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Pre and postoperative magnetic resonance imaging for evaluation of cancer rectum

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Abstract
Background: Colorectal carcinoma (CRC) ranked as the second most prevalent form of cancer among individuals. Diagnostic imaging helps in planning before surgery by establishing a relationship between the carcinoma's mass and the surrounding anatomy, which consequently helps in selecting the optimal surgical approach and limiting the probability of injury to the neighboring structures. It could additionally help in estimating and predicting the therapeutic response and detecting the recurrence of the tumor. MR imaging has proven to be the most prevalent cross-sectional imaging technique for post-rectal cancer patients' follow-up, it's mainly used to diagnose pelvic cancer recurrence and assess the extent of recurrence, which enables early resection and prolonged survival.
Aim of the work: In the current study, we have attempted to evaluate the role of both functional and dynamic MRI in the staging of patients having cancer in their rectum before surgical operation and following up after it.
Material and Methods: After signing a written consent, thirty patients were enrolled in this prospective clinical trial at Tanta University Hospitals - the Department of Radio Diagnosis and Medical Imaging. Duration from November 2018 to March 2022. All patients had a full patient history**,** medical examination**,** lab investigations (CBC, carbohydrate antigen 19-9 (CA 19-9)**,** Renal function test, and carcinoembryonic antigen(CEA))**,** and dynamic and functional MRI which include: Weighted fast spin echo sequences, pre-contrast three-dimensional T, pre-contrast two-dimensional T, weighted fast gradient echo sequences, pre-contrast two-dimensional proton density-weighted sequences (saturation recovery turbo fast gradient echo, SRTF, or fast gradient echo, FLASH); and Pre- and post-dynamic contrast-enhanced T Weighted SRTF or FLASH sequences MRI examination included: Pre contrast (2D T2 weighted images, 2D T1 weighted images, Diffusion-weighted images. And Post-contrast (T1 weighted images after IV administration of contrast).
Results: The most common location of the tumor found by MRI was in the Middle rectum. MRI findings after chemoradiotherapy of 12 cases revealed a downstaging of cases, 9 of them became eligible for surgery. MRI findings of our studied cases after surgery revealed: 21 studied cases were free-restricted and 4 cases were restricted diffusion, 21(84%) cases had clear operative beds, and 4 (16%) cases had unclear operative beds.
Conclusion: We conclude that post-operative MRI has a golden standard value not only for follow-up post-operative complication and detection of recurrent rectal carcinoma but furthermore for predicting the appropriateness of curative surgery and facilitating decisions on palliative resection, which have a significant impact on survival rate.

Keywords: CRC, MRI, post-operative

Introduction
Rectal cancer is the second-leading cause of cancer in the large intestine and is also considered one of the most widespread malignant neoplasms among individuals.
Colorectal cancers (CRCs) ranked as the second most prevalent cancer for humans and one of the world's biggest public health threats [1].
Every year, several new cases are successfully diagnosed because of increased availability, accessibility, and the use of advanced screening techniques. Rectal cancer treatment and management differ from other tumors occurring in other regions of the digestive tract or even the colon due to the position of the rectum and its neighboring organs [2].
Rectal cancer has clinical signs that are distinct from other tumors of the digestive tract. Rectal cancer has received a lot of attention in recent years as a distinct entity from other regions of the colon in terms of diagnosis and treatment.

These tumors can be detected at an earlier stage with the help of novel imaging techniques. Multiple treatment techniques, such as postoperative and preoperative radio- or chemotherapies, and surgery, have resulted in improved survival rates for patients [2].

Accurate staging is crucial for selecting the best treatment plan and, as a result, achieving the best clinical results. Radiologic tests become more valuable in both rectal cancer staging and the assessment of response to neoadjuvant treatment. Furthermore, imaging enhances preoperative planning by outlining links between the surrounding anatomy and the tumor, establishing the most appropriate surgical approach, and reducing the risk of harm to neighboring tissues [3].

In the context of rectal cancer, magnetic resonance imaging (MRI) is now known as the leading modality of pelvic imaging [4]. The fundamental reason for such dominance is the excellent soft tissue contrast between the surrounding soft tissues and the targeted tumor on T2-weighted MRI, which additionally enables imaging across several planes [5]. Multidisciplinary meetings utilizing MRI have enhanced the chances of choosing the most suitable treatment options for rectal cancer patients [6-9].

MRI reflects the link between a tumor and the mesorectal fascia, which signifies the safe margin of circumferential resection during full mesorectal excision [10], It can also be useful in the prognosis and evaluation of therapeutic response, as well as in detecting tumor recurrence [11].

Furthermore, diffusion-weighted (DW)-MRI and, dynamic contrast-enhanced (DCE)-MRI can be utilized for evaluating treatment's biological and functional impacts [12].

MR imaging has proven to be the most prevalent cross-sectional imaging technique for post-rectal cancer patients' follow-up, it's mainly used to diagnose pelvic cancer recurrence and assess the extent of recurrence, which enables early resection and prolonged survival [13, 14].

Aim of the study

In the current study, we have attempted to evaluate the role of both functional and dynamic MRI in the staging of patients having cancer in their rectum before surgical operation and following up after it.

Patients and Methods

After signing a written consent, thirty patients were enrolled in this prospective clinical trial at Tanta University Hospitals - the Department of Radio Diagnosis and Medical Imaging. Duration from November 2018 to March 2022- about 3 years and 4 months, the age of studied cases was 25-65 years old, 18 (60%) males and 12 (40%) females.

Inclusion criteria: Both sexes were included in the study. Patients with stage I, II or III rectal cancer (rectal adenocarcinoma) who are scheduled for surgical resection. Following -up of patients with rectal cancer who already underwent surgical resection.

Exclusion criteria: Cases who are not fit for surgery. Stage IV cancer rectum cases. Patients with ferromagnetic aneurysm clips. Patients with cochlear or ocular implants. Patients who have metallic foreign bodies. Patients with allergy to contrast media. Patients with implanted pacemakers or defibrillation.

Patients Assessment

All patients had a full patient history, medical examination, lab investigations (CBC, carbohydrate antigen 19-9 (CA 19-9), Renal function test, and carcinoembryonic antigen(CEA)), and dynamic and functional MRI which include: Weighted fast spin echo sequences, pre-contrast three-dimensional T, pre-contrast two-dimensional T, weighted fast gradient echo sequences, pre-contrast two-dimensional proton density-weighted sequences (saturation recovery turbo fast gradient echo, SRTF, or fast gradient echo, FLASH); and Pre- and post-dynamic contrast-enhanced T Weighted SRTF or FLASH sequences MRI examination included: Pre contrast (2D T2 weighted images, 2D T1 weighted images, Diffusion-weighted images. And Post-contrast (T1 weighted images after IV administration of contrast).

Results

Table 1: Distribution of the enrolled patients regarding MRI findings: (n = 28)

MRI findings			No.	%
TNM staging	T	1	8	28.5
		2	12	42.9
		3	8	28.5
N				
		0	16	57.1
		1	10	35.7
		2	2	7.1
Initial status of sphincter affection				
	Intact		23	82.1
	Internal sphincter only invaded		3	10.7
	Internal & external sphincters invaded		2	7.1
Mesorectal fat affected			0	0
Mesorectal fascia included			2	7.1
Extramural vascular invasion			2	7.1
DWI				
	Free		0	0
	Restricted		28	100
ADC				
	High		0	0
	Low		28	100
Dynamic MRI				
	Enhancement		28	100
	NO enhancement		0	0

Table 2: Distribution of the studied cases (group 2) after chemo radiotherapy: (n = 12)

After treatment with neoadjuvant	No.	%
T		
0	1	8.3
1	3	25
2	7	58.3
3	1	8.3
N		
0	10	83.3
1	1	8.3
2	1	8.3
Initial status of sphincter affection		
Intact	11	91.6
Internal sphincter only invaded	1	8.3
Internal & external sphincters invade	0	0
Mesorectal fat affection	0	0
Mesorectal fascia invasion	1	8.3
Extramural vascular invasion	1	8.3
Circumferential resection margin		
Positive	3	25
Negative	9	75
DWI		
Free	1	8.3
Restricted	11	91.6
ADC		
Low	11	91.6
High	1	8.3
Dynamic MRI		
Enhancement	11	91.6
No enhancement	1	8.3

Table 3: Distribution of the studied cases according to MRI finding after surgery (n=25):

After surgery	No.	%
Diffusion weighted		
Restricted	4	16
Free	21	84
ADC		
Low	4	16
High	21	84
Operative bed		
Clear	21	84
Not clear	4	16
Complications		
Positive	8	32
Negative	17	68

Table 4: Proficiency of apparent diffusion coefficient (ADC) detection in rectal cancer diagnosis.

ROC curve between Post and Pre					
Cutoff	Sens.	Spec.	PPV	NPV	Accuracy
<1.2	78.0	90.50	84.7	79.8	83.6%

Case Presentation

Case no (1)

A 60-year-old female complaining of blood from the rectum and diagnosed as having cancer rectum. She underwent chemoradiotherapy for 5 months.

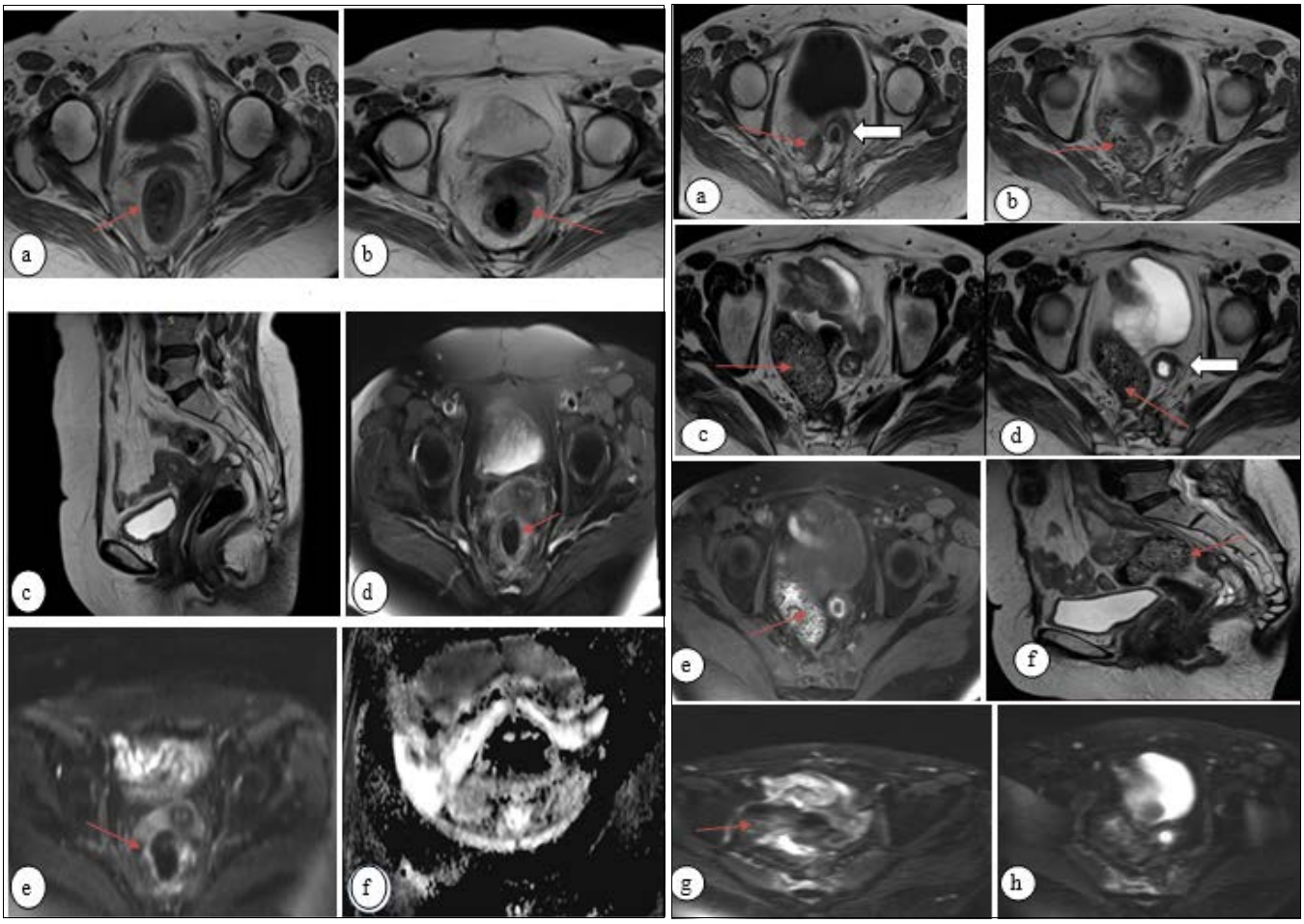
MRI finding

Preoperative

- **Figure (a):** Axial T1WI MRI showing segmental mild circumferential mural thickening involving the upper rectum encroaching on the lumen (red arrow).
- **Figure (b & c):** Axial T2WI MRI and sagittal T2 WI MRI showing nonhomogeneous high T2 signals with nonhomogeneous enhancement at post. Gadolinium series (red arrow).
- **Figure (d):** Axial T1 fatsat showing stranding and fine nodularity of the surrounding mesorectal fat & fascia more at left side. (Red arrow)
- The involved segment measures a maximum length of 5 cm and a maximum thickness of about 1.2 cm.
- **Figure (e & f):** DWI MRI and ADC showing partially restricted diffusion (Red arrow in figure e) with a hypointense signal of rectal mass, a value of about.98 $x10^{-3}$ mm^2/sec.

Post-operative

- **Figure (a, and b):** Axial T1WI MRI showing Segmental Circumferential mild mural thickening involving the upper rectum associated with stranding and fine nodularity of the surrounding mesorectal fat & fascia, that might represent post-operative & therapeutic sequel with the possibility of mild residual/recurrence couldn't be excluded. (White arrow)
- **Figure (c, d, and f):** Axial T2WI and sagittal T2WI showing high resolution of mural thickening with Evidence of surgical removal of the uterus and adenexa.(White arrow)
- Newly developed presacral loculated fluid collection and abnormal soft tissue signal, likely representing post-operative changes with granulation tissue formation rather than metastatic deposits. (Red arrow in figure a, b, c, d, and e)
- **Figure (g, and h):** DWI MRI showing ADC value of about 1.02 x 10-3 mm2/sec and Restricted diffusion. (Red arrow)
- We noticed an improvement in ADC value than its value in preoperative imaging.
- Diagnosis: post-operative and therapeutic sequel.



Pre-operative Post-operative

Case no (2)

A 52-year-old male complaining of bloody rectum and altered bowel habits, was accordingly diagnosed as having a cancer rectum and underwent chemoradiotherapy for 6 months.

MRI finding:

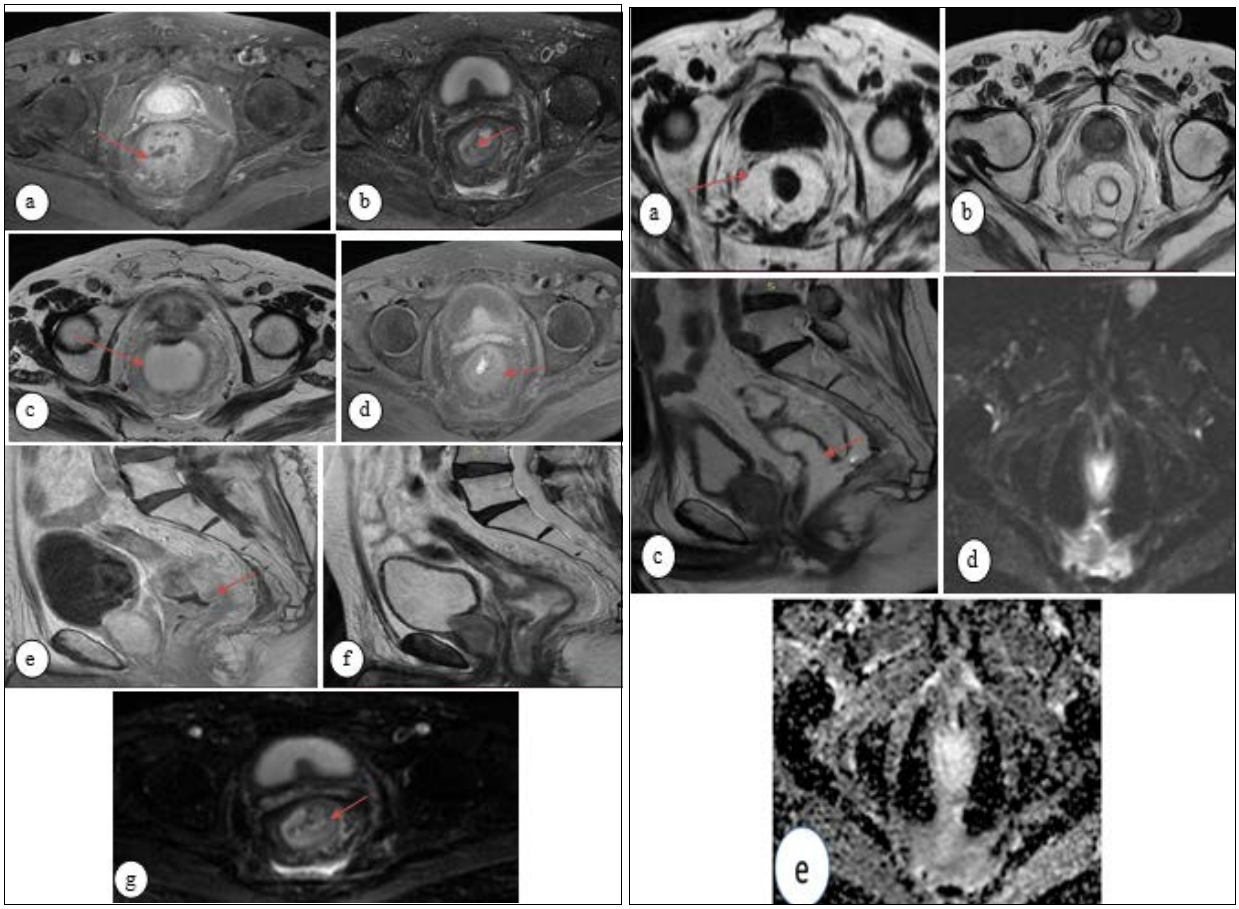
Pre-operative

- Figures (a, and b): Axial low-resolution T1WI MRI and Axial T2WI showing mid rectal polypoidal circumferential mass for around 5.7cm and roughly collectively measures 4x3.5cm in axial plan with maximum one lip thickness of 1.9 cm. (Red arrow)
- Figure (c): Axial T2WI with contrast showing a high bright signal due to post-radiation edema. (Red arrow)
- Figure (d): Axial T1FS showing no mesorectal fascia involvement.
- Figures (e, and f): sagittal T1W1 and sagittal high-resolution T2WI showing the lower edge of the lesion is 7cm from the anal verge. (Red arrow)
- Figure (g): DWI MRI showing ADC value of about $0.97x10^{-3}$ mm^2/sec (hypointense signal) with restricted diffusion (Red arrow).

Postoperative

(a) Axial T1 FSE (b) Axial T2 FST (c)Sagittal T2 FST (d) DWI (e)ADC

- A complete response to surgery with no residual tumor
- Normal T1 and T2
- Figure (d, and e); DWI MRI showing free restriction and ADC value of about 1.38 x10-3 mm2/sec that confirms the total resolution of the tumor.



Pre-operative Post-operative

Discussion

Rectal cancer which is one of the most prevalent malignant tumors of the gastrointestinal tract is considered to be one of the most common cancers in all developed countries. MRI has proven to be the most prevalent cross-sectional imaging technique for the assessment and staging of rectal cancer so it could help surgeons to achieve negative surgical margins. MRI also guarantees an accurate assessment of the sphincter complex and MRF for surgical planning [15].

High-resolution pelvic MRI has become absolutely crucial in rectal cancer staging and therapy decisions. It is also critical in determining the diagnostic accuracy of MRI in predicting the circumferential resection margin (CRM) of rectal cancer before surgical operations [16].

In the current study, we have attempted to evaluate the role of both functional and dynamic MRI in the staging of patients having cancer in their rectum before surgical operation and following up after it.

This study was carried out on 28 patients at the Department of Radio Diagnosis and Medical Imaging, Tanta University Hospital.

The mean age of the enrolled cases was between 31-42 years old with a male predominance of 57.1% and a female of 42.9%, In the study, most of the patients were in the age group of (40-50) years old.

Another study by El-Kady *et al*. (2014) reported a greater age and female predominance [17] since it involved 50 individuals with rectal carcinoma. 27 were females while the rest were males, with a close ratio of 54%:46% respectively. Their ages also varied from 20 to 80 years old, with a mean of 50 years old. The peak age was aimed at the seventh decade. The examination was deemed satisfactory by all patients, with no reports of pain or problems [17].

Additional study by De La Pinta, *et al*. (2019) [16] included about 74 males and 43 females with a total number of 117 enrolled patients with primary cancer in the rectum, where their median age was 67.9 years (ranges between 41- 85 years)

Regarding this study, the main complaint was rectal bleeding in 64.2% of cases, altered bowel habits in 50%, generalized symptoms of cachexia in 35.7%, and abdominal pain in 14.2%

El-Kady *et al*. (2014) similarly reported a relevant point [17]. Their research discovered that almost 94% of these cases complained of rectum bleeding, with 86% also complaining of altered bowel habits. 70% of individuals had widespread cachexia symptoms. While 32% of patients reported abdominal discomfort. None of these individuals presented with intestinal obstruction or remote organ metastasis of unknown primary [17].

Because of the rapid evolution of surgical procedures and shifting to neoadjuvant chemotherapy-radiation therapies, as well as stage T3 tumors prognostic heterogeneity, A precisely correct preoperative staging is crucial, especially in terms of nodal (N) and tumor (T) staging, the tumor's relationship to the potential CRM, and the extent of invasion of cancer outside the muscularis propria. The proper and relevant assessment of these factors enables patients to be triaged to either immediate surgical resection or short- or long-term chemotherapy-radiation therapy or solely radiation therapy with a suitable CRM modification before the surgical operation [18].

In our study, the most prevalent site of tumor discovered by MRI was in the Middle rectum (5-10 cm from the anorectal

junction) in 35.7%, followed by the lower rectum (5 cm from the anorectal junction) in 28.5%, and while the upper rectum (>10 cm from the anorectal junction) in 7.1%.

According to El-Kady *et al*. (2014) [17], tumor location is classified as upper rectal neoplasm (>10 cm), middle rectal neoplasm (5-10 cm), lower rectal neoplasm (5 cm), widespread upper and middle involvement, widespread middle and lower involvement), and diffuse anorectal involvement, this classification is based on the distance between the ano-rectal junction (ARJ) and the lower border of the tumor **[17]**.

In our study, we found that 16 patients out of 28 patients (57.1%) were eligible for surgery (group I), while 12 out of 28 patients (42.9%) received neoadjuvant chemoradiotherapy for downstaging (group II). Our results were higher than the reported results of the study done by Abu Rashed, *et al*. 2019]15] showing 11 out of 30 patients (36.3%) were eligible for surgery, while 19 patients (63.3%) received neo-adjuvant chemoradiotherapy.

- Our studied cases underwent primary staging.
- The MRI findings revealed: 8 studied cases (28.5 %) were categorized as T1 stage, all of them show no evidence of lymph node enlargement (N0), no soft tissue mass at mesorectal fat, and no invasion of mesorectal fascia. 12 cases(42.9 %) were categorized as T2 stage, 8 of them with no evidence of lymph nodes enlargement (N0), and 4 with evidence of regional lymph node enlargement and categorized as N1 (1-3 regional lymph nodes involvement), no soft tissue mass at mesorectal fat, no invasion of mesorectal fascia., 8 cases (28.5 %) were categorized as T3 stage, 6 of them were categorized as N1 (1-3 regional lymph nodes involvement) with no soft tissue mass at mesorectal fat, no invasion of mesorectal fascia, and 2 of them were categorized as N2 (4 or more regional lymph node involvement) with no soft tissue mass at mesorectal fat, but with invasion of mesorectal fascia.
- Initial TNM staging by De La Pinta, *et al*. 2019 [16] found that Pre-CRT MRI suggested that twenty patients (17.15%) had cT4 lesions, eighty-seven patients (74.3%) had cT3 lesions, and ten patients (8.55%) had cT2 lesions.
- All studied cases (100%) showed diffusion restriction with ADC values ranging from.68 to 1.05 s/mm2 (with a cut value of 1.20 X 10 -3 s/mm2).
- 23 studied cases (82.1 %) showed intact sphincters, 3 cases (10.7 %) showed invasion of the internal sphincter and 2 cases (7.1 %) showed invasion of both internal and external sphincters. 2 studied cases (7.1 %) showed extramural vascular invasion. MRF only invaded in 2 studied cases (7.1%), EMVI founded in 2 patients (7.1%)
- El-Kady, *et al*. (2014) [17] discovered that in thirty cases the sphincteric mechanism was intact. Invasion of the internal sphincter was observed in only nine patients. Just five patients demonstrated negative MRF involvement, compared to forty-five participants who demonstrated positive involvement, while Seven patients were discovered to have both external and internal sphincter invasion. thirty-nine patients demonstrated positive MRF depth of involvement via nodal lesions, in addition to fifteen others demonstrated both positive EMVI and MRF depth of involvement [17].

  Beets, *et al*. (2013) [19] reported that the mesorectal fascia involvement and the depth of transmural tumor invasion were properly predicted in about100% and 83% of the participants, respectively, using contrast-enhanced thin section MRI (slice thickness, 3 mm) on a 1.5-T scanner with a phased-array coil [19].

  Furthermore, Rao, *et al*. (2007) [20] evaluated the impact of high-resolution MRI in the MRF involvement predilection and discovered that the mesorectal fascia had been involved in 15 patients identified by pathologists with a cutoff distance of 2 mm between the mesorectal fascia and the tumor. The entire sensitivity for predicting mesorectal fascia involvement was about 88% [20].

  After the collection of data, we found that we have 16 cases categorized as T1/T2 and N0 (resectable) so they underwent surgical resection. (Group 1)

  12 studied cases were categorized as T2/T3 with evidence of lymph node involvement (irresectable), so they underwent chemoradiotherapy for 3-6 months for downstaging. (Group 2)

TNM restaging of our 12 patients (group 2) depending on MR findings and DWI after chemoradiotherapy revealed:

Out of the 4 patients who were categorized as T2N1: 3 patients become eligible for surgical resection as they showed no lymph node involvement (downstaging), 2 of them were categorized as T2N0, and 1 was categorized as T1N0, 1 patient showed no residual tumor and no lymph node involvement, with no restricted diffusion.

Out of the 6 patients, who were categorized as T3N1: 5 patients become eligible for surgical resection as they showed downstaging, 3 of them were categorized as T2N0, and 2 of them were categorized as T1N0, 1 patient showed down staging but still not eligible for surgical resection, categorized as T2N1.

Out of the 2 patients who were categorized as T3N2: 1 patient showed a progressive course and 1 patient become eligible for surgery, categorized as T2N0.

After chemoradiotherapy, Internal and external sphincters are intact in 11 cases (91.6%), the internal sphincter only invaded in 1 case (8.3%) and no cases showed invasion of both internal and external cases, Mesorectal fascia is invaded in 1 case (8.3%).

The ADC value of rectal masses after neo-adjuvant CRT ranged from 0.86 mm2 x 10-3 /sec to 1.3 mm2 x 10-3 /sec denoting fair response to the treatment.

In a research by El-Kady E, *et al*. [17] downstaging was divided into five groups based on tumor regression grade (TRG). Forty-one patients (following the first course of neoadjuvant treatment) and forty-five others (following a recommended additional clinical course) with TRG1,2, and 3 showed a substantial increase in ADC value. No tumor was detected among thirteen patients. While sixteen of them had pure low T2 signals as a result of post-management fibrotic alterations. A total of twelve participants had an intermediate signal from the remaining tumor and a mixed low T2 signal from the fibrotic response, three patients had a high T2 signal from mucinous alterations and edema, as well as 1 patient had a mixed both high and low T2 signal. Additional neo-adjuvant treatment sessions were clinically recommended and directed for four patients with TRG5 and two patients with TRG4 (17) [17].

This goes with Kim, *et al*. (2009) [21] who mentioned that including DWI into conventional MRI is critical for

improving the accuracy of assessing tumor response following CRT [21].

Sun, *et al*. (2010) [22] further highlighted that the relevance of DWI extends to the very early response detection. (22)

Regarding this study, by using a cut-off ADC value of 1.20 103mm2/s for discriminating of non-complete responders from complete responders (CR), we found that the usage of ADC value for properly distinguishing between responders from non-responders was beneficial. Our findings matched those of a prior study done by Kim *et al*, 2010 [21] who showed a 100% negative predictive value (23 of 23 cases) when using an ADC of 1.20 103 mm2/s as the threshold value in discriminating the CR group from the non-CR group.

TNM restaging of our patients depending on MR findings and DWI after surgery which revealed

21 studied cases showed free restriction with high ADC value and 4 cases showed restricted diffusion, 21 studied cases (84%) showed clear operative bed and 4 cases (16%) showed unclear operative bed, 8 studied cases (32%) showed post-operative complications such as: infection, fibrosis and GIT complications, 17 cases (68%) showed no postoperative complications.

Limitations of our study

The study has certain limitations, including the limited sample population, which means that our findings must be verified by further clinical research.

Conclusion

DW-MRI has been a totally noninvasive procedure with no radiation exposure that is fundamental for the early staging of cancer rectum and post-neoadjuvant therapy evaluation to assess the grade of tumor response, which greatly influences the selection of operation plan as well as decreases the local recurrence of the tumor, hence enhancing both surgical results and the overall survival rate. It has an important role in accurate post-operative assessment and detection of recurrence in cancer rectum patients. Thus, we conclude that post-operative MRI has a golden standard value not only for follow-up post-operative complication and detection of recurrent rectal carcinoma, but also aids in predicting the appropriateness of curative surgery and assisting in informed palliative resection decisions, which has a significant impact on the survival rates.

Conflict of Interest

Not available

Financial Support

Not available

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