjuvant CRT and in post-CRT restaging to assess treatment response. This imaging technique is vital for guiding surgical approaches and oncological treatment alternatives (5-8).

Patients with LARC receive personalized CRT treatments. In recent years, there has been an increasing demand for more detailed and reliable radiological response assessments of such Patients with LARC receive personalized CRT treatments. In recent years, there has been an increasing demand for more detailed and reliable radiological response assessments of such patients. Post-CRT MRI plays a critical role in the decision-making process for managing rectal cancer by providing crucial information on prognostic factors, such as tumor grade, circumferential resection margin (CRM) status, mesorectal fascia (MRF) involvement, the presence of extramural vascular invasion (EMVI) and the mucin content of the tumor (9-11).

MRI is the most sensitive noninvasive imaging method for staging rectal cancer patients. High-resolution T2-weighted (T2-W) images are regarded as the most sensitive sequences for evaluation. However, existing MRI techniques face certain limitations in assessing post-CRT treatment responses, particularly in regions affected by post-radiation fibrosis. Consequently, it is crucial to incorporate functional MRI sequences, such as diffusion-weighted imaging (DWI) sequences, in order to enhance the distinction between the tumor and fibrosis are increasingly being adopted in clinical MRI protocols to reliably determine the tumor response and achieve a balance between oncological safety and patient quality of life (5,11-14).

Dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI), the magnetization transfer ratio, and textural analysis (i.e., radiomics) are being investigated to overcome some limitations in the restaging of rectal cancer post-CRT. However, none of these techniques are currently used in routine clinical practice (6).

To reduce costs, shorten imaging and assessment times, and avoid unnecessary sequences that might negatively impact patient comfort, abbreviated MRI protocols have emerged as alternatives to standard protocols (13). According to the ESGAR guidelines, the MRI protocol for staging rectal cancer should include T2-W sequences in three planes and DWI, which can provide adequate disease assessment in approximately 10-15 min, thus mimicking an abbreviated protocol (9). However, non-contrast and contrast-enhanced fat-suppressed (FS) T1-W sequences are not routinely recommended during DCE-MRI or after the administration of contrast agents (5,8,12). Combining morphological and functional assessments using T2-W sequences with DWI and DCE-MRI sequences could be beneficial for the restaging of rectal cancer. Because T1 and postcontrast T1-weighted sequences are not recommended because they do not provide optimum information about the anatomy (5,12,15-18).

Currently, the accuracy of MRI is lower in post-CRT staging than in pre-CRT assessment. Furthermore, there is no consensus on a standard protocol or the utility of DCE-MRI and DWI for post-CRT staging (12). DCE-MRI is part of the routine imaging protocol for assessing tumor response after neoadjuvant CRT, as it provides a reliable basis for evaluating tumor response after an initial contrast-enhanced study. It is recommended that post-CRT tumor restaging be performed using the same protocol and scanner as the initial staging phase (5,8,12,19,20). Although AB-MRI protocols are considered promising for significantly shortening imaging

time while maintaining diagnostic accuracy in breast and prostate cancer, and other cancer types, few studies have evaluated their effectiveness in the post-CRT restaging of rectal cancer (5,6,11,20-24).

The aim of the present study was to compare the effectiveness of two post-CRT abbreviated rectal MRI protocols in evaluating tumor response to neoadjuvant CRT in patients with LARC. This comparison was also evaluated against pretreatment DCE-MRI findings.

Materials and methods

Study population. The images used in the present study were created during assessments performed Recep Tayyip Erdogan University Faculty of Medicine, Training and Research Hospital Radiology Department between December 2015 and December 2021. Our exclusion criteria include low image quality, claustrophobia, refusal to participate in the study, patients who cannot be pathologically confirmed, contraindications to contrast agents, and cases where MRI could not be performed before or after neoadjuvant chemoradiotherapy. After applying the exclusion criteria, a total of 62 patients were included in the study. In order to evaluate the treatment response after the exclusion criteria, 62 patients diagnosed with rectal cancer who underwent neoadjuvant CRT and standard contrast-enhanced rectal MRI examination before (for staging purposes) and after CRT (for evaluating the treatment response) were included in the study. The patients had a median age of 58 years (range: 37-85 years), and 54.8% were male. The AB-MRI protocols, which were obtained via retrospective screening and re-analysis of standard contrast-enhanced MRI (T2-W, postcontrast T1-W, and DWI) data registered in picture archiving and communication systems (PACS), included the AB1 (T2-W and DWI) and AB2 (postcontrast FS T1-W and DWI) protocols. Two radiologists, blinded to the results, reached a consensus after jointly reviewing images obtained using standard MRI sequences at baseline and protocol AB-MRI sequences obtained after treatment.

Written informed consent was obtained from each subject following a detailed explanation of the objectives and protocol of the study, which was conducted in accordance with the ethical principles in the 'Declaration of Helsinki' and approved by the Recep Tayyip Erdogan University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (Date of Approval: 07/06/2022; Reference/Protocol No.: 2022/134). Informed consent was obtained from the participants whose images were used in the publication.

Assessments. Demographic data, tumor histopathology, metastatic lymph node status, and residual tumor size were recorded for each patient. The pretreatment MRI and post-CRT (with two AB-MRI protocols) data included measurements of lesion length, lesion width, lymph node size, tumor stage, CRM, EMVI, mucoid accumulation in the lumen (MAIN), extramural extension, mucinous response, MRF involvement, and MRI-based tumor regression grade (mrTRG). TNM classification was used for staging rectal cancer (7). Additionally, the reliability and concordance of the AB1 and AB2 protocols in assessing tumor response were analyzed.

mrTRG was classified based on four grades: Grade 1 (significant fibrosis but no residual tumor), grade 2 (significant

fibrosis and minimal residual tumor), grade 3 (fibrosis and tumor) and grade 4 (significant residual tumor and minimal fibrosis). EMVI was defined as positive when minimal or <25% fibrotic change was detected on the treated tumor component within the extramural venous structure. Mucinous response was categorized as poor (i.e., the tumor remained non-mucinous or mucinous after treatment) or good (i.e., there was a non-mucinous to mucinous conversion after treatment or the presence of tumor cell necrosis with mucinous structures persisting between them).

MRI protocol. Prior to medical treatment and following neoadjuvant CRT, MRI was conducted using a 3 Tesla MRI system (GE Healthcare Discovery MR750, Waukesha, WI) and a pelvic phased-array surface coil (eight-channel body coil). The contrast agent gadobutrol (Gadovist; Bayer AG) was injected and the remaining contrast agent in the catheter used for MRI was flushed with 20 ml of saline to flush the remaining contrast agent from the catheter after the contrast injection at a flow rate of 2 ml/sec at 0.1 mmol/kg body weight. Post-contrast T1-WI was obtained approximately 2 min after the injection of the contrast age.

The MRI protocol for staging rectal cancer and evaluating treatment response included the following sequences: axial FS T1-W imaging, axial non-fat-saturated T2-W imaging, axial fat-saturated T2-W imaging, postcontrast fat-saturated T1-W imaging, coronal fat-saturated T2-W imaging, sagittal high-resolution DWI, and axial DWI. For the purpose of response assessment, abbreviated protocols created from the full MRI protocol were AB1, consisting of T2-WI and DWI, and AB2, consisting of post-contrast axial FS T1-WI and axial DWI.

Statistical analysis. Statistical analysis was performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp.). The conformity of the variables to the normal distribution was examined visually (histogram and probability graphs) and using the Kolmogorov-Smirnov method. The Friedman test was used to compare the difference between continuous variables, with Bonferroni's correction for pairwise results. The McNemar test was used to assess the statistical difference for related categorical variables. Reliability analysis was performed using the intraclass correlation test with consideration of intraclass correlation coefficient (ICC) values <0.5, between 0.5 and 0.75, between 0.75 and 0.9, and >0.9, to indicate poor, moderate, good and excellent reliability, respectively. Agreement between the AB1 and AB2 protocols was analyzed using Cohen's κ coefficient values and interpreted as poor (<0.20), fair (0.20-0.40), moderate (0.41-0.60), good (0.61-0.80) and very good (0.81-1.00). Absolute agreement was calculated as the percentage of the same results for the variables. Data are expressed as the median, confidence interval (CI) and n (%) where appropriate. P<0.05 was considered to indicate a statistically significant difference.

Results

Patients. The median patient age was 58 years (range, 37-85 years), and 54.8% of the patients were male. The histological subtype was adenocarcinoma in 90.3% of the patients, and surgical metastatic lymphanedopathy (LAP) was noted in 43.5% of the patients (Table I).

Table I. Demographic characteristics.

Characteristic	Value
Age, years[a]	58 (37-85)
Sex, n (%)	
Female	28 (45.2)
Male	34 (54.8)
Histological subtype, n (%)	
Adenocarcinoma	56 (90.3)
Mucinous cancer	6 (9.7)
Surgical metastatic LAP, n (%)	
No	35 (56.5)
Yes	27 (43.5)
Residual tumor[a] mm	29.5 (0-124)
ADC, mm^2/sec[a]	
Pre-treatment	0.91 (0.50-1.58)
Post-treatment	1.21 (0.13-1.8)

[a]Data are presented as median (range). LAP, lymphadenopathy; ADC, apparent diffusion coefficient.

Tumor response to neoadjuvant CRT. As shown in Figs. 1 and 2, and Table II, the post-CRT AB1 and AB2 protocols revealed increases in the percentages of T0-T2 stage tumors (from 0% for pretreatment to 22.5% for AB1 and 24.2% for AB2) and decreases in the percentages of T4a (from 38.7 to 17.7% for AB1 and 19.4% for AB2) and T4b (from 11.3 to 0.0% for both AB1 and AB2) stage tumors. There were also decreases in the rate of lymph node positivity (from 90.3 to 50.0% for AB1 and 51.6% for AB2), CRM involvement (from 72.6 to 38.7% for both protocols), MRF involvement (from 58.1 to 38.7% for AB1 and 42.0% for AB2), EMVI (from 72.6 to 48.4% for AB1 and 38.7% for AB2), MAIN (from 40.3 to 17.7% for AB1 and 14.5% for AB2) and extramural extension (from 61.3 to 43.5% for AB1 and 41.9% for AB2).

As shown in Table II, the rate of poor mucinous response was 48.4% for the pretreatment MRI and 85.5 and 29.0% for the post-CRT AB1 and AB2 protocols, respectively. Post-CRT mrTRG was at grade 3 in nearly half of the imaging assessed by the AB1 (43.5%) and AB2 (46.8%) protocols.

Lesion and lymph node characteristics. As shown in Table III, the post-CRT AB1 and AB2 protocols revealed significant decreases in median lesion length from 63 mm (range, 28-132 mm) for pretreatment MRI to 37.5 mm (range, 0-128 mm) for AB1 and 37.5 mm (range, 0-120 mm) for AB2 (both P<0,001). There were also significant decreases in lesion width from 19 mm (range, 12-56 mm) to 14.0 mm (range, 0-23 mm) and 12 mm (range, 0-24 mm), respectively (both P<0.05), and significant decreases in lymph node size from 9 mm (range, 0-19 mm) to 6 mm (0-14 mm) and 6 mm (range, 0-13 mm), respectively (both P<0.05).

Reliability and agreement analysis for the AB1 and AB2 protocols. As shown in Table IV, the post-CRT AB1 and AB2 protocols had excellent reliability in identifying lesion

Table II. Tumor response to neoadjuvant chemoradiotherapy.

		Post-treatment AB-MRI protocol	
Parameter	Pretreatment	AB1 (T2-WI and DWI)	AB2 (post-contrast FS T1-WI and DWI)
Tumor stage, n (%)			
0	0 (0.0)	1 (1.6)	0 (0.0)
1	0 (0.0)	2 (3.2)	3 (4.8)
2	0 (0.0)	11 (17.7)	12 (19.4)
3a	1 (1.6)	3 (4.8)	2 (3.2)
3b	10 (16.1)	21 (33.9)	20 (32.3)
3c	14 (22.6)	4 (6.5)	6 (9.7)
3d	6 (9.7)	9 (14.5)	7 (11.3)
4a	24 (38.7)	11 (17.7)	12 (19.4)
4b	7 (11.3)	0 (0.0)	0 (0.0)
Lymph node positivity, n (%)			
No	6 (9.7)	31 (50.0)	30 (48.4)
Yes	56 (90.3)	31 (50.0)	32 (51.6)
CRM involvement, n (%)			
No	17 (27.4)	38 (61.3)	38 (61.3)
Yes	45 (72.6)	24 (38.7)	24 (38.7)
MRF involvement, n (%)			
No	26 (41.9)	38 (61.3)	36 (58.1)
Yes	36 (58.1)	24 (38.7)	26 (41.9)
EMVI, n (%)			
No	17 (27.4)	32 (51.6)	38 (61.3)
Yes	45 (72.6)	30 (48.4)	24 (38.7)
MAIN, n (%)			
No	37 (59.7)	51 (82.3)	53 (85.5)
Yes	25 (40.3)	11 (17.7)	9 (14.5)
Extramural extension, n (%)			
No	24 (38.7)	35 (56.5)	36 (58.1)
Yes	38 (61.3)	27 (43.5)	26 (41.9)
Mucinous response, n (%)			
Poor	30 (48.4)	53 (85.5)	18 (29.0)
Good	32 (51.6)	9 (14.5)	44 (71.0)
mrTRG, n (%)			
Grade 1 (significant fibrosis, no residue tumor)		5 (8.1)	5 (8.1)
Grade 2 (significant fibrosis, minimal residue tumor)		13 (21.0)	15 (24.2)
Grade 3 (fibrosis and tumor)		27 (43.5)	29 (46.8)
Grade 4 (significant residual tumor, minimal fibrosis)		17 (27.4)	13 (21.0)

AB, abbreviated; T2-WI, T2-weighted imaging; T1-WI, T1-weighted imaging; DWI, diffusion-weighted imaging; FS, fat-suppressed; CRM, circumferential resection margin; EMVI, extramural venous invasion; MAIN, mucoid accumulation in lumen; MRF, mesorectal fascia; mrTRG, MRI-based tumor regression grade; MRI, magnetic resonance imaging.

length (ICC, 0.988; 95% CI, 0.980-0.993; P<0.001), lesion width (ICC, 0.972; 95% CI, 0.953-0.983; P<0.001) and lymph node size (ICC, 0.979; 95% CI, 0.963-0.988; P<0.001). Cohen's κ coefficient indicated very good agreement between the AB1 and AB2 protocols in terms of identifying lymph node positivity (κ, 0.903; absolute agreement, 95.2%), CRM involvement (κ, 0.864; absolute agreement, 93.5%), EMVI (κ, 0.805; absolute agreement, 90.3%), MAIN (κ, 0.881; absolute agreement, 96.8%) and MRF involvement (κ, 0.838; absolute agreement, 91.9%). There was good agreement between the AB1 and AB2 protocols in identifying extramural extension (κ, 0.769; absolute agreement, 88.7%). However, no agreement was observed between the protocols in terms of identifying mucinous response (κ, 0.084; absolute agreement, 41.9%).
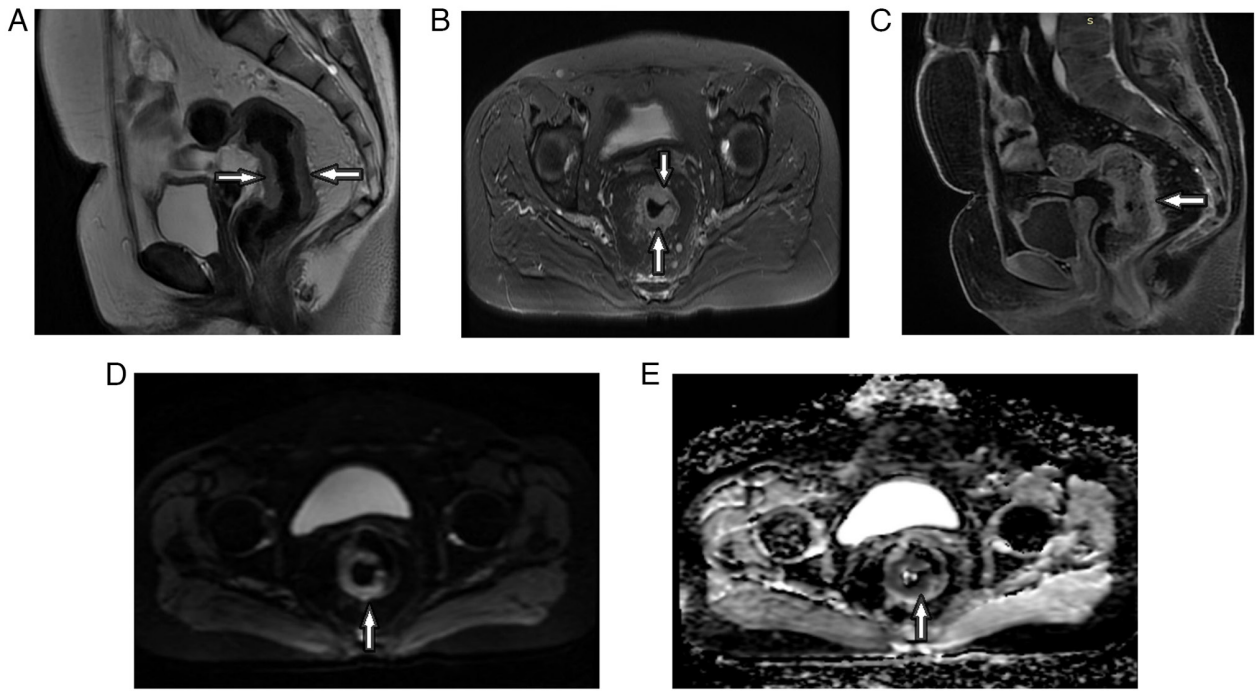
Figure 1. (A) Sagittal and (B) Axial T2-weighted, (C) Post-contrast sagittal and T1-weighted MRI of a 53-year-old female patient with the complaint of rectal bleeding, who was found to have a polypoid mass lesion in the middle part of the rectum in colonoscopy and who had a family history of rectal cancer. (D) Diffusion-weighted imaging MRI of the rectum (E) Apparent diffusion coefficient value MRI of the rectum.The rectum wall thickness is 12 mm in the 45 mm long segment in the middle 1/3, and increased wall thickness, linear intensities compatible with extramural venous invasion, and metastatic lymph nodes, the largest of which is 12x7 mm, are observed.A mass lesion with medium-level signal intensity and diffusion restriction is observed (T4N1 and the pathology result was interpreted as rectal adenocarcinoma.
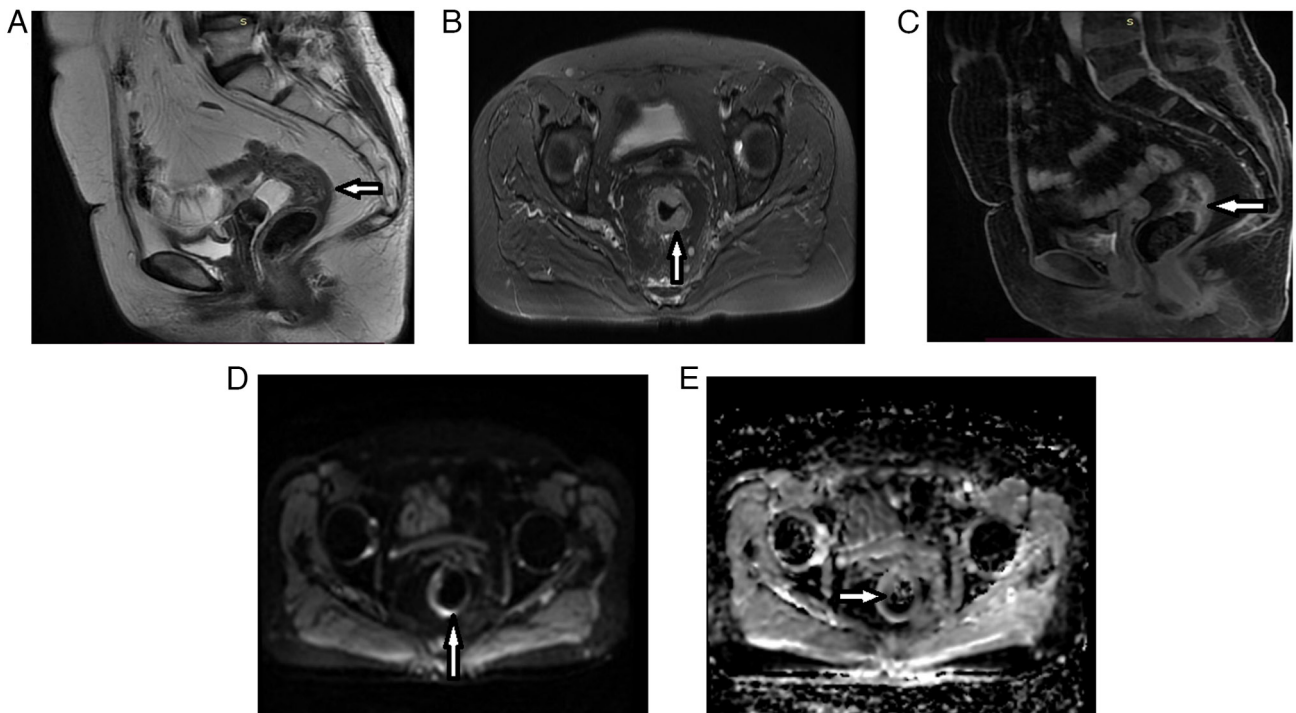

Figure 2. (A) Post-neoadjuvant chemoradiotherapy sagittal and (B) Axial T2-weighted, (C) Postcontrast sagittal T1-weighted MRI of the same patient (Fig.1) (D) Diffusion weighted imaging MRI of the rectum (E) Apparent diffusion coefficient value MRI of the rectum. A mass lesion with lymph nodes extending to the mesorectal fascia (MRF), extramural venous invasion (EMVI), decrease in revtal wall thickness and mrTRD 3 is observed in the middle part of the rectum. The pathological stage of the patient who underwent low anterior resection was reported as pT2NOMx.

Cross-analysis of the pretreatment and post-CRT protocols. As shown in Figs. 3, and 4, and Table V, the post-CRT AB1 and AB2 protocols revealed similar improvements in lymph node positivity (disappeared after CRT in 44.6 and 42.8% of

Table III. Lesion and lymph node characteristics.

| | | Post-treatment AB-MRI protocol | | |
Characteristic	Pretreatment	AB1 (T2-WI and DWI)	AB2 (post-contrast FS T1-WI and DWI)	P-value
Lesion length along long axis mm (n=62)	63.0 (28.0-132.0)	37.5 (0-128.0)[a]	37.5 (0-120.0)[a]	<0.001[b]
Lesion width mm (n=62)	19.0 (12.0-56.0)	14.0 (0-23.0)[a]	12.0 (0-24.0)[a]	<0.001[b]
Lymph node size mm (n=53)	9.0 (0-19.0)	6.0 (0-14.0)[a]	6.0 (0-13.0)[a]	<0.001[b]

[a]$P<0.05$ vs. pretreatment values. [b]Friedman's test with Bonferroni corrected P-values for pairwise comparisons (significance at $P<0.017$. Data are presented as median (range). AB, abbreviated; T2-WI, T2-weighted imaging; T1-WI, T1-weighted imaging; DWI, diffusion-weighted imaging; FS, fat-suppressed; MRI, magnetic resonance imaging.

Table IV. Reliability and agreement analysis for abbreviated magnetic resonance imaging protocols.

| | AB1 (T2-WI and DWI) and AB2 (post-contrast FS T1-WI and DWI) | |
Parameters	ICC (CI)	P-value[a]
Lesion length mm	0.988 (0.980-0.993)	<0.001
Lesion width, mm	0.972 (0.953-0.983)	<0.001
Lymph node size mm	0.979 (0.963-0.988)	<0.001

Parameters	Cohen's κ value	Absolute agreement, %	P-value[b]
Lymph node positivity	0.903	95.2	<0.001
CRM involvement	0.864	93.5	<0.001
EMVI	0.805	90.3	<0.001
MAIN[a]	0.881	96.8	<0.001
Extramural extension	0.769	88.7	<0.001
MRF involvement	0.838	91.9	<0.001
Mucinous response	0.084	41.9	0.190

[a]Intra class correlation test; [b]κ test. AB, abbreviated; T2-WI, T2-weighted imaging; T1-WI, T1-weighted imaging; DWI, diffusion-weighted imaging; FS, fat-suppressed; ICC, intra class coefficient; CI, confidence interval; CRM, circumferential resection margin; EMVI, extramural venous invasion; MAIN, mucoid accumulation in lumen.

patients, respectively), CRM involvement (disappeared in 48.6 and 46.0% of patients, respectively), and MRF involvement (disappeared in 41.7 and 38.9% of patients, respectively). The AB1 and AB2 protocols yielded lower rates of improvement for EMVI (disappeared in 33.3% vs. 46.7% of patients, respectively), MAIN (disappeared in 60.0% vs. 68.0% of patients, respectively), and, especially, mucinous response.

Cross-analysis of the pretreatment and post-CRT protocols. As shown in Table VI, the post-CRT AB1 and AB2 protocols revealed had lower recovery rates for mucoid response (lost in 10.3 and 48.3% of patients, respectively).

Cross-analysis of the AB1 and AB2 protocols. As shown in Table VII, with regard to patients with lymph node positivity, MRF involvement, CRM involvement, mucinous response, extramural extension, MAIN and EMVI in the AB1 protocol, the AB2 protocol confirmed the findings in

96.8, 95.8, 91.7, 88.9, 85.2, 81.8 and 80.0% of the patients, respectively.

Discussion

In the present study, some of the patients who received neoadjuvant CRT experienced improvements in clinical and pathological outcomes, such as reductions in tumor, lesion and lymph node sizes, and decreases in lymph node positivity, CRM and MRF involvement, EMVI, MAIN. These findings suggest that neoadjuvant CRT supports sphincter-sparing surgery and even nonsurgical treatment approaches in some cases, alongside tumor shrinkage (in over 50% of cases) and pathological complete response (pCR) (in 15-38% of cases) (7,8). Therefore, the use of an abbreviated rectal MRI protocol via T2-W and DWI or postcontrast FS T1-W and DWI series facilitates the assessment of tumor response after neoadjuvant CRT in rectal cancer patients. It also allows
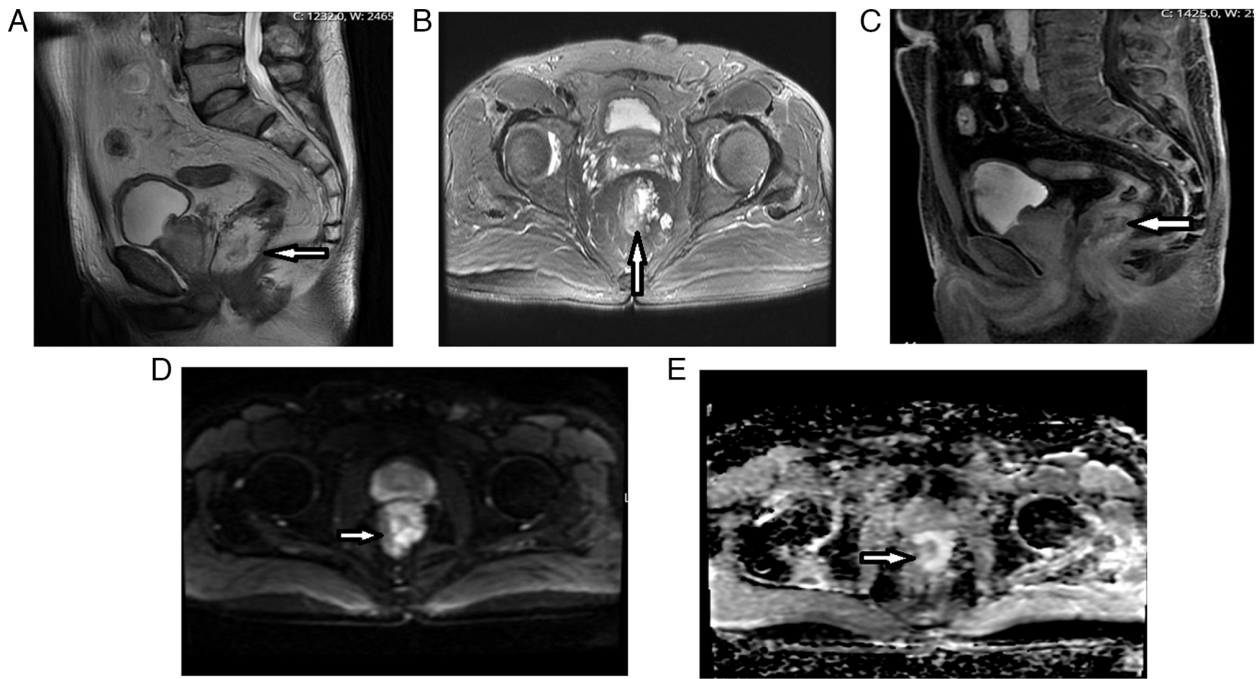
Figure 3. (A) Sagittal and (B) axial T2-weighted MRI of a 64-year-old male patient with a polypoid mass lesion in the lower part of the rectum that did not allow colonoscopy to pass, admitted with complaints of rectal bleeding and inability to pass gas-stool, and no family history of rectal cancer. (C) Postcontrast sagittal T1-weighted MRI (D) Diffusion-weighted imaging MRI of the rectum (E) Apparent diffusion coefficient value MRI of the rectum. In the lower part of the rectum, the rectum is 50 mm long, 17 mm thick, extending to the mesorectal fascia (MRF) and extramural venous invasion (EMVI) is observed, and multibl lymph nodes reaching 14x8 mm in size in the left mesorectum are detected in T2-weighted series. A mass lesion showing signal intensity and diffusion restriction is observed (T4N1). The pathology result was interpreted as adeno ca containing mucinous component.
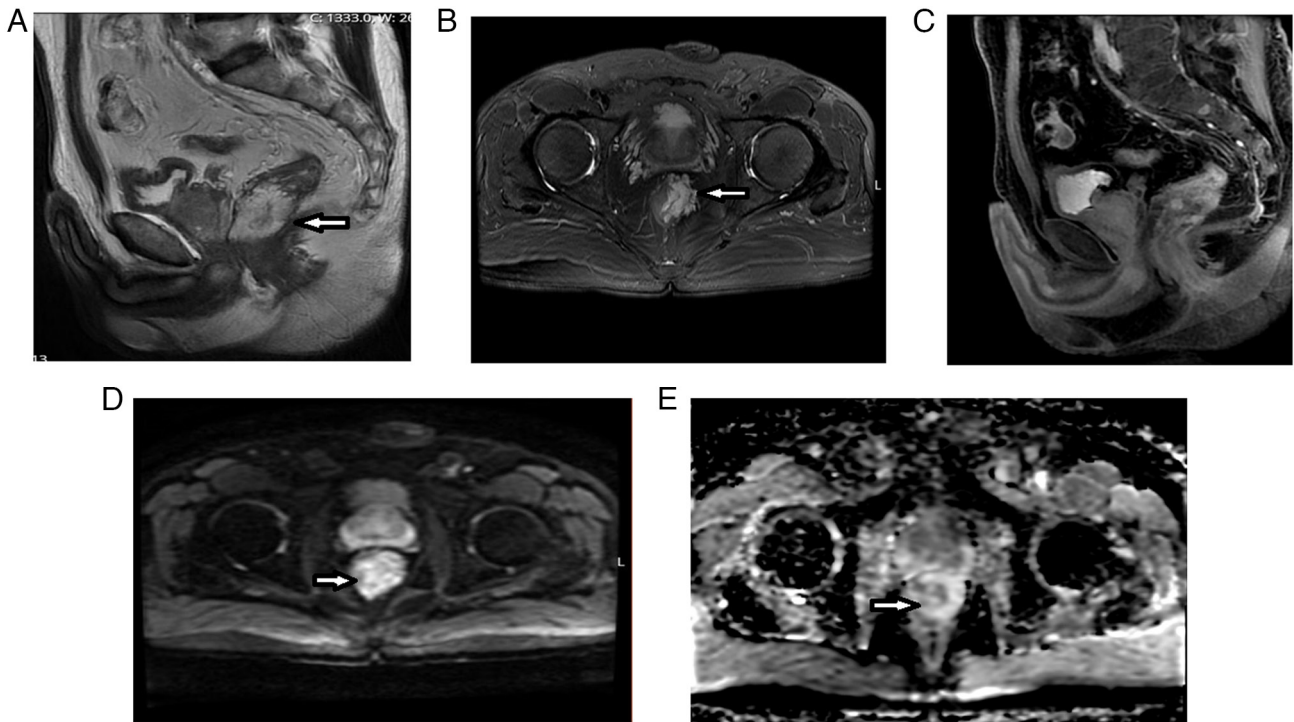

Figure 4. (A) Post-neoadjuvant CRT sagittal (B) Axial T2-weighted, (C) Postcontrast sagittal T1-weighted MRI of male patient from Fig. 3 (D) Diffusion weighted imaging MRI of the rectum (E) Apparent diffusion coefficient value MRI of the rectum In the lower part of the rectum, a lesion, which was evaluated as MRI-based tumor regression grade 4, showing high signal intensity and diffusion restriction, is observed in T2-weighted series that does not respond to treatment after CRT, which surrounds the rectum. The pathological stage was reported as pT4N1Mx. MRI, magnetic resonance imaging; CRT, chemoradiotherapy.

for a reduction in examination time without compromising imaging quality during post-CRT follow-up.

Diffusion-weighted imaging (DWI) is considered an optional MRI sequence that is sensitive to the movement

Table V. Cross-analysis of pretreatment and post-treatment protocols.

| | Post-treatment AB-MRI protocol | | | |
| | AB1 (T2-WI and DWI) | | AB2 (post-contrast FS T1-WI and DWI) | |
Pretreatment MRI	No	Yes	No	Yes
Lymph node positivity (n=62)				
No (n=6)	6 (100.0)	0 (0.0)	6 (100.0)	0 (0.0)
Yes (n=56)	25 (44.6)	31 (55.4)	24 (42.9)	32 (57.1)
P-value[a]	<0.001		<0.001	
CRM involvement (n=62)				
No (n=25)	20 (80.0)	5 (20.0)	21 (84.0)	4 (16.0)
Yes (n=37)	18 (48.6)	19 (51.4)	17 (45.9)	20 (54.1)
P-value[a]	0.011		0.007	
EMVI (n=62)				
No (n=17)	17 (100.0)	0 (0.0)	17 (100.0)	0 (0.0)
Yes (n=45)	15 (33.3)	30 (66.7)	21 (46.7)	24 (53.3)
P-value[a]	<0.001		<0.001	
MAIN (n=62)				
No (n=37)	36 (97.3)	1 (2.7)	36 (97.3)	1 (2.7)
Yes (n=25)	15 (60.0)	10 (40.0)	17 (68.0)	8 (32.0)
P-value[a]	0.001		<0.001	
Extramural extension (n=62)				
No (n=24)	23 (95.8)	1 (4.2)	22 (91.7)	2 (8.3)
Yes (n=38)	12 (31.6)	26 (68.4)	14 (36.8)	24 (63.2)
P-value[a]	0.003		0.004	
MRF involvement (n=62)				
No (n=26)	23 (88.5)	3 (11.5)	22 (84.6)	4 (15.4)
Yes (n=36)	15 (41.7)	21 (58.3)	14 (38.9)	22 (61.1)
P-value[a]	0.008		0.031	

[a]McNemar test .AB, abbreviated; T2-WI, T2-weighted imaging; T1-WI, T1-weighted imaging; DWI, diffusion-weighted imaging; FS, fat-suppressed; CRM, circumferential resection margin; EMVI, extramural venous invasion; MAIN, mucoid accumulation in lumen; MRF, mesorectal fascia; MRI, magnetic resonance imaging.

Table VI. Cross-analysis of pretreatment and post-treatment protocols.

| | Post-treatment AB-MRI protocol | | | |
| | AB1 (T2-WI and DWI) | | AB2 (post-contrast FS T1-WI and DWI) | |
Mucinous response (n=62)	Poor	Good	Poor	Good
Good (n=33)	27 (81.8)	6 (18.2)	4 (12.1)	29 (87.9)
Poor (n=29)	26 (89.7)	3 (10.3)	15 (51.7)	14 (48.3)
P-value[a]	0.353		<0.001	

[a]McNemar test.

of water molecules *in vivo* and is used for tumor and lymph node detection in primary staging (2,6). The movement caused by diffusion is influenced by the characteristics of tissues and cells, the integrity of cell membranes, and the

Table VII. Cross analysis of AB1 and AB2 protocols.

AB1 (T2-WI and DWI)	AB2 (post-contrast FS T1-WI and DWI)	
	No	Yes
Lymph node positivity (n=62)		
No	29 (93.5)	2 (6.5)
Yes	1 (3.2)	30 (96.8)
P-value	1.0	
CRM involvement (n=62)		
No	36 (94.7)	2 (5.3)
Yes	2 (8.3)	22 (91.7)
P-value	>0.999	
EMVI (n=62)		
No	32 (100)	0 (0)
Yes	6 (20.0)	24 (80.0)
P-value	0.031	
MAIN (n=62)		
No	51 (100)	0 (0)
Yes	2 (18.2)	9 (81.8)
P-value	0.500	
Extramural extension (n=62)		
No	32 (91.4)	3 (8.6)
Yes	4 (14.8)	23 (85.2)
P-value	>0.999	
MRF involvement (n=62)		
No	35 (92.1)	3 (7.9)
Yes	1 (4.2)	23 (95.8)
P-value	0.625	
Mucinous response (n=62)		
Good	1 (11.1)	8 (88.9)
Poor	18 (34.6)	35 (63.4)
P-value	0,111	

Data were analyzed by McNemar test AB abbreviated; T2-WI, T2-weighted imaging; T1-WI, T1-weighted imaging; DWI, diffusion-weighted imaging; FS, fat-suppressed; CRM, circumferential resection margin; EMVI, extramural venous invasion; MAIN, mucoid accumulation in lumen; MRF, mesorectal fascia.

viscosity of fluids. This type of imaging can be particularly useful in the restaging of tumors after CRT (6,8,24-27). This is because patients who respond to treatment often develop fibrosis or necrosis accompanied by a decrease in cellular density, (which leads to an increase in the apparent diffusion coefficient (ADC) value (5,28,29). ADC is a quantitative parameter used to assess the magnitude of water diffusion movement within tissues and provides information related to tissue cellularity. ADC values have been proven to be associated with tumor cellularity and grade. ADC parameters have been validated as potential predictors for early therapeutic response in various types of cancer, including head and neck cancer, Hodgkin lymphoma, lung cancer, breast cancer, and prostate cancer (2).

DCE-MRI studies of rectal cancer have been recognized as significant for pre- and post-CRT staging (15). While contrast-enhanced T1-W imaging does not contribute to an increase in diagnostic accuracy in the local staging of rectal cancer, it can be particularly useful during post-CRT staging. This type of imaging helps radiologists better identify local recurrence and assess common iliac and lower para-aortic nodes and incidental pelvic findings. Additionally, it has proven valuable in cases of mucinous neoplasms where T2 signal intensities might closely resemble those of fat (5,6,15,30).

Indeed, a morphological and functional evaluation combining the T2-W sequence with DWI and DCE-MRI sequences has been shown to be useful in assessing post-CRT tumor response in rectal cancer patients (5,12,15-18). Likewise, besides the excellent reliability and very good agreement between the AB1 and AB2 protocols in identifying several tumor response criteria in the present study, the AB2 protocol yielded significantly higher percentages of disappearances of EMVI and MAIN and poor mucinous response after CRT compared to the AB1 protocol. These findings seem to support the suggested value of including DWI and T1-W sequences in addition to T2-W sequences in the MRI-based restaging of rectal cancer patients (5,6).

The mrTRG scores provide important information in follow-up evaluations after CRT. The theoretical success of pCR is higher in patients with mrTRG 1 and 2, and these individuals show improved disease-free survival and overall survival compared with those with higher-grade mrTRG (9,11,31,32). In the present study, the post-CRT AB1 and AB2 protocols yielded similar results regarding the prevalence of mrTRG 1 (8.1% for each) and 2 (21.0% for AB1 and 24.2% for AB2). This suggests that at least one-third of our advanced-stage rectal cancer patients could become candidates for organ-preserving treatments after neoadjuvant CRT. However, post-CRT MRI is not reliable for making determinations about more radical surgical dissection or organ-preserving strategies due to its inadequacy in distinguishing between residual viable tumors and CRT-related changes (such as edema, necrosis, and, especially, fibrotic changes). Therefore, T2-W imaging carries a risk of tumor overstaging because CRT-induced fibrotic changes (low signal intensity on T2-W images) at the interface between the tumor and mesorectal fat as well as CRT-induced submucosal edema (thickened and intermediate to high signal intensity on T2-W images) on the rectal wall adjacent to the tumor can be misinterpreted as residual tumors (6,11,20,29).

Although fibrotic changes manifest as reduced signal intensity on T2-W images, the dark signal intensity observed on MRI does not solely indicate fibrotic change; approximately 50% of viable residual tumor may remain in the fibrotic tissue (12,31-34). Hence, determining tumor relationships with the surrounding structures on the sole basis of T2 signal intensity changes is likely to jeopardize oncologic safety. Meanwhile, supplementary functional MRI sequences, such as DWI, have yielded encouraging outcomes in the MRI-based restaging of tumors by distinguishing between residual tumor (manifesting as high signal intensity on DWI) and fibrosis (manifesting as low signal intensity on high b-value DWI) (6,11,14,33,34). Notably, our findings revealed considerable tumor downstaging due to the post-CRT AB1 and AB2 protocols, including increases

in T0-T2 stage tumors (to 22.5 and 24.2%, respectively) and decreases in T4a (from 38.7 to 17.7 and 19.4%, respectively) and T4b (from 11.3 to 0.0%) stage tumors. These results seem notable given that the AB1 and AB2 protocols both included DWI and that DWI-based restaging has been shown to have improved sensitivity and offers a solution for overcoming the risk of tumor overstaging in T2-W imaging (20,29).

In addition to the frequent intermixing of fibrosis (i.e., decreased T2-W signal intensity) with viable tumor tissues, the development of a mucinous response (i.e., increased T2-W signal intensity) after CRT in rectal tumors challenges the prediction of residual tumor viability in T2-W MRI protocols (11,14,35). Following CRT, non-mucinous tumors have the potential to transform into mucinous tumors, presenting with a mucinous (or colloid degeneration) response. This response signals a positive reaction to treatment and a more favorable prognosis. In contrast, mucinous tumors can exhibit an acellular mucin response (i.e., a pathological response specific to mucinous tumors) without affecting recurrence-free survival, or they may not respond to CRT, resulting in an elevated risk of local recurrence and a poorer outcome (6,20,36). In the present study, a conversion from a poor mucinous response to a good mucinous response was observed in 3 out of 29 patients (10.3%) based on pretreatment MRI and 14 out of 29 patients (48.3%) based on the post-CRT AB1 and AB2 protocols, indicating a significant discrepancy between the AB1 and AB2 protocols in detecting changes in mucinous status. The presence of intermingled tumor cells with fibrosis and mucin is likely the reason behind the low level of agreement between mrTRG and pathological tumor regression grade (pTRG) (11,37).

The very good agreement in determining CRM involvement between the AB1 and AB2 protocols is important given that CRM is one of the key components in determining the rate of local tumor recurrence after CRT; Positive CRM involvement has been observed in 25-26% of patients with CRM in previous studies (9,11,38). In addition, the protocols had very high concordance in terms of MRF involvement in the current study, which seems important as applying MRF involvement in addition to CRM (implementation of distance from MRF) is likely to overcome certain limitations of post-CRT MRI in detecting positive CRM [i.e., low positive predictive value (PPV)], making more aggressive and additional treatment unnecessary (11,34,39-41).

The potential utility of DWI in predicting tumor clearance at the MRF after CRT has been documented. The positive predictive value (PPV) of the AB 1 protocol for MRF involvement was higher (82-91%) compared to T2W imaging alone (30-45%) (42). In this context, the presence of CRM and MRF involvement in the post-CRT AB1 (38.7% for each) and AB2 (38.7% for CRM and 42.0% for MRF) protocols is noteworthy. This finding is significant due to the potential introduction of additional treatment options, such as extramesorectal excision or multivisceral resection, boost radiotherapy at the site of MRF invasion, and upfront chemotherapy. This is also true for patients who are CRM and MRF positive after CRT (11).

The post-CRT AB1 and AB2 protocols revealed comparable enhancements in lymph node positivity, which disappeared after CRT in 44.6 and 42.8% of the patients, respectively. Additionally, there were significant reductions in lymph node size, which decreased from a median of 9 to 6 mm for each protocol. These results suggest that a substantial number of

irradiated lymph nodes might vanish following CRT. Reliable predictors of negative node status after surgery include a reduction in lymph node size of at least 70% and a nodal size of less than 2.5 mm in the short axis (6,43,44).

Persistent EMVI on post-CRT MRI has been shown to increase the risk of metastatic disease and to serve as an independent negative prognostic marker for disease-free survival; regression or persistence of EMVI after neoadjuvant therapy has been associated with improved survival (45,46). In the present study, the AB1 and AB2 protocols showed the disappearance of EMVI in 33.3 and 46.7% of patients who had EMVI on pretreatment MRI, respectively. Furthermore, regarding patients who had EMVI or MAIN according to the AB1 protocol, the AB2 protocol revealed the absence of EMVI and MAIN in 20% of those cases, indicating a potential discordance between the AB1 and AB2 protocols in the detection of changes in EMVI and MAIN.

Post-CRT MRI is regarded as the primary option for assessing treatment response. It not only functions as a surgical roadmap but also helps identify complete responders and facilitate organ-preserving treatments. However, current MRI techniques have certain limitations in evaluating post-CRT treatment response, jeopardizing the reliability and safety of tumor response evaluation. Furthermore, the use of post-CRT MRI-based data to inform treatment strategies remains controversial (11,14). Given the risk of radiological interpretation resulting in either a faulty decision for organ-preserving treatment or unnecessary radical surgery, improved knowledge of specific morphology and diffusion signal patterns and the complementary use of functional MRI sequences (such as DWI) in addition to morphological (T2-W) MRI are important for increasing post-CRT MRI's ability to identify complete responders and ensuring the absence of extramural tumor infiltration and residual metastatic lymph nodes (11,14). In this context, the present study's findings on the similar effectiveness of abbreviated post-CRT MRI protocols and the use of DWI, especially in determining CRM and MRF involvement, are significant.

The present study has some limitations. The main limitation is the lack of data on tumor response on post-CRT AB protocols in relation to postoperative pathological findings. Additionally, the impact of tumor histological findings and subtype on treatment response with each MRI protocol, as well as the assessment of residual tumor size based on the largest dimension rather than the three-dimensional volume measurement, are limitations that otherwise would extend the knowledge obtained in the current study.

In conclusion, the use of an abbreviated rectal MRI protocol has been shown to be a reliable method for evaluating tumor response in patients with rectal cancer following neoadjuvant CRT. Both AB protocols demonstrated excellent reliability and good to very good agreement in identifying improved outcomes in post-CRT clinicopathological results, including reductions in lesion length, lesion width, lymph node size, lymph node positivity, CRM involvement, EMVI, MAIN and MRF involvement. However, there were variations in the diagnostic performance of the T2-WI and T1-WI sequences in the detection of changes in EMVI, MAIN and, especially, mucinous response. Larger-scale prospective studies in patients with LARC are needed to evaluate the comparative effectiveness of AB-MRI protocols

and to assess how specialized sequences could overcome MRI limitations in accurately assessing treatment response.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

FT and YM confirm authenticity of all the raw data. FT conceived the study and reviewed the manuscript. YM conceived the study and analyzed data. NOM analyzed data. SR designed the experiments and wrote the manuscript. MGG interpreted data. ET performed experiments, interpreted data and wrote and reviewed the manuscript. All authors have read and approved the manuscript.

Ethics approval and consent to participate

The study was evaluated and approved by Erdogan University Faculty of Medicine Non-interventional Clinical Research Ethics Committee (approval no. 2022/134). The principles outlined in the Declaration of Helsinki have been followed.

Patient consent for publication

Informed consent was obtained from the participants whose images were used in the publication. Consent was obtained before MRI and for use of images for study purposes.

Competing interests

The authors declare that they have no competing interests.

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